New York State
Brownfield Cleanup Program
Development of Soil Cleanup Objectives
Technical Support Document
2020 Addendum

Prepared By:
New York State Department of Environmental Conservation
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Introduction:
As required in ECL 27-1415(6)(c), the New York State Department of Environmental Conservation (NYSDEC) is required to update the Soil Cleanup Objectives (SCOs) tables every 5 years. NYSDEC has reviewed those tables and a summary of the changes made are provided below. This is an addendum to the Technical Support Document (TSD) issued in September 2006 and is available on NYSDEC's website.

Applicability:

Once the revisions to 6 NYCRR Part 375, including revised SCOs are adopted, the revised SCOs will apply to any State Superfund or Environmental Restoration site for which a remedy has not been selected by the Department and for any Brownfield Site for which the Remedial Action Work Plan has not been approved by the Department.

Updating the list of chemicals:

Adding:
Two chemicals were added to the list of volatile organic chemicals (VOCs), aniline and nitrobenzene. These chemicals were identified as contaminants of concern for at least one site since the initial publication of Subpart 375-6, and SCOs were developed to address the contamination at those sites. These chemicals are included in this revision to allow for sampling for these chemicals at other sites where they may be present. . These chemicals can be analyzed for using the same EPA Standard Method used for other VOCs, so little or no increased cost as expected.

Moving:
Two chemicals had changes to the category they were listed under.

- Dibenzofuran was initially listed under the category of PCBs/Pesticides. This semivolatile organic chemical is not a pesticide or a PCB, so it is more appropriate to include it under the "Semivolatile organic compound" list.
- 1,4-dioxane is a volatile organic chemical in its pure form. However, because of the way 1,4-dioxane interacts with water, it behaves more like a semivolatile compound as it exists in environmental media. The United States Environmental Protection Agency (USEPA) has listed it as a semivolatile organic compound in their contract lab protocol (CLP), and the preferred analytical method for this compound is EPA method 8270, which is used to evaluate semivolatile organic compounds. Special sampling methods to prevent volatilization are not necessary. 1,4-dioxane has therefore been moved to the semivolatile organic compound list.

Removing: 2,4,5 TP Acid (Silvex) is an herbicide used to defoliate broadleaf plants that was banned from use in the United States for food crops since 1970, and for all uses since 1985.

No herbicides are included in the USEPA “Target Analyte List”, which NYSDEC references as the list of chemicals that are to be evaluated at remediation sites (DER-10). Silvex is the only herbicide included in the SCOs. The rest of the pesticides are insecticides.

The Technical Support Document describes the process used to select the chemicals for the SCOs. Silvex was not on the original list developed by NYSDEC. It was added to the list as a result of public comment (there was not a record of who made that request).

The TSD indicated that they used the following criteria in considering the comments:

- the chemical is listed on typical analytical scans,
- the chemical is typically found at sites, and
- the chemical is typically found in soils.

11 Compounds were added to the priority list following public comment (listed below). Silvex is the only one of those not on the TAL/TCL list:

- barium,
- beryllium,
- selenium,
- silver,
- acenaphthene,
- acenaphthylene,
- pyrene,
- 2-methylphenol (o-creosol),
- 3-methylphenol, (m-creosol)
- 4-methylphenol, (p-creosol)
- Silvex

Over 11,000 samples from over 260 sites have been analyzed for Silvex. This chemical was detected in 180 samples at 17 sites, with a maximum concentration of 0.056 mg/kg. The unrestricted use SCO for this chemical is 3.8 mg/kg. Silvex has also been analyzed by Suffolk County as part of their groundwater program, and it has not been detected. There are no sites that have identified Silvex as a contaminant of concern. Silvex was detected in the groundwater at 6 sites at levels up to 0.88 ug/l, which is significantly below the groundwater standard of 10 ug/l. This testing fails to demonstrate that Silvex

is “typically found in soils” and is “typically found at sites” and supports removing the chemical from the SCO tables.

If there is a site where herbicides were disposed, then NYSDEC would require testing for the herbicides suspected of being disposed, which might include Silvex, but which would likely include other herbicides not on the SCO list.

Protection of Public Health SCOs

In response to NYSDEC’s request, the New York State Department of Health (DOH) has reviewed the health based SCOs. There have been numerous updates in the toxicity data and in the methods and data used to estimate soil-related exposures. DOH has used these updates to derive revised health based SCOs for 81 contaminants and new SCOs for 4 more. Those changes and their derivation are described in the attached document, “New York State Brownfield Cleanup Program Development of Soil Cleanup Objectives Technical Support Document 2020 Addendum” Prepared By: New York State Department of Environmental Conservation and New York State Department of Health March 2020.

Protection of Public Health SCOs are calculated for 3 forms of mercury: elemental mercury (CAS Number 7439-97-6), mercury inorganic salts, organic mercury. The SCO table will list only total mercury and will cite the lowest values for these 3 forms. The only ELAP certified method available is for Total Mercury. Analysis for the three forms listed above are not certified by ELAP and are not widely available. If mercury is found in soil above the published SCO, then subsequent analysis of the separate species of mercury can be taken into consideration during the remedy selection process. Mercury SCOs for the protection of groundwater and the protection of ecological resources are only available for total mercury.

Protection of Groundwater SCOs

Clarification of Section 7.5: The Technical Support Document indicates that a dilution attenuation factor (DAF) of 100 is used to account for the mechanisms that prevent all of the contamination that leaves the contaminated soil from impacting groundwater, including:

1) volatilization;
2) sorption and desorption;
3) leaching and diffusion;
4) transformation and degradation; and

5) change in concentration of contaminants after reaching and/or mixing with the groundwater surface.

While a DAF of 100 was used for organic compounds to develop the original SCOs, a DAF of 20 was used to calculate the original SCOs for inorganic chemicals, based on the assumption that volatilization, sorption, and transformation would not play a significant role in fate and transport of inorganic chemicals.

It is noted that some substances are much more susceptible to these mechanisms than others. None of the chemicals in the PCBs/Pesticides group are volatile, and all have limited degradation potential. In the VOC group, many of the chemicals are both highly volatile and are readily degraded by aerobic bacteria. Yet, the same DAF is applied uniformly. Degradation can also be site dependent, since aerobic conditions would rapidly degrade some VOCs, while other VOCs are only bio-degraded anaerobically. Since these variations are not accounted for in the SCOs, they must be taken into consideration during the selection of the remedy. For example, sites with chlorinated solvents (trichloroethene or tetrachloroethene) often will require groundwater treatment even if no soil results exceed the protection of groundwater SCO, while sites with PCB concentrations exceeding the protection of groundwater SCO will very seldom have groundwater contamination issues. Caution is therefore required if protection of groundwater SCOs are applied outside the remedy selection process.

Revisions to Section 7.7: The below revisions to Section 7.7 reflect the following changes in the procedure for calculating the protection of groundwater SCOs in the 2020 update of Part 375. The key revisions to this section include:

1. One of the “authoritative bodies” was no longer available.
2. A number of chemicals leach differently as pH varies. The pH assumed in calculating the protection of groundwater SCOs is now indicated, and a reference is cited to provide additional information.
3. A number of different equations are available to calculate the Koc from the Kow. NYSDEC has cited the equation from the principal authoritative body listed below (HHRAP). The source of the previously provided equation was not identified.
4. We have provided a table indicating the protection of groundwater SCOs that have changed in this update, along with the criteria used to calculate these values.

7.7 Hierarchy of Authoritative Bodies

1. HHRAP: USEPA (United States Environmental Protection Agency). 1998. Human Health Risk Assessment Protocol for Hazardous Waste Combustion

Facilities. Region 6: Office of Solid, Waste and Emergency Response. EPA530D-D-98-001A. July 1998. https://archive.epa.gov/epawaste/hazard/tsd/td/web/html/risk.html. The appendix listing Koc values was replaced by The Hazardous Waste Companion Database (ACCESS). This database updates and replaces the hard-copy listing of chemical-specific parameter values originally found in Appendix A of the 1998 HHRAP. USEPA has committed to maintaining the database, and will post periodic updates on the same web site;

2. ATSDR: Agency for Toxic Substances and Disease Registry. Toxicological Profiles for various chemicals. https://www.atsdr.cdc.gov/toxprofiledocs/index.html
3. HSDB: US National Library of Medicine. 2004. Hazardous Substances Data Base. Bethesda MD. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB
4. SGDSS: US EPA. 2002. Supplemental Guidance for Developing Soil Screening Levels for Superfund Sites. OSWER 9355.4-24. December 2002. (Prepared for USEPA Office of Emergency and Remedial Response)

The order of the references listed above was used as a hierarchy for finding the chemical-specific parameters of: logKow, Koc, and solubility. For any parameters not found in the first reference, the second reference was consulted and so forth until a value for the parameter was found, or the hierarchy of references was exhausted.

HHRAP (Reference #1) provided a single K_{oc} value for a majority of the chemicals. The K_{oc} for Xylene (mixed) is a geometric mean of the Koc for 3 isomers.

The following have been identified as being particularly sensitive to variations in pH: pentachlorophenol, Arsenic, Barium, Beryllium, Cadmium, Chromium(+III), Chromium(+VI), Mercury, Nickel, Silver, Selenium, Thallium, and Zinc. The values used for these chemicals reflect a pH of 6.8. Kd values for different pH conditions can be found in Exhibits C2 and C4 of the SGDSS (reference 5).

The equation to estimate K_d using K_{oc}, taken from EPA's Human Health Risk Assessment Protocol for Hazardous Waste Combustion Facilities (Reference #1), is $K_d = f_{oc} * K_{oc}$ where f_{oc} is estimated between 0.002 and 0.024 but the mid-range value of 0.01 is generally used.

If K_{oc} was not found in the reference hierarchy, K_{oc} was calculated with one of the following equations, taken from Appendix A of HHRAP (Reference 1) (appendix A, Page A-2-11):

For semi-volatile, nonionizing organic compounds:

Log Koc=0.00028+(0.983*Log Kow)

For volatile nonionizing organics, chlorinated benzenes and chlorinated pesticides

Log Koc = 0.0784 + (0.7919 * log Kow)

Table 7-1. Protection of Groundwater SCOs for Inorganic Chemicals

CAS	Contaminant	Kd	ref	GW (ug/l)	Calculated SCO	2006 SCO	2020 SCO
7440-38-2	Arsenic	29	1	25	14.5	16[f]	16[f]
7440-39-3	Barium	41	1	1000	820	820	820
7440-41-7	Beryllium	790	1	3	47	47	47
7440-43-9	Cadmium	75	1	5	7.5	7.5	7.5
16065-83-1	Chromium III	1,800,000	1	50	1,800,000	NS	NS
18540-29-9	Chromium VI	19	1	50	19	19	19
7440-50-8	Copper	430		200	1,720	1,720	1,720
57-12-5	Cyanide	9.9	1	200	40	40	40
7439-92-1	Lead	900	1	25	450	450	450
7439-96-5	Manganese	65		300	390	2000[f]	2,000[f]
7439-97-6	Mercury	52	1	0.7	.73	.73	.73
7440-02-0	Nickel	65	1	100	130	130	130
7782-49-2	Selenium	5	1	10	1.0	4[f]	4[f]
7440-22-4	Silver	8.3	1	50	8.3	8.3	8.3
7440-66-6	Zinc	62	1	2000	2,480	2,480	2,480

Table 7-2. Protection of Groundwater SCOs for Organic Chemicals

CAS	Contaminant	Ref	Koc	GW Criteria (ug/l)	Calculate SCO	2006 SCO	2020 SCO
71-55-6	1,1,1-Trichloroethane	1	1.35E+02	5	0.68	0.68	0.68
75-34-3	1,1-Dichloroethane	1	5.34E+01	5	0.27	0.27	0.27
75-35-4	1,1-Dichloroethene	1	6.50E+01	5	0.33	0.33	0.33
95-63-6	1,2,4-Trimethylbenzene*	3	1.18E+03	5	5.90	3.60	5.9
95-50-1	1,2-Dichlorobenzene	1	3.79E+02	3	1.1	1.1	1.1
107-06-2	1,2-Dichloroethane	1	3.80E+01	0.6	0.02	0.02	0.02
156-59-2	1,2-Dichloroethene (cis)	1	3.83E+01	5	0.19	0.25	0.19
156-60-5	1,2-Dichloroethene (trans)	1	3.80E+01	5	0.19	0.19	0.19
108-67-8	1,3,5-Trimethylbenzene*	1	6.12E+02	5	3.1	8.4	3.1
541-73-1	1,3-Dichlorobenzene	1	8.50E+02	3	2.6	2.4	2.6
106-46-7	1,4-Dichlorobenzene	1	6.16E+02	3	1.8	1.8	1.8
123-91-1	1,4-Dioxane*	1	5.40E-01	50	0.03	0.1[e]	0.1[e]
93-72-1	2,4,5-TP Acid	3	1.22E+02	0.26	0.3	3.8	0.3
78-93-3	2-Butanone (methyl ethyl ketone)	1	1.93E+00	50	0.1	0.12	0.10
72-54-8	4,4'-DDD	1	4.58E+04	0.3	14	14	14
72-55-9	4,4'-DDE	1	4.64E+04	0.2	9.3	17	9.3
50-29-3	4,4'-DDT	1	6.75E+05	0.2	135	136	135

CAS	Contaminant	Ref	Koc	GW Criteria (ug/l)	Calculate SCO	2006 SCO	2020 SCO
83-32-9	Acenaphthene	1	4.90E+03	20	98	98	98
208-96-8	Acenapthylene	3	7.30E+03	50	365	107	365
67-64-1	Acetone	1	5.80E-01	50	0.03	0.05	0.03
309-00-2	Aldrin	1	4.87E+04	0.004	0.19	0.19	0.19
319-84-6	Alpha-BHC	1	1.76E+03	0.01	0.02	0.02	0.02
62-53-3	aniline	1	7.67E+00	5	0.04	New	0.04
120-12-7	Anthracene	1	2.35E+04	50	1,175.00	1,000 [c]	1,000 [c]
56-55-3	Benz(a)anthracene	1	3.58E+05	0.002	0.72	1 [f]	1 [f]
71-43-2	Benzene	1	6.17E+01	1	0.06	0.06	0.06
50-32-8	Benzo(a)pyrene	1	9.69E+05	0.023	22	22	22
205-99-2	Benzo(b)fluoranthene	1	1.05E+06	0.002	2.1	1.7	2.1
191-24-2	Benzo(g,h,i)perylene	3	3.29E+06	50	1,000	1,000 [c]	1,000 [c]
207-08-9	Benzo(k)fluoranthene	1	9.92E+05	0.002	2	1.7	2
319-85-7	Beta-BHC	1	2.14E+03	0.04	0.09	0.09	0.09
56-23-5	Carbon tetrachloride	1	1.52E+02	5	0.76	0.76	0.76
5103-71-9	Chlordane (alpha)	3	9.05E+04	.05	4.5	2.9	4.5
108-90-7	Chlorobenzene	1	2.24E+02	5	4.5	1.1	4.5
67-66-3	Chloroform	1	5.25E+01	7	0.37	0.37	0.37
218-01-9	Chrysene	1	4.01E+05	0.002	0.80	1 [f]	1 [f]
319-86-8	Delta-BHC	3	2.27E+03	0.04	0.1	0.25	0.1
53-70-3	Dibenz(a,h)anthracene	1	1.79E+06	50	89,500.00	1,000 [c]	1,000 [c]
132-64-9	Dibenzofuran	3	2.19E+03	50	110	210	110
60-57-1	Dieldrin	1	2.55E+04	0.004	0.1	0.1	0.1
959-98-8	Endosulfan I	3	1.29E+03	50	65	102	65
33213-65-9	Endosulfan II	3	8.81E+02	50	44	102	44
1031-07-8	Endosulfan sulfate	3	9.48E+02	50	47	1,000	47
72-20-8	Endrin (technical)	1	1.08E+04	0.002	0.02	0.06	0.06
100-41-4	Ethylbenzene	1	2.04E+02	5	1.0	1.0	1.0
206-44-0	Fluoranthene	1	4.91E+04	50	2,455	1,000 [c]	1,000 [c]
86-73-7	Fluorene	1	7.71E+03	50	386	386	386
58-89-9	Gamma-BHC (lindane)	3	1.06E+03	0.05	0.05	0.1	0.05
76-44-8	Heptachlor	1	9.53E+03	0.04	0.38	0.38	0.38
118-74-1	Hexachlorobenzene	1	8.00E+04	0.04	3.2	3.2	3.2
193-39-5	Indeno(1,2,3-cd)pyrene	1	3.08E+06	0.002	6.6	8.2	6.6
108-39-4	m-Cresol(s)	1	8.45E+01	1	0.08	0.33 [e]	0.33 [e]
1634-04-4	Methyl tert-butyl ether	3	6.65E+00	10	0.1	0.93	0.1

CAS	Contaminant	Ref	Koc	GW Criteria (ug/l)	Calculate SCO	2006 SCO	2020 SCO
75-09-2	Methylene chloride	1	1.00E+01	5	0.05	0.05	0.05
91-20-3	Naphthalene	1	1.19E+03	10	12	12	12
104-51-8	n-Butylbenzene	3	3.52E+03	5	18	12	18
98-95-3	nitrobenzene	1	1.19E+02	0.4	0.05	New	.08 [f]
103-65-1	n-Propylbenzene	3	1.00E+03	5	5	3.9	5
95-48-7	o-Cresol(s)	1	8.26E+01	1	0.08	0.33 [e]	0.33 [e]
106-44-5	p-Cresol(s)	1	7.38E+01	1	0.07	0.33 [e]	0.33 [e]
87-86-5	Pentachlorophenol	1	5.92E+02	1	0.59	0.8	0.80 [e]
85-01-8	Phenanthrene	1	2.65E+04	50	1,325.00	1,000 [c]	1,000 [c]
108-95-2	Phenol	1	2.98E+01	1	0.03	0.33 [e]	0.33 [e]
1336-36-3	Polychlorinated biphenyls (PCBs) Geometric Mean of Arochlors		3.44+04	0.09	3.2	3.2	3.2
129-00-0	Pyrene	1	6.80E+04	50	3,400	1,000 [c]	1,000 [c]
135-98-8	sec-Butylbenzene	3	4.98E+03	5	25	11	25
98-06-6	tert-Butylbenzene	3	2.15E+03	5	11	5.9	11
127-18-4	Tetrachloroethene	1	2.65E+02	5	1.3	1.3	1.30
108-88-3	Toluene	1	1.40E+02	5	0.70	0.7	0.70
79-01-6	Trichloroethene	1	9.43E+01	5	0.47	0.47	0.47
75-01-4	Vinyl chloride	1	1.54E+01	2	0.03	0.02	0.03
1330-20-7	Xylene	1	2.46+02	5	1.2	1.6	1.2

[a] The SCOs for residential, restricted-residential and ecological resources use were capped at a maximum value of 100 ppm. See TSD section 9.3.

[b] The SCOs for commercial use were capped at a maximum value of 500 ppm. See TSD section 9.3.

[c] The SCOs for industrial use and the protection of groundwater were capped at a maximum value of 1000 ppm. See TSD section 9.3.

[d] The SCOs for metals were capped at a maximum value of 10,000 ppm. See TSD section 9.3.

[e] For constituents where the calculated SCO was lower than the contract required quantitation limit (CRQL), the CRQL is used as the SCO value.

[f] For constituents where the calculated SCO was lower than the rural soil background concentration as determined by NYSDEC and DOH rural soil survey, the rural soil background concentration is used as the Track 2 SCO value for this use of the site.

Section 9.4 Detection Limits:

In some cases, the calculated SCOs are below levels at which laboratories can report the results with certainty. In these cases, the calculated values have been replaced with the lowest level that laboratories are able to achieve, referred to as the Contract Required Quantitation Levels (CRQL). The CRQL corresponds to the lowest concentration level on the analytical method calibration curve. Section 27-1415.6(c) of the Environmental Conservation Law requires that the tables of SCOs be updated every five years. These updates will incorporate improvements in detection and quantitation limits by the laboratories and include revised CRQLS as appropriate.

New York State
Brownfield Cleanup Program

Development of Soil Cleanup Objectives

Technical Support Document

2020 Addendum

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INTRODUCTION/BACKGROUND

Legislation establishing New York State's Brownfield Cleanup Program (i.e., Article 27, Title 14 of the Environmental Conservation Law, ECL § 27-1415) required the Department of Environmental Conservation (NYS DEC), in consultation with the Department of Health (NYS DOH), to develop regulations that create an approach for the remediation of contamination at Brownfield sites (NYS 2006a). ECL § 27-1415.6 established the requirements for soil cleanup objectives (SCOs), which are contaminant-specific remedial action objectives for soil (i.e., contaminant soil concentrations expressed in ppm [parts per million] or mg/kg [milligrams of contaminant per kilogram of soil]) based on a site's current, intended, or reasonably anticipated future use.

These SCOs are listed in the Brownfield Cleanup Program regulation (Title 6, New York Codes Rules and Regulations [6 NYCRR], sub-Part 375-6 [NYS, 2006b]) in tables of contaminant-specific SCOs that are protective of public health (human health-based SCOs) or the environment (groundwater or ecological SCOs). Section 27-1415.6(b) of the legislation states that SCOs "... shall not exceed an excess cancer risk of one-in-one million for carcinogenic endpoints and a hazard index of one for non-cancer endpoints; provided, however, that if the background soil concentration for a contaminant in rural soils in New York state exceeds such risk level the contaminant specific action objective for such contaminant may be established equal to such background concentration."

New York State set SCOs for 85 priority soil contaminants in 2006. ECL § 27-1415.6.c states that SCOs initially promulgated under the Brownfield Cleanup Program shall be updated every five years. DEC requested that DOH update its health-based SCOs in anticipation of proposing revisions to the 6 NYCRR Part 375 regulations.

Human health-based SCOs are estimates of contaminant-specific soil levels that are without appreciable risk of either non-cancer or cancer health effects. They are based on a combination of toxicity assessment and exposure assessment. Since 2006, there have been substantial changes in the toxicity data for numerous priority soil contaminants, and in the methods and data used to estimate soil-related exposures. Updated toxicity information and exposure parameters were used to derive revised health-based SCOs for 81 priority contaminants and new SCOs for 7 additional priority contaminants. The revisions based on the updated information are summarized below, organized according to the specific sections of the original New York State Brownfield Cleanup Program Development of Soil Cleanup Objectives Technical Support Document (2006 TSD) (NYS 2006c).

Section 4.0 Target Chemicals

4.1 Identification of Target Chemicals

Based on the methods summarized in Section 4.1 of the 2006 TSD (NYS 2006c), aniline (CAS Number 62-53-3), elemental mercury (CAS Number 7439-97-6), mercury inorganic salts, organic mercury, nitrobenzene (CAS Number 98-95-3), perfluorooctane sulfonic acid (CAS Number 1763-23-1), and perfluorooctanoic acid (CAS Number 335-67-1) were added to the Soil Cleanup Objectives Priority List, and 2-(2,4,5-trichlorophenoxy)propionic acid (Silvex) was removed.

Section 5.0 Protection of Human Health

5.1.1.3 Selection of Toxicity Values for Non-Cancer Effects
5.1.1.5 Selection of Toxicity Values for Cancer Effects

Review of the toxicity values for priority contaminants available from authoritative bodies was completed in 2018. For each contaminant, decisions were made to retain or change the toxicity values recommended in 2006, using the same selection criteria outlined in the original 2006 TSD. Fact sheets for each contaminant containing a summary of the available toxicity values, the selected value, and a brief rationale in support of the selection are found in Appendix Ad-A. Table Ad-1 lists the 2018 toxicity values for each soil contaminant, as well as toxicity values used in the original 2006 TSD (NYS 2006c).

5.2.2 Exposure Assessment Parameters and Values

There were no changes to the five land-use categories (totaling 10 exposure scenarios) evaluated in 2006 or to the exposure pathways considered within each exposure scenario. The structure of all formulas used for each exposure pathway is unchanged. The only exposure-assessment changes related to the selection of parameter values for the various exposure pathways.

Review and evaluation of the latest information on soil exposure was completed in 2018. This process ensured that exposure estimates used to calculate the SCOs are consistent with new data and recommended risk assessment methods. When deciding to retain or revise a value for each exposure factor used to derive the 2006 health-based chronic SCOs, two general criteria were considered:

(1) Maintaining consistency with updated US EPA values when possible and appropriate. In 2014, the United States Environmental Protection Agency (US EPA, 2014) updated its guidance on recommended values for standard default exposure factors used to evaluate exposures of adults and children to environmental chemicals at hazardous waste sites. The US EPA recommended values were adopted when the values were judged to be reasonable estimates or were updated conventional defaults (based on new data) for exposure-factor values appropriate for use in deriving SCOs. Examples of these values include:

- adult body weight of 80 kg instead of 70 kg,
- child (age 2 years) body weight of 15 kg instead of 13.3 kg,
- 26-year residency at a single home instead of 70 years,
- increased incidental soil ingestion rates for child residents and outdoor workers, and
- revised age categories for “lifetime” cancer risk assessment.

(2) The existence of or lack of new data for New York State-specific parameter values. When a New York State-specific value for an exposure factor was used to calculate the 2006 SCOs, new data on the factor were reviewed. The New York State-specific value was revised if supported by the more recent data. Otherwise, these state-specific values remained unchanged. Examples of these values include:

- number of days per year where outdoor exposure to soil is possible ("warm season") increased from 217 to 224,
- increased adult incidental ingestion rates for indoor dust containing outdoor soil from 0 mg/day to 24 mg/day,
- In some cases, a 2006 New York State-specific exposure-factor was mandated by the enabling legislation and the value was based on professional judgement because of inadequate empirical data for that factor. No new data were found to support revising those values. Examples of these values include:

    - allocation of 20% of total contaminant dose to soil-related exposures,
    - default adjustment factors that consider doses received via home-grown produce consumption and home-produced animal product consumption,
    - nearly all elements of the New York State-specific child visitor (commercial settings) and adolescent trespasser (industrial settings) exposure scenarios.

Tables Ad-2.1, Ad-2.2, and Ad-2.3 contain a list of more than 240 exposure factors and their 2006 and 2018 values. The 2018 values were used in the calculation of the revised health-based SCOs.

5.3 Calculation of Chronic Human Health-based Soil Cleanup Objectives

The revised toxicity and exposure values described above were used to calculate health-based chronic SCOs for children and adults based on the chronic non-cancer effects of all contaminants, and SCOs for children/adults (i.e., children developing into adults) based on the cancer effects of those contaminants with toxicity values for cancer effects. Other than the revised toxicity and exposure parameter values, the calculations followed exactly the same structure as described in Section 5.3 of the 2006 TSD (NYS 2006c).

5.4 Calculation of Acute Soil Ingestion SCOs

SCOs based on the acute toxicity of contaminants in a child exhibiting pica behavior (i.e., a child who persistently eats non-food substances such as soil**)** were recalculated using a revised child body weight and following the procedure described in Section 5.4 of the 2006 TSD. The revised SCOs based on acute soil ingestion are shown in Table Ad-3.

5.6 Final Human Health-based SCOs

After revised SCOs were calculated for all land-use categories, final health-based SCOs for each contaminant were obtained following the same procedure as described in Section 5.6 of the 2006 TSD. Table Ad-4 presents the final health-based SCOs based on consideration of chronic cancer and noncancer health risks, acute health risks, dermal irritancy health risks, and the rural background concentration data (when available) for each contaminant.

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Table Ad-1. Toxicity Values for Priority Contaminants [1]

Substance	CAS RN [2]	Oral Toxicity Values				Inhalation Toxicity Values			
		Reference Dose (mg/kg/day)		Cancer Potency Factor $(mg/kg/day)^{-1}$		Reference Concentration (mcg/m^3)		Unit Risk $(mcg/m^3)^{-1}$	
		2006	2018	2006	2018	2006	2018	2006	2018
acenaphthene	83-32-9	0.06		- [3]		210 [4]		- [3]	
acenaphthylene	208-96-8	0.06 [5]		- [3]		210 [4,5]		- [3]	
acetone	67-64-1	0.9		- [3]		30,000		- [3]	
aldrin	309-00-2	0.00003		17		0.10 [4]		0.0049 [6]	
aniline*	62-53-3	- [7]	0.007	- [7]	0.0034	- [7]	1	- [7]	0.00000097 [6]
anthracene	120-12-7	0.3		- [3]		1000 [4]		- [3]	
arsenic		0.0003		1.5		0.03	0.015	0.0015	
barium		0.02	0.2	- [3]		0.5		- [3]	
benz[a]anthracene	56-55-3	0.03 [8]	0.0003 [9]	0.903 [10]	0.1 [10]	100 [4,8]	0.002 [11]	0.00011 [10]	0.00006 [10]
benzene	71-43-2	0.004	0.0005	0.055	0.1	30	3	0.0000078	0.000016
benzo[a]pyrene	50-32-8	0.03 [8]	0.0003	9.03	1	100 [4,8]	0.002	0.0011	0.0006
benzo[b]fluoranthene	205-99-2	0.03 [8]	0.0003 [9]	0.903 [10]	0.1 [10]	100 [4,8]	0.002 [11]	0.00011 [10]	0.00006 [10]
benzo[g,h,i]perylene	191-24-2	0.03 [8]	0.0003 [9]	- [3]		100 [4,8]	0.002 [11]	- [3]	
benzo[k]fluoranthene	207-08-9	0.03 [8]	0.0003 [9]	0.0903 [10]	0.01 [10]	100 [4,8]	0.002 [11]	0.000011 [10]	0.000006 [10]
beryllium		0.002		- [3]		0.007		0.0024	
n-butylbenzene	104-51-8	0.1 [12]	0.05	- [3]		400 [12]	180 [4]	- [3]	
sec-butylbenzene	135-98-8	0.1 [12]	0.037 [12]	- [3]		400 [12]	130 [4,12]	- [3]	
tert-butylbenzene	98-06-6	0.1 [12]	0.037 [12]	- [3]		400 [12]	130 [4,12]	- [3]	
cadmium		0.0007	0.0001	0.38	0.067	0.02	0.01	0.0042	
cadmium (child)		- [13]	0.000011	- [13]		- [13]		- [13]	
carbon tetrachloride	56-23-5	0.0007	0.004	0.13	0.07	2	100	0.000015	0.000006
chlordane	12789-03-6	0.0005		0.35		0.7		0.0001	
chlordane (child)	12789-03-6	- [13]	0.000033	- [13]		- [13]		- [13]	
chlorobenzene	108-90-7	0.02		- [3]		60	50	- [3]	
chloroform	67-66-3	0.01		0.031		50	100	0.000000068	
chromium (III) (soluble salts)		0.005		- [3]		- [14]		- [3]	
chromium (III) (insoluble salts)		1.5		- [3]		60		- [3]	
chromium (VI)		0.003	0.0009	-	0.5	0.1		0.05	
chrysene	218-01-9	0.03 [8]	0.0003 [9]	0.0903 [10]	0.01 [10]	100 [4,8]	0.002 [11]	0.000011 [10]	0.000006 [10]
copper		0.14		- [3]		490 [4]		- [3]	

Substance	CAS RN [2]	Oral Toxicity Values				Inhalation Toxicity Values			
		Reference Dose (mg/kg/day)		Cancer Potency Factor $(mg/kg/day)^{-1}$		Reference Concentration (mcg/m^3)		Unit Risk $(mcg/m^3)^{-1}$	
		2006	2018	2006	2018	2006	2018	2006	2018
cyanide	57-12-5	0.02	0.0006	- [3]		25	0.8	- [3]	
DDD	72-54-8	0.0005		0.125		1.8 [4]		0.000036 [6]	
DDE	72-55-9	0.012		0.185		42 [4]		0.000053 [6]	
DDT	50-29-3	0.0005		0.189		1.8 [4]		0.000054 [6]	
dibenz[a,h]anthracene	53-70-3	0.03 [8]	0.0003 [9]	9.03 [10]	1 [10]	100 [4,8]	0.002 [11]	0.0011 [10]	0.0006 [10]
dibenzofuran	132-64-9	0.002	0.001	- [3]		7 [4]	4 [4]	- [3]	
1,2-dichlorobenzene	95-50-1	0.021	0.3	- [3]		200		- [3]	
1,3-dichlorobenzene	541-73-1	0.003		- [3]		10 [4]		- [3]	
1,4-dichlorobenzene	106-46-7	0.03	0.07	0.011		800		0.0000031 [6]	
1,1-dichloroethane	75-34-3	- [14]		0.0057		- [14]		0.0000016	
1,1-dichloroethene	75-35-4	0.05		- [3]	0.27 [15]	200	4.4	- [3]	0.000076
1,2-dichloroethane	107-06-2	0.045		0.047		400		0.000013 [6]	
cis-1,2-dichloroethene	156-59-2	0.01	0.002	- [3]		35 [4]	60	- [3]	
trans-1,2-dichloroethene	156-60-5	0.02		- [3]		60		- [3]	
dieldrin	60-57-1	0.00005		8.32		0.18 [4]		0.0024 [6]	
1,4-dioxane	123-91-1	0.1	0.026	0.011	0.1	3600	30	0.0000031 [6]	0.000005 [6]
endosulfan (technical)	115-29-7	0.00067	0.002	- [3]		2.3 [4]	5.6	- [3]	
endrin	72-20-8	0.0003		- [3]		1 [4]		- [3]	
ethyl benzene	100-41-4	0.1		0.0035 [15]		2000	260	0.000001	
fluoranthene	206-44-0	0.04		- [3]		140 [4]		- [3]	
fluorene	86-73-7	0.04		- [3]		140 [4]		- [3]	
heptachlor	76-44-8	0.0015		0.79		5.2 [4]		0.00023 [6]	
heptachlor (child)	76-44-8	- [13]	0.00003	- [13]		- [13]		- [13]	
hexachlorobenzene	118-74-1	0.0008	0.00001	1.09		2.8 [4]	0.035 [4]	0.00029 [6]	0.00031 [6]
alpha-hexachlorocyclohexane	319-84-6	0.0005		3.4		1.8 [4]		0.00097 [6]	
beta-hexachlorocyclohexane	319-85-7	0.00001		0.96		0.035 [4]		0.00027 [6]	
delta-hexachlorocyclohexane	319-86-8	0.025		- [3]		88 [4]		- [3]	
gamma-hexachlorocyclohexane	58-89-9	0.00004	0.000012	0.71		0.14 [4]	0.042 [4]	0.0002 [6]	
indeno[1,2,3-cd]pyrene	193-39-5	0.03 [8]	0.0003 [9]	0.903 [10]	0.1 [10]	100 [4,8]	0.002 [11]	0.00011 [10]	0.00006 [10]
manganese		0.05		- [3]		0.15	0.09	- [3]	
manganese (child)		- [13]	0.03	- [13]		- [13]		- [13]	
mercury (elemental)*	7439-97-6	- [14]		- [3]		0.09	0.03	- [3]	

Substance	CAS RN [2]	Oral Toxicity Values				Inhalation Toxicity Values			
		Reference Dose (mg/kg/day)		Cancer Potency Factor $(mg/kg/day)^{-1}$		Reference Concentration (mcg/m^3)		Unit Risk $(mcg/m^3)^{-1}$	
		2006	2018	2006	2018	2006	2018	2006	2018
mercury (inorganic salts)*		0.00016		- [3]		- [14]		- [3]	
mercury (organic)*		- [7]	0.0001	- [3]		- [7]	0.35	- [3]	
methylene chloride	75-09-2	0.06	0.006	0.0062	0.002	400		0.000000037	0.00000001
methyl ethyl ketone	78-93-3	0.6		- [3]		5000		- [3]	
2-methylphenol	95-48-7	0.05	0.1	- [3]		180 [4]	350 [4]	- [3]	
3-methylphenol	108-39-4	0.05	0.1	- [3]		180 [4]	350 [4]	- [3]	
4-methylphenol	106-44-5	0.005	0.1	- [3]		18 [4]	350 [4]	- [3]	
methyl *tert*-butyl ether	1634-04-4	0.033		0.0034		8000		0.00000026	
naphthalene	91-20-3	0.02		- [3]		9		- [3]	0.000034
nickel		0.02		- [3]		0.09	0.014	0.00048	
nitrobenzene*	98-95-3	- [7]	0.002	- [7]	0.14 [15]	- [7]	9	- [7]	0.00004
pentachlorophenol	87-86-5	0.001		0.12	0.4	3.5 [4]		0.000034 [6]	0.000114
pentachlorophenol (child)	87-86-5	- [13]	0.001	- [13]		- [13]		- [13]	
perfluorooctane sulfonic acid*	1763-23-1	- [7]	0.000002	- [7]	12.8	- [7]	0.0063 [4]	- [7]	0.0036 [6]
perfluorooctanoic acid*	335-67-1	- [7]	0.0000015	- [7]	5.3	- [7]	0.0052 [4]	- [7]	0.0015 [6]
phenanthrene	85-01-8	0.03 [8]	0.0003 [9]	- [3]		100 [4,8]	0.002 [11]	- [3]	
phenol	108-95-2	0.3		- [3]		20		- [3]	
n-propylbenzene	103-65-1	0.1 [16]		- [3]		400 [12]	260 [16]	- [3]	
pyrene	129-00-0	0.03		- [3]		100 [4]		- [3]	
selenium		0.005		- [3]		18 [4]		- [3]	
silver		0.005		- [3]		18 [4]		- [3]	
tetrachloroethene	127-18-4	0.01	0.006	0.05	0.0021	100	30	0.000001	0.0000061
toluene	108-88-3	0.2	0.08	- [3]		300	5000	- [3]	
1,1,1-trichloroethane	71-55-6	0.28	2	- [3]		2200	5000	- [3]	
trichloroethene	79-01-6	0.00146	0.0005	0.00572	0.046	40	2	0.000002	0.0000041
1,2,4-trimethylbenzene	95-63-6	0.05	0.01	- [3]		6	60	- [3]	
1,3,5-trimethylbenzene	108-67-8	0.05	0.01	- [3]		6	60	- [3]	
vinyl chloride (child and adult exposure)	75-01-4	0.003		1.5		100		0.0000088	
vinyl chloride (adult exposure)	75-01-4	0.003		0.75		100		0.0000044	
xylenes	1330-20-7	0.2		- [3]		100		- [3]	
zinc		0.3		- [3]		1000 [4]		- [3]	

CAS RN: Chemical Abstracts Service Registry Number
mg/kg/day: milligrams per kilogram per day
mcg/m^3: micrograms per cubic meter
*Denotes a chemical added to the list of priority contaminants for this update. Updates to toxicity values for perfluorooctane sulfonic acid and perfluorooctanoic acid were made in 2019.

(1) Toxicity values for lead and polychlorinated biphenyls are not listed because the New York State Department of Health used chemical-specific risk assessment approaches and federal guidelines to establish soil cleanup objectives for these substances.
(2) Chemical Abstracts Service Registry Numbers are not included for metals except for elemental mercury. The toxicity values for metals are intended for use with various inorganic forms found in the environment.
(3) The carcinogenic potency of the substance has either not been studied, the studies of their carcinogenic potency did not show a dose-related increased in cancer incidence, or some evidence of carcinogenic potency has been observed but the quality of the studies or the data do not allow quantitative estimation of carcinogenic potency.
(4) A reference concentration is calculated from the recommended reference dose for chemicals that are systemic toxicants, assuming a 70 kilogram individual inhales 20 cubic meters of air per day. See also Footnote 24 for Tables Ad-2.1 to Ad-2.3.
(5) Based on acenaphthene.
(6) A unit risk is calculated from the recommended cancer potency factor for chemicals that are systemic carcinogens, assuming a 70 kilogram individual inhales 20 cubic meters of air per day. See also Footnote 24 for Tables Ad-2.1 to Ad-2.3.
(7) Substance not on the list of priority contaminants in 2006.
(8) Based on pyrene reference dose.
(9) Based on benzo[a]pyrene reference dose.
(10) Based on benzo[a]pyrene and application of recommended relative potency factors.
(11) Based on benzo[a]pyrene reference concentration.
(12) Based on isopropylbenzene (cumene).
(13) Child toxicity value not available.
(14) The contaminant lacks non-cancer toxicity data sufficient for the derivation of a reference dose or reference concentration.
(15) A cancer potency factor is calculated from the recommended unit risk assuming a 70-kilogram individual inhales 20 cubic meters of air per day. See also Footnote 24 for Tables Ad-2.1 to Ad-2.3.
(16) Based on ethylbenzene.

Tables Ad-2.1 to Ad-2.3. Comparison of 2006 and 2018 Values for Exposure Factors Used to Calculate Soil Cleanup Objectives

Table Ad-2.1. Exposure Factors and Values Applicable to All Substances

Land-Use Category, Receptor, Endpoint, Parameter	2006 Value	2018 Value
Unrestricted, Restricted Residential, Residential Settings – Child, Noncancer(1)		
Age Range	2 to 3 years	0 to 6 years
Body Weight*	13.3 kg	15 kg
Incidental Ingestion Rate - Outdoor Soil*	80 mg/day	200 mg/day
Incidental Ingestion Rate - Household Dust*	80 mg/day	
Fraction of Household Dust that is Outdoor Soil*	0.50	
'Soil in Household Dust' Incidental Ingestion Rate*	40 mg/day(2)	
Outdoor Soil Exposure Season (NYS Warm Season)*	217 days/year	224 days/year(3)
Soil Ingestion Exposure Frequency (During NYS Warm Season)*	5 days/week	7 days/week
Household Dust Ingestion Exposure Frequency (Year-Round)*	7 days/week	
Incidental Ingestion Rate - Total Soil (Time-Weighted Average)	74 mg/day	137 mg/day(4)**
Soil Vapor Inhalation Duration (During NYS Warm Season)*	24 hours/day	
Soil Vapor Inhalation Frequency (During NYS Warm Season)*	7 days/week	
Soil Particle Inhalation Duration (During NYS Warm Season)*	3 hours/day(5)	24 hours/day
Soil Particle Inhalation Frequency (During NYS Warm Season)*	5 days /week	7 days /week
Soil Adherence Factor*	0.2 mg/cm^2	
Skin Surface Area*	1870 cm^2	2373 cm^2
Soil Dermal Contact Frequency (During NYS Warm Season)*	5 days/week	7 days/week
Dust Dermal Contact Frequency (Year-Round)*	7 days/week	
Unrestricted, Restricted Residential, Residential Settings – Adult, Noncancer(1)		
Body Weight*	70 kg	80 kg
Incidental Ingestion Rate - Outdoor Soil*	100 mg/day	
Incidental Ingestion Rate – Household Dust*	0 mg/day	24 mg/day
Fraction of Household Dust that is Outdoor Soil*	0.50	
'Soil in Household Dust' Incidental Ingestion Rate*	0 mg/day(6)	12 mg/day(7)
Outdoor Soil Exposure Season (“NYS Warm Season”)*	217 days/year	224 days/year(3)
Soil Ingestion Exposure Frequency (During NYS Warm Season)*	2 days/week	7 days/week
Household Dust Ingestion Exposure Frequency (Year-Round)*	0 days/week(6)	7 days/week
Incidental Ingestion Rate - Total Soil (Time-Weighted Average)	17 mg/day	66 mg/day(8)
Soil Vapor Inhalation Duration (During NYS Warm Season)*	24 hours/day	
Soil Vapor Inhalation Frequency (During NYS Warm Season)*	7 days/week	

Soil Particle Inhalation Duration (During NYS Warm Season)*	3.9 hours/day	24 hours/day
Soil Particle Inhalation Frequency (During NYS Warm Season)*	7 days/week	
Soil Adherence Factor*	0.07 mg/cm^2	
Skin Surface Area*	4850 cm^2	6032 cm^2
Soil Dermal Contact Frequency (During NYS Warm Season)*	2 days/week	7 days/week
Dust Dermal Contact Frequency (Year-Round)*	0 days/week[9]	7 days/week
Unrestricted, Restricted Residential, Residential Settings – Cancer[1]		
Body Weight – Age Class 0 to <1 year	9.1 kg	8.3 kg
Body Weight – Age Class 1 to <2 years	12.3 kg	11.4 kg
Body Weight – Age Class 2 to <6 years*	16.2 kg	17.4 kg
Body Weight – Age Class 6 to <16 years*	39.8 kg	44.3 kg
Body Weight – Age Class 16 to <26 years*	70 kg	80 kg
Incidental Ingestion Rate - Total Soil (Time-Weighted Average) – Age Class 0 to <1 year	0 mg/day[10]	88.5 mg/day
Incidental Ingestion Rate - Total Soil (Time-Weighted Average) – Age Class 1 to <2 years	74 mg/day	137 mg/day
Incidental Ingestion Rate - Total Soil (Time-Weighted Average) – Age Class 2 to <6 years	74 mg/day	137 mg/day
Incidental Ingestion Rate - Total Soil (Time-Weighted Average) – Age Class 6 to <16 years	17 mg/day	137 mg/day
Incidental Ingestion Rate - Total Soil (Time-Weighted Average) – Age Class 16 to <70 years	17 mg/day	Not Applicable
Incidental Ingestion Rate - Total Soil (Time-Weighted Average) – Age Class 16 to <26 years	Not Applicable	66 mg/day
Exposure Duration – Age Class 0 to <1 year	1 year	
Exposure Duration – Age Class 1 to <2 years	1 year	
Exposure Duration – Age Class 2 to <6 years	4 years	
Exposure Duration – Age Class 6 to <16 years	10 years	
Exposure Duration – Age Class 16 to <26 years	54 years	10 years[11]**
Body Weight – Age Class 16 to <18 years (dermal only)*	61.3 kg	71.6 kg
Body Weight – Age Class 18 to <70 years (dermal only)*	70 kg	Not Applicable
Body Weight – Age Class 18 to <26 years (dermal only)*	Not Applicable	80 kg
Skin Surface Area – Age Class 0 to <1 year	1870	1260
Skin Surface Area – Age Class 1 to <2 years	1870	1590
Skin Surface Area – Age Class 2 to <6 years*	1870	2040
Skin Surface Area – Age Class 6 to <16 years*	4526	4020
Skin Surface Area – Age Class 16 to <18 years*	4526	4256
Skin Surface Area – Age Class 18 to <70 years*	4850	Not Applicable
Skin Surface Area – Age Class 18 to <26 years*	Not Applicable	6032
Soil Adherence Factor – Age Class 0 to <1 year*	0.2	
Soil Adherence Factor – Age Class 1 to <2 years*	0.2	
Soil Adherence Factor – Age Class 2 to <6 years*	0.2	
Soil Adherence Factor – Age Class 6 to <16 years*	0.07	
Soil Adherence Factor – Age Class 16 to <18 years*	0.07	
Soil Adherence Factor – Age Class 18 to <70 years*	0.07	Not Applicable
Soil Adherence Factor – Age Class 18 to <26 years*	Not Applicable	0.07

Exposure Frequency – Age Class 0 to <1 year (dermal only)	0 days/year[10]	144 days/year[12]
Exposure Frequency – Age Class 1 to <2 years (dermal only)	155 days/year	287 days/year[13]
Exposure Frequency – Age Class 2 to <6 years (dermal only)*	155 days/year	287 days/year[13]
Exposure Frequency – Age Class 6 to <16 years (dermal only)*	155 days/year	287 days/year[13]
Exposure Frequency – Age Class 16 to <18 years (dermal only)*	155 days/year	287 days/year[13]
Exposure Frequency – Age Class 18 to <70 years (dermal only)*	62 days/year	Not Applicable
Exposure Frequency – Age Class 18 to <26 years (dermal only)*	Not Applicable	287 days/year[13]
Averaging Time	70 years	
Commercial Settings – Child, Noncancer[14]		
Age Range	2 to 3 years	0 to 6 years
Body Weight*	13.3 kg	15 kg
Incidental Ingestion Rate - Outdoor Soil*	53 mg/day	50 mg/day[15]
Incidental Ingestion Rate – Indoor Dust*	0 mg/day[16]	
Fraction of Indoor Dust that is Outdoor Soil*	Not Applicable	Not Applicable
'Soil in Indoor Dust' Incidental Ingestion Rate*	0 mg/day[16]	
Outdoor Soil Exposure Season (“NYS Warm Season”)*	217 days/year	224 days/year[3]
Soil Ingestion Exposure Frequency (During NYS Warm Season)*	2 days/week	
Indoor Dust Ingestion Exposure Frequency (Year-Round)*	0 days/week[16]	
Incidental Ingestion Rate - Total Soil (Time-Weighted Average)	9 mg/day	9 mg/day[17]
Soil Vapor Inhalation Duration (During NYS Warm Season)*	2 hours/day	
Soil Vapor Inhalation Frequency (During NYS Warm Season)*	2 days/week	
Soil Particle Inhalation Duration (During NYS Warm Season)*	2 hours/day	
Soil Particle Inhalation Frequency (During NYS Warm Season)*	2 days/week	
Soil Adherence Factor*	0.20 mg/cm^2	
Skin Surface Area*	1870 cm^2	2373 cm^2
Soil Dermal Contact Frequency (During NYS Warm Season)*	2 days/week	
Soil Dermal Contact Frequency (full year)	60 days/year	
Dust Dermal Contact Frequency (Year-Round)*	0 days/week[16]	
Commercial Settings – Adult, Cancer & Noncancer[18]		
Body Weight*	70 kg	80 kg
Incidental Ingestion Rate - Outdoor Soil*	50 mg/day	100 mg/day[19]
Incidental Ingestion Rate – Indoor Dust*	0 mg/day[16]	
Fraction of Indoor Dust that is Outdoor Soil*	Not Applicable	
'Soil in Indoor Dust' Incidental Ingestion Rate*	0 mg/day[16]	
Outdoor Soil Exposure Season (“NYS Warm Season”)*	217 days/year	224 days/year[3]

Soil Ingestion Exposure Frequency (During NYS Warm Season)*	4 days/week	5 days/week
Indoor Dust Ingestion Exposure Frequency (Year-Round)*	0 days/week[16]	
Incidental Ingestion Rate - Total Soil (Time-Weighted Average)	17 mg/day	40 mg/day[20]**
Soil Vapor Inhalation Duration (During NYS Warm Season)*	12 hours/day	8 hours/day
Soil Vapor Inhalation Frequency (During NYS Warm Season)*	4 days/week	5 days/week
Soil Particle Inhalation Duration (During NYS Warm Season)*	12 hours/day	8 hours/day[21]
Soil Particle Inhalation Frequency (During NYS Warm Season)*	4 days/week	5 days/week
Soil Adherence Factor*	0.2 mg/cm^2	0.12 mg/cm^2
Skin Surface Area*	2480 cm^2	3527 cm^2
Soil Dermal Contact Frequency (During NYS Warm Season)*	4 days/week	5 days/week
Dust Dermal Contact Frequency (Year-Round)*	0 days/week[16]	
Exposure Duration (cancer only)	25 years	
Averaging Time (cancer only)	70 years	
Industrial Settings – Child, Noncancer[22]		
Age Range	15 years	11 to <16 years
Body Weight*	58.1 kg	57 kg
Incidental Ingestion Rate - Outdoor Soil*	100 mg/day[22]	
Incidental Ingestion Rate – Indoor Dust*	0 mg/day[16]	
Fraction of Indoor Dust that is Outdoor Soil*	Not Applicable	
'Soil in Indoor Dust' Incidental Ingestion Rate*	0 mg/day[16]	
Outdoor Soil Exposure Season (“NYS Warm Season”)*	217 days/year	224 days/year[3]
Soil Ingestion Exposure Frequency (During NYS Warm Season)*	1 day/week	
Indoor Dust Ingestion Exposure Frequency (Year-Round)*	0 days/week[16]	
Incidental Ingestion Rate - Total Soil (Time-Weighted Average)	8.5 mg/day	9 mg/day[23]
Soil Vapor Inhalation Duration (During NYS Warm Season)*	4 hours/day	
Soil Vapor Inhalation Frequency (During NYS Warm Season)*	1 day/week	
Soil Particle Inhalation Duration (During NYS Warm Season)*	4 hours/day	
Soil Particle Inhalation Frequency (During NYS Warm Season)*	1 day/week	
Soil Adherence Factor*	0.07 mg/cm^2	
Skin Surface Area*	4256 cm^2	
Soil Dermal Contact Frequency (During NYS Warm Season)*	1 day/week	
Soil Dermal Contact Frequency (full year)	30 days/year	
Dust Dermal Contact Frequency (Year-Round)*	0 days/week[16]	
Industrial Settings – Adult, Cancer & Noncancer[18]		
Body Weight*	70 kg	80 kg
Incidental Ingestion Rate - Outdoor Soil*	50 mg/day	100 mg/day[19]

Incidental Ingestion Rate – Indoor Dust*	0 mg/day[16]	
Fraction of Indoor Dust that is Outdoor Soil*	Not Applicable	
'Soil in Indoor Dust' Incidental Ingestion Rate	0 mg/day[16]	
Outdoor Soil Exposure Season (“NYS Warm Season”)*	217 days/year	224 days/year[3]
Soil Ingestion Exposure Frequency (During NYS Warm Season)*	2 days/week	5 days/week
Indoor Dust Ingestion Exposure Frequency (Year-Round)*	0 days/week[16]	
Incidental Ingestion Rate - Total Soil (Time-Weighted Average)	8.5 mg/day	40 mg/day[20]**
Soil Vapor Inhalation Duration (During NYS Warm Season)*	12 hours/day	8 hours/day
Soil Vapor Inhalation Frequency (During NYS Warm Season)*	2 days/week	5 days/week
Soil Particle Inhalation Duration (During NYS Warm Season)*	12 hours/day	8 hours/day
Soil Particle Inhalation Frequency (During NYS Warm Season)*	2 days/week	5 days/week
Soil Adherence Factor*	0.2 mg/cm^2	0.12 mg/cm^2
Skin Surface Area*	2480 cm^2	3527 cm^2
Soil Dermal Contact Frequency (During NYS Warm Season)*	2 days/week	5 days/week
Dust Dermal Contact Frequency (Year-Round)*	0 days/week[16]	
Exposure Duration (cancer only)	25 years	
Averaging Time (cancer only)	70 years	

Table Ad-2.2. Exposure Factors and Values Applicable to All Land-Use Categories

Parameter	2006 Value	2018 Value
Default Absorption Fraction for Route-to-Route Dose Extrapolation	1	
Body Weight for Route-Route Dose Extrapolation	70 kg[24]	
Inhalation Rate for Route-to-Route Dose Extrapolation	20 m^3/day	
Adjustment for Persistent, Bioaccumulative & Toxic Substances	0.1[25]	
Adjustment for Homegrown Produce and Home-Produced Animal Product Consumption	0.1[25]	
Adjustment for Homegrown Produce Consumption	0.2[25]	
Default Relative Source Contribution (Decimalized)	0.2	
Age Dependent Adjustment Factor (Ages 0 to 2)	10	
Age Dependent Adjustment Factor (Ages 2 to <16)	3	
Age Dependent Adjustment Factor (Ages ≥16)	1	
Soil Vapor and Particle Dispersion Models		
Particulate Emission Factor	1.21 E+09 m^3/kg	
Dispersion Term (the inverse of the mean air concentration at the center of a square 0.5-acre area source)	83.53 g/m^2-s per kg/m^3	
Representative cities for particulate transport model	Cleveland, OH; Harrisburg, PA; Hartford, CT; Philadelphia, PA	
Brownfield Surface Area	0.5 acres	
Respirable Fraction Emission Rate	0.036 g/m^2-hr	
Brownfield Percentage of Vegetative Cover (decimalized)	0.5	
Mean Annual Wind Speed	4.69 m/s	
Equivalent Threshold Friction Velocity[26]	11.32 m/s	
Wind Speed Distribution Function[27]	0.194	
Mass-limit Volatilization Factor[28]	2.67 E+04 m^3/kg	
Average Duration of Volatilization	70 years[29]	
Brownfield Dry Soil Bulk Density	1.5 kg/L	
Brownfield Depth of Contamination	4.6 m[30]	

Table Ad-2.3. Exposure Factors and Values Applicable to Specific Substances

Parameter and Contaminant	2006 Value	2018 Value
New or Revised Dermal Absorbed Fractions (Decimalized)		
aniline	Not Applicable	0.1
4,4'-DDD	0	0.1
4,4'-DDE	0	0.1
dieldrin	0	0.1
endosulfan (technical)	0	0.1
endrin	0	0.1
heptachlor	0	0.1
alpha-hexachlorocyclohexane	0	0.1
beta-hexachlorocyclohexane	0	0.1
delta-hexachlorocyclohexane	0	0.1
gamma-hexachlorocyclohexane	0.04	0.1
mercury (elemental)	Not Applicable	0
mercury (organic)	Not Applicable	0
nitrobenzene	Not Applicable	0.1
perfluorooctane sulfonic acid	Not Applicable	0
perfluorooctanoic acid	Not Applicable	0
New Rural Soil Background Concentrations[(31)]		
aniline	Not Applicable	None Available
cyanide	-	2.3 mg/kg
hexachlorobenzene	-	0.03 mg/kg
mercury (elemental)	-	None Available
mercury (organic)	-	0.009 mg/kg
nickel	-	30 mg/kg
nitrobenzene	Not Applicable	0.08 mg/kg
perfluorooctane sulfonic acid	Not Applicable	None Available [TBD]
perfluorooctanoic acid	Not Applicable	None Available [TBD]
phenanthrene	-	1.1 mg/kg
New Volatility Determinations		
aniline	Not Applicable	Volatile
mercury (elemental)	Not Applicable	Volatile
mercury (organic)	Not Applicable	Volatile
nitrobenzene	Not Applicable	Volatile
perfluorooctane sulfonic acid	Not Applicable	Non-volatile
perfluorooctanoic acid	Not Applicable	Non-volatile
New Persistent, Bioaccumulative & Toxic Determinations		
aniline	Not Applicable	Not PBT
mercury (elemental)	Not Applicable	PBT
mercury (organic)	Not Applicable	PBT
nitrobenzene	Not Applicable	Not PBT
perfluorooctane sulfonic acid	Not Applicable	PBT
perfluorooctanoic acid	Not Applicable	PBT
New Mutagenic Mode of Action Determinations		
aniline	Not Applicable	Non-mutagenic
nitrobenzene	Not Applicable	Non-mutagenic

perfluorooctane sulfonic acid	Not Applicable	Non-mutagenic
perfluorooctanoic acid	Not Applicable	Non-mutagenic

Notes for Tables Ad-2.1 to Ad-2.3.:

*Values are averages assumed for the entire exposure period.

**This determination had a relatively substantial impact on the final chronic health-based SCOs.

Unrestricted, Restricted Residential, Residential Settings – Child Incidental Ingestion Rate (Total Soil, Time-Weighted Average). The TWA was substantially increased due primarily to an increase in the average incidental soil ingestion rate during the assumed 224-day NYS "Warm Season" from 80 mg/day to 200 mg/day. The increase improves consistency between US EPA and NYS DOH risk assessment approaches.

Unrestricted, Restricted Residential, Residential Settings - Exposure Duration for Age Class 16 to 26 years. The magnitude of lifetime cancer risk from residence on brownfields was substantially reduced by a decrease in the exposure duration from an assumed 70-year lifetime to an upper percentile residency period estimate of 26 years. Consistent with US EPA guidance, a person residing on brownfields is assumed to be potentially exposed to brownfield soil only from birth to age 26 years.

Commercial and Industrial Settings – Adult Incidental Ingestion Rate (Total Soil, Time-Weighted Average). The TWAs were substantially increased due primarily to an increase in the adult incidental soil ingestion rate during the 224-day NYS Warm Season. Consistent with US EPA guidance, an outdoor worker/landscaper working on one or more brownfields is now assumed to incidentally ingest an average of 100 mg/day of outdoor soil, including the outdoor soil component of indoor dust, during the NYS Warm Season. The prior NYS DOH ingestion rate assumptions were 17 mg/day (commercial setting adult) and 8.5 mg/day (industrial setting adult).

(1) Hypothetical child and adult receptors in the unrestricted, restricted residential, and residential land use scenarios are residents. For the unrestricted scenario, children and adults are members of a farm family (or otherwise consume an unusual volume of food grown or raised on-site).

(2) 80 mg dust/day x 0.5 mg soil/mg dust = 40 mg soil/day

(3) Mean continuous frost-free period for La Guardia Airport, which is near Astoria, Queens (1941-2015).

(4) Child TWA IR = [200 mg/day x (224 days/365 days) x (7 days/7 days)] + [40 mg/day x (126 days /365 days x (7 days/7 days)] + [0 mg/day x (15 days /365 days) x (7 days/7 days)] = 137 mg/day

(5) Soil particle exposures were previously assumed to occur only while outdoors. Soil particle erosion is dependent on the cube of wind speed, so that brief (one to two-minute duration) wind gusts are highly influential, and during wind gusts respirable soil particle transport through open windows is reasonably anticipated. We now consider constant particle exposure during the 224-day NYS Warm Season, which is consistent with US EPA guidance.

(6) The adult resident soil ingestion rate was previously assumed to include ingestion of the outdoor soil component of household dust. The scientific literature now supports a specific soil-in-household dust ingestion rate for adult residents of 12 mg/day.

(7) 24 mg dust/day x 0.5 mg soil/mg dust = 12 mg soil/day

(8) Adult TWA IR = [100 mg/day x (224 days/365 days) x (7 days/7 days)] + [12 mg/day x (126 days/365 days) x (7 days/7 days)] + [0 mg/day x (15 days/365 days)] = 66 mg/day

(9) The adult resident was previously assumed to have no contact with the outdoor soil component of household dust. The updated approach assumes contact with the outdoor soil component of indoor household dust year-round, except for 15 vacation days.

(10) Children under 1 year of age were previously assumed not to ingest, or have skin contact with, outdoor soil or the outdoor soil component of indoor household dust. The updated approach assumes incidental ingestion of outdoor soil, as well as the outdoor soil component of indoor household dust, beginning at age 6 months.

(11) For purposes of cancer risk assessment, a person resides at brownfields from birth to age 26 years, rather than from birth to age 70 years. The shorter (26-year) duration is consistent with current US EPA risk assessment practice.

(12) A child age 0 to 1 years is assumed to have dermal contact with outdoor soil, or the outdoor soil component of indoor dust, only between the ages of 6 and 12 months. The exposure frequency (EF) is therefore one-half that of a child ages 1 to 2 years: EF = 287 days/year x 0.5 = 144 days/year.

(13) Based on the assumption that outdoor soil contact occurs 224 days/year, that there is no dermal contact with soil or household dust during vacation 15 days/year, and that 50% of household dust is outdoor soil, the child and adult resident exposure frequency (EF) is calculated: EF = 224 days/year + [(365 days/year – 224 days/year - 15 days/year) x 0.5] = 287 days/year.

(14) In the commercial exposure scenario the hypothetical child is an occasional commercial (or passive-recreational) brownfield site visitor with little opportunity for soil exposure.

(15) The commercial brownfield child visitor is assumed to have less contact with soil compared with a child resident, so the child visitor incidental ingestion rate is not an upper percentile value for a child resident, but rather a central tendency value.

(16) Ingestion and dermal exposures to the outdoor soil component of workplace dust, and from tracking of soil from brownfields into the home, are likely to be relatively trivial compared with the high-normal incidental ingestion rate selected for this receptor, and are therefore adequately reflected in the selected incidental ingestion rate.

(17) Child TWA IR = (50 mg/day x (224 days/365 days) x (2 days/7 days)] + [0 mg/day x (15 days/365 days)] = 9 mg/day

(18) Hypothetical adults on commercial and industrial properties are outdoor workers/landscapers as described by US EPA guidance, with a downward adjustment to account for the default NYS Warm Season of 224 days/year.

[19] US EPA recommendation for an outdoor worker/landscaper. This value includes outdoor soil and the outdoor soil component of indoor (workplace) dust.

[20] Outdoor Worker TWA IR = [100 mg/day x (202 days/365 days) x (5 days/7 days)] + [0 mg/day x (15 days/365 days)] = 40 mg/day

[21] US EPA recommends that risk assessors assume the standard 8-hour work day for outdoor workers/landscapers.

[22] In the industrial exposure scenario the hypothetical child is a brownfield site trespasser with soil exposure on only 30 days/year, and an incidental ingestion rate on those days that is the same as the rate assumed for adults residing on a brownfield (100 mg/kg).

[23] Child Trespasser IR = [100 mg/day x (224 days/365 days) x (1 day/7 days)] + [0 mg/day x (15 days/365 days)] = 9 mg/day

[24] A body weight of 70 kg, rather than 80 kg, is used for route-to-route dose extrapolation because when authoritative bodies required adult body weights during the development of toxicity values, a body weight of 70 kg was most often employed. See, for example, posterior predictions for representative internal human doses in US EPA's Toxicological Review of Trichloroethylene (US EPA, 2011), and the oral RfD summary for silver in US EPA's IRIS database (US EPA, 1991).

[25] These are the Department's generic adjustments employed to calculate SCOs for unrestricted parcels (Persistent, Bioaccumulative & Toxic Substances factor, and Homegrown Produce Consumption and Home-Produced Animal Product Consumption factor) and residential parcels (Homegrown Produce Consumption factor only).

[26] The minimum friction velocity that is required to initiate movement of a brownfield soil particle resting on the soil surface, adjusted for monitor height. The US EPA's recommended default value is used.

[27] The wind speed distribution function is derived from the mean annual wind speed and the threshold friction velocity. The US EPA's recommended default value is used.

[28] The mass-limit volatilization factor represents the degree of vapor release from brownfield soil when it is assumed that contaminant release from soil occurs at a constant rate over a specified period.

[29] The volatile analyte is assumed to be released from brownfield soil, exhausting the contaminant mass over a 70-year period. The 70-year duration was selected to reflect a likely condition at brownfields, involving a slow release of soil volatiles over several decades. Choosing a lower value for this parameter (*e.g.*, a residential duration of 26 years) would imply rapid contaminant release, and would result in higher estimates of soil particle inhalation exposure.

[30] Soil contamination to a depth of 4.6 meters (15 feet) below the ground surface was specified. SCOs developed for commercial and industrial land uses are applicable to this depth.

(31) New Rural Soil Background Concentrations are estimated 98th percentile values based on results from the Department's Statewide Rural Soil Survey and/or reviews of the scientific literature, derived in a manner that avoids the establishment of RSBCs that are below normally achieved reporting limits. The RSBC for organic mercury is 3% of the RSBC for total mercury, based on the observation that 3% is an approximate upper-bound organic mercury percentage for most soils absent an obvious source of organic mercury contamination (see US EPA 1997).

Table Ad-3. 2018 Acute Soil Ingestion SCOs [(1)]

Contaminant	SCO_{acute} (mg/kg)
barium	410
cadmium	9.7
copper	280
cyanide (free)	28
nickel	320
pentachlorophenol	6.9
phenol	830

[(1)] 2018 acute soil cleanup objectives are based on a 13.8 kilogram child who ingests 10 grams of soil per exposure event.

Table Ad-4. 2018 Soil Cleanup Objectives After Consideration of Chronic Cancer and Noncancer Health Risks, Acute Health Risks, Dermal Irritancy Risk, and Rural Soil Background Concentrations

Substance	Unrestricted (mg/kg)	Residential (mg/kg)	Restricted Residential (mg/kg)	Commercial (mg/kg)	Industrial (mg/kg)
acenaphthene	130	240	980	9,500	16,000
acenaphthylene	130	240	980	9,500	16,000
acetone	2,000	3,800	19,000	300,000	360,000
aldrin	0.0048 (1)	0.0088	0.044	0.33	0.33
aniline	5.5	6.7	8.1	36	36
anthracene	640	1,200	5,000	47,000	65,000 (2)
arsenic	16 (1)	16 (1)	16 (1)	16 (1)	16 (1)
barium	410 (3)	410 (3)	410 (3)	410 (3)	73,000
benz(a)anthracene	1.0 (1)	1.0 (1)	1.4	37	37
benzene	0.68	1.2	3.7	20	20
benzo(a)pyrene	1 (1)	1 (1)	1 (1)	3.7	3.7
benzo(b)fluoranthene	1 (1)	1 (1)	1.4	37	37
benzo(g,h,i)perylene	0.64	1.2	4.9	47	78
benzo(k)fluoranthene	0.8 (1)	1.2	4.9	47	78
beryllium	4.4	8.8	43	670	750
n-butylbenzene	100	190	650	5,000	5,000
sec-butylbenzene	75	140	470	3,600	3,600
tert-butylbenzene	75	140	470	3,600	3,600
cadmium	2.5 (1)	2.5 (1)	2.5 (1)	3.7	4.4
carbon tetrachloride	1	1.9	7.1	41	41
chlordane	0.014	0.14	0.65	8.2	11
chlorobenzene	40	73	220	1,500	1,500
chloroform	2.4	4.8	24	180	180
chromium (III)	30 (1)	30 (1)	110	1,700	2,000
chromium (VI)	0.033	0.066	0.33	11	11

Substance	Unrestricted (mg/kg)	Residential (mg/kg)	Restricted Residential (mg/kg)	Commercial (mg/kg)	Industrial (mg/kg)
chrysene	1 (1)	1.2	4.9	47	78
copper	280 (3)	280 (3)	280 (3)	280 (3)	56,000
cyanide	2.3 (1)	2.6	13	28 (3)	240
4,4'-DDD	0.12	1.2	5	33	33
4,4'-DDE	0.081	0.78	3.4	22	22
4,4'-DDT	0.079	0.78	3.8	27	27
dibenz(a,h)anthracene	0.1 (1)	0.1 (1)	0.14	3.7	3.7
dibenzofuran	2.1	4.2	18	180	290
1,2-dichlorobenzene	480	740	1,400	7,000	7,000
1,3-dichlorobenzene	6.1	11	38	280	280
1,4-dichlorobenzene	5.8	10	24	130	130
1,1-dichloroethane	11	19	47	240	240
1,2-dichloroethane	1.4	2.4	5.8	30	30
1,1-dichloroethene	0.24	0.41	0.98	5.1	5.1
cis-1,2-dichloroethene	4.4	8.7	41	590	590
trans-1,2-dichloroethene	41	75	240	5,200	12,000
dieldrin	0.005 (1)	0.017	0.075	0.48	0.48
1,4-dioxane	0.73	1.4	5.7	36	36
endosulfan	4.3	8.4	35	360	580
endrin	0.13	1.2	5.3	55	87
ethylbenzene	18	32	76	390	390
fluoranthene	85	170	660	6,200	11,000
fluorene	85	170	660	6,200	11,000
heptachlor	0.013	0.12	0.53	5.1	5.1
hexachlorobenzene	0.03 (1)	0.042	0.18	1.8	2.9
alpha-hexachlorocyclohexane	0.022	0.042	0.18	1.2	1.2
beta-hexachlorocyclohexane	0.021	0.042	0.18	1.8	2.9
delta-hexachlorocyclohexane	54	100	440	4,500	7,200

Substance	Unrestricted (mg/kg)	Residential (mg/kg)	Restricted Residential (mg/kg)	Commercial (mg/kg)	Industrial (mg/kg)
gamma-hexachlorocyclohexane	0.025	0.05	0.21	2.1	3.4
indeno(1,2,3-cd)pyrene	0.5 (1)	0.5 (1)	1.4	37	37
lead	- (4)	- (4)	- (4)	- (4)	- (4)
manganese	2,000 (1)	2,000 (1)	2,000 (1)	10,000	11,000
mercury (elemental)	0.26 (5)	0.26 (5)	0.26 (5)	1.1	1.1
mercury (inorganic salts)	0.07 (5)	0.7 (5)	3.5	53	64
mercury (organic)	0.043 (5)	0.38	1.3	9.8	9.8
methyl *tert*-butyl ether	21	40	150	890	890
methylene chloride	8.3	17	81	2,000	2,100
methyl ethyl ketone	1300	2500	10,000	100,000	100,000
2-methylphenol (o-cresol)	210	420	1800	18,000	29,000
3-methylphenol (m-cresol)	210	420	1800	18,000	29,000
4-methylphenol (p-cresol)	210	420	1800	18,000	29,000
naphthalene	43	84	350	3,600	5,800
nickel	44	87	320 (3)	320 (3)	5,900
nitrobenzene	0.45	0.77	1.8	8.9	8.9
pentachlorophenol	0.18	0.34	1.3	6.9 (3)	7.0
perfluorooctane sulfonic acid	0.00088	0.0088	0.044	0.44	0.44
perfluorooctanoic acid	0.00066	0.0066	0.033	0.5	0.6
phenanthrene	1.1 (1)	1.2	4.9	47	78
phenol	640	830 (3)	830 (3)	830 (3)	87,000
polychlorinated biphenyls	- (4)	- (4)	- (4)	- (4)	- (4)
n-propylbenzene	200	370	1,100	7,700	7,700
pyrene	64	120	500	4,700	8,000
selenium	11	22	110	1,700	2,000
silver	11	22	110	1,700	2,000
tetrachloroethene	12	15	18	81	81
toluene	1,800	3,600	13,000	27,000	27,000
1,1,1-trichloroethane	4,000	7,300	22,000	150,000	150,000

Substance	Unrestricted (mg/kg)	Residential (mg/kg)	Restricted Residential (mg/kg)	Commercial (mg/kg)	Industrial (mg/kg)
trichloroethene	0.91	1.7	6.4	54	54
1,2,4-trimethylbenzene	21	41	150	1400	1400
1,3,5-trimethylbenzene	21	41	150	1400	1400
vinyl chloride	0.05	0.099	0.48	7.1	7.1
xylenes	290	440	730	3,500	3,500
zinc	660	1300	6600	100,000	120,000

Notes:

mg/kg = milligrams per kilogram of soil or parts per million

The New York State Department of Environmental Conservation will reduce some of the soil cleanup objectives in this table to protect groundwater, or to accommodate ecological toxicity, ecological rural soil background concentrations, contract required quantitation limits, and “caps” (default upper limits that consider, among other factors, violations of critical modeling assumptions regarding soil adherence to skin, wind dispersion, absence of free-phase contamination, etc., at very high soil contaminant levels).

(1) The lowest health-based SCO was below the RSBC, so the RSBC was selected.

(2) The dermal irritancy SCO was below the chronic health-based SCO, therefore the dermal irritancy SCO was selected.

(3) The acute health-based SCO was below the chronic health-based SCO, so the acute SCO was selected. The acute health-based SCOs, which are based on soil ingestion by a child, are not considered in the selection of SCOs for industrial land use.

(4) Toxicity values for lead and polychlorinated biphenyls are not listed because the NYS DOH used chemical-specific risk assessment approaches and federal guidelines to establish SCOs for these substances.

(5) The SCO applies when all forms of mercury (elemental, inorganic, organic) are quantified. Otherwise, only the total mercury concentration is considered, in which case the RSBC for total mercury of 0.3 mg/kg is applicable.

Appendix Ad-A

Toxicity Value Fact Sheets for Priority Contaminants

Chemical Name: Acenaphthene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Acenaphthene (CAS Number 83-32-9)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2004) ♦ US EPA ODW (2004) ♦ US EPA HEAST (1997)	0.06	175	NOEL	3,000	Based on hepatotoxicity in male and female mice in a 90-day oral gavage study. Study LOEL = 350 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The US EPA value is the only available reference dose for acenaphthene from an authoritative body from listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the US EPA reference dose (0.06 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for acenaphthene.

3. Review Dates

Summary table completion: July, 2004; no revision January 2018
Toxicity value recommendation: September, 2004; no revision January 2018

4. References for Summary Table

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (Office of Drinking Water). 2004. 2004 Edition of the Drinking Water Standards and Health Advisories. EPA 822-R-04-005. Office of Water. U.S. Environmental Protection Agency Washington, DC. Last accessed (01/18/2018) at http://www.epa.gov/waterscience/drinking/

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acenaphthene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Acenaphthene (CAS Number 83-32-9)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Human and animal data are not available.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for acenaphthene is not available.

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acenaphthene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Acenaphthene (CAS Number 83-32-9)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for acenaphthene is not available from the authoritative bodies listed in item number 5 (below). Acenaphthene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for acenaphthene is 0.06 mg/kg/day. Therefore, a reference concentration of 210 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for acenaphthene.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005 no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acenaphthene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Acenaphthene (CAS Number 82-32-9)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for acenaphthene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acenaphthylene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Acenaphthylene (CAS Number 208-96-8)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
--	--	--	--	--	No information available from listed sources.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.
UF: uncertainty factor.

2. Recommendation and Rationale

An oral reference dose for acenaphthylene is not available. An oral reference dose is available for acenaphthene, which is structurally and chemically similar to acenaphthylene. The similarity between the two chemicals provides a basis for using toxicity data for acenaphthene to represent acenaphthylene. Therefore, the US EPA reference dose for acenaphthene (0.06 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for acenaphthylene (see Oral Non-Cancer Toxicity Value Documentation for acenaphthene).

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water

Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acenaphthylene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Acenaphthylene (CAS Number 208-96-8)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Human data are not available. Data from animal studies are inadequate.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10^{-6} dose), where 1 x 10^{-6} dose = 1 x 10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for acenaphthylene is not available.

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acenaphthylene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Acenaphthylene (CAS Number 208-96-8)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for acenapthylene is not available from the authoritative bodies listed in item number 5 (below). Acenaphthylene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure and for which an oral reference dose for a chemically similar surrogate (acenaphthene) based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for the chemical surrogate (acenaphthene) is 0.06 mg/kg/day. Therefore, based on the chemical surrogate and exposure route extrapolation, a reference concentration of 210 mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for acenaphthene.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acenaphthylene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Acenaphthylene (CAS Number 208-96-8)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for acenaphthylene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acetone
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Acetone (CAS Number 67-64-1)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2003) • US EPA HEAST (1997)	0.9	900	NOEL	1000	Based on kidney toxicity (nephropathy) in male rats exposed by drinking water for 13 weeks. Study LOEL = 1700 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The US EPA value is the only available reference dose for acetone from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore the US EPA reference dose (0.9 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for acetone.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 (97-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section.
https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acetone
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Acetone (CAS Number 67-64-1)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Available epidemiology and animal studies show no evidence of carcinogenicity.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for acetone is not available.

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. http://www.epa.gov/iris/index.html. Agency consensus date: 05/29/2003. Last revised: 07/31/2003.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System

- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acetone
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Acetone (CAS Number 67-64-1)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
ATSDR (2002)	3×10^4 *	2.97×10^6	LOEL	100	Based on neurological effects in a 6 week human study.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.
*The ATSDR value is reported as 13 parts per million (ppm). For acetone, 1 ppm = 2.37 mg/m^3.

2. Recommendation and Rationale

The ATSDR value is the only available reference concentration for acetone from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the ATSDR reference concentration (30,000 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for acetone.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological Profile for acetone. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. https://www.atsdr.cdc.gov/toxprofiledocs/index.html

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System

National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Acetone
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Acetone (CAS Number 67-64-1)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Inadequate human and animal data, and generally negative results in genotoxicity studies.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An inhalation unit risk for acetone is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Aldrin
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Aldrin (CAS Number 309-00-2)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2003) • US EPA OPP (1997) • US EPA ODW (2002) • US EPA HEAST (1997)	3×10^{-5}	0.025	LOEL	1000	Based on increased liver-to-body weight ratio and liver histopathological changes in male and female rats in a 2-year dietary study.
WHO (2017)	1×10^{-4}	0.025	NOEL	250	Based on NOELs of 1 mg/kg in diet of dogs and 0.5 mg/kg in diet of rats, equivalent to 0.025 mg/kg/day in both species. Limited information is available on the precise studies and points of departure used to obtain the reference dose.
ATSDR (2002)	3×10^{-5}	0.025	LOEL	1000	Based on same study and analysis as US EPA IRIS (2004).
RIVM (2001)	1×10^{-4}	0.025	LOEL	250	Based on liver toxicity in rats in same study as US EPA IRIS (2004), and on liver toxicity in dogs in a 25-month dietary study.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The basis for the various reference doses for aldrin are essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (0.025 mg/kg/day). Limited documentation for the WHO reference dose designates the level of 0.025 mg/kg/day a NOEL in rats and dogs. However, this exposure level produced increased liver to body weight ratios and histopathological liver lesions in rats, and is thus considered a LOEL. The RIVM reference dose uses an uncertainty factor of 2.5 for using a LOEL rather than a NOEL as the point of departure, while the US EPA and ATSDR reference doses use an uncertainty factor of 10 for this purpose. The lower uncertainty factor for the RIVM value is based on the marginal nature of the liver effects at the LOEL. However, the effect is not necessarily marginal considering the presence of histopathological lesions. An uncertainty factor of 10 for use of a LOEL is considered appropriate and is also most consistent with accepted risk assessment practices of United States health agencies. The US EPA reference dose (3×10^{-5} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for aldrin.

3. Review Dates

Summary table completion: February, 2004; revised January, 2018
Toxicity value recommendation: March, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological Profile for Aldrin and Dieldrin. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. p.244-248.

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 (97-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2002. Office of Drinking Water, Drinking Water Standards and Health Advisories. Washington, DC. EPA 822-R-02-038.

US EPA OPP (United States Environmental Protection Agency Office of Pesticide Programs). 1997. Reference Dose Tracking Report. Washington, DC: Office of Pesticide Programs, Health Effects Division. HED reviewed 08/08/86.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2017. Guidelines for drinking water quality, 4th Ed. World Health Organization, Geneva. https://www.who.int/water_sanitation_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Aldrin
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Aldrin (CAS Number 309-00-2)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2003) • US EPA OPP (1997) • Cal EPA (2004)	5.8×10^{-8}	17	linearized multistage model, extra risk	body surface area[2]	Chronic dietary studies showed aldrin increased the incidence of liver tumors in both sexes of three strains of mice. There was no sex or strain effect. The cancer potency factor is the geometric mean of three separate cancer potency factors; each derived from a different dose response dataset.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.

2. Recommendation and Rationale

The US EPA IRIS cancer potency factor is the only available cancer potency factor from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the US EPA IRIS cancer potency factor (17 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for aldrin. The aldrin risk specific dose calculated from this toxicity value is 5.8×10^{-8} mg/kg/day.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency), 2004. Office of Environmental Health Hazard Assessment. Toxicity Criteria Database. Last accessed (01/17/2018) at https://oehha.ca.gov/chemicals

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA OPP (United States Environmental Protection Agency Office of Pesticide Programs). 1997. Reference Dose Tracking Report. Washington, DC: Office of Pesticide Programs, Health Effects Division. HED reviewed 08/08/86.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Aldrin
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Aldrin (CAS Number 309-00-2)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for aldrin is not available from the authoritative bodies listed in item number 5 (below). Aldrin is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for aldrin is 3×10^{-5} mg/kg/day. Therefore, a reference concentration of 0.1 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for aldrin.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Aldrin
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Aldrin (CAS Number 309-00-2)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for aldrin is not available from the authoritative bodies listed in item number 5 (below). Aldrin is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral cancer potency factor based on cancer effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a unit risk from the cancer potency factor. The recommended oral cancer potency factor for aldrin is 17 per mg/kg/day. Therefore, a unit risk of 4.9×10^{-3} per mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for aldrin. The risk specific air concentration calculated from this toxicity value is 2×10^{-4} mcg/m^3.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Aniline*
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Aniline (CAS Number 62-53-3)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA OSRTI Also used by: ♦ US EPA RSL	0.007	7	LOEL	1000	Based on erythrocytic and splenic toxicity in rats exposed via the diet in a 104-week study.
HC PSAP	0.0014	7.2	LOEL	5000	Based on same study, species, and effects used by US EPA OSRTI.
NYS DEC (1997)	0.15	150	LOEL	1000	Based on fatty metamorphosis, fibrosis and papillary hyperplasia of the spleen, hemosiderosis of the liver and kidney, and endometrial stromal polyps in rats exposed via the diet in an 8-week study.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Aniline is a new priority contaminant and this is a new fact sheet. Aniline was not identified as a priority contaminant in the 2006 Technical Support Document for the Development of Soil Cleanup Objectives in the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA and HC PSAP reference doses for aniline are based on the same 104-week dietary study in rats. This study is preferred over the study used by NYS DEC as the basis of a chronic reference dose because the study length was substantially longer (104 weeks compared to 8 weeks). The US EPA applied a total uncertainty factor of 1000 to the LOEL to compensate for animal-to-human extrapolation (10), the use of a LOEL (10), and human variation (10). HC PSAP used the same uncertainty factors but added a 5-fold uncertainty factor for limited evidence of carcinogenicity. Given that cancer risks are evaluated separately in the Brownfield Cleanup Program, the US EPA reference dose (0.007 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for aniline.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table and Recommendation and Rationale

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/25/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Aniline. Albany, NY: Division of Water

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund. Last accessed (01/25/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/25/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Aniline*
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Aniline (CAS Number 62-53-3)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ♦ US EPA RSL	1.8×10^{-4}	5.7×10^{-3}	linearized multistage model	body surface area[2]	Based on the combined incidence of splenic sarcomas, fibrosarcomas, stromal sarcomas, capsular sarcomas and hemangiosarcomas in male rats exposed via the diet to aniline hydrochloride in a 104-week study.
CA EPA CPF	1.8×10^{-4}	5.7×10^{-3}	linearized multistage model	body surface area[2]	CA EPA CPF adopted the US EPA IRIS derivation and cancer potency factor.
NYS DEC (1997)	2.9×10^{-4}	3.4×10^{-3}	linearized multistage model	$BW^{¾}$ [3]	Based on same study, species, sex, and tumors used by US EPA IRIS.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.
[2]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$.

*Aniline is a new priority contaminant and this is a new fact sheet. Aniline was not identified as a priority contaminant in the 2006 Technical Support Document for the Development of Soil Cleanup Objectives in the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The cancer potency factors for aniline derived by authoritative bodies are all based on the same study and effects (the combined incidence of splenic sarcomas, fibrosarcomas, stromal sarcomas, capsular sarcomas, and hemangiosarcomas in male rats exposed via the diet in a 104-week study). The only difference in the derivations is the method used to extrapolate animal doses to equivalent human doses. The NYS DEC derivation used $BW^{3/4}$ scaling while the US EPA/CA EPA derivations used body surface area scaling. Since $BW^{3/4}$ scaling is the current recommendation of the US EPA and CA EPA, the NYS DEC cancer potency factor (3.4×10^{-3} per mg/kg/day) is the toxicity value recommended for

use in the derivation of an oral cancer-based soil cleanup objective for aniline. The aniline risk specific dose calculated from this toxicity value is 2.9×10^{-4} mg/kg/day.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/25/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Aniline. Albany, NY: Division of Water

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/25/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/25/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Aniline*
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Aniline (CAS Number 62-53-3)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL	1	3400	$NOEL_{ADJ-HEC}$[3]	3000	Based on lack of observed toxicity in rats, guinea pigs and mice exposed via inhalation for 6 hours/day, 5 days/week for 20 to 26 weeks ($NOEL_{EXP}$ = 19 mg/m^3 and $NOEL_{ADJ}$[2] = 3.4 mg/m^3) and supported by the observation of splenic toxicity in rats exposed via inhalation for 6 hours/day, 5 days/week for 2 weeks ($LOEL_{EXP}$ = 64.7 mg/m^3 and $LOEL_{ADJ}$[2] = 11.6 mg/m^3).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

[2]$NOEL_{ADJ}$ or $LOEL_{ADJ}$ = $NOEL_{EXP}$ or $LOEL_{EXP}$ x 6 hours/24 hours x 5 days/7 days.

[3]$NOEL_{ADJ-HEC}$: adjusted NOEL human equivalent concentration (HEC), which equals $NOEL_{ADJ}$ x 1 (default ratio for the ratio of the animal blood:air partitioning coefficient to the human blood:air partitioning coefficient for aniline).

$NOEL_{EXP}$: experimental no-observed-effect level; $NOEL_{ADJ}$: $NOEL_{EXP}$ adjusted to continuous exposure; $LOEL_{EXP}$: experimental lowest-observed-effect level; $LOEL_{ADJ}$: $LOEL_{EXP}$ adjusted to continuous exposure; UF: uncertainty factor.

*Aniline is a new priority contaminant and this is a new fact sheet. Aniline was not identified as a priority contaminant in the 2006 Technical Support Document for the Development of Soil Cleanup Objectives in the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA reference concentration for aniline is the only value from an authoritative body listed in item 5 (below). The animal point of departure ($NOEL_{ADJ}$) for splenic toxicity was converted to a human $NOEL_{ADJ-HEC}$ using the US EPA recommended dosimetric adjustment for extrarespiratory effects of category 3 gases. This compensates for animal-human differences in the pharmacokinetics of

inhaled aniline. The US EPA applied a 3000-fold uncertainty factor to compensate for animal-to-human extrapolation (10), use of subchronic study (10), human variation (10) and the lack of appropriate reproductive studies (3). The US EPA reference concentration (1 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for aniline.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table and Recommendation and Rationale

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/25/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/25/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Aniline*
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for Aniline (CAS Number 62-53-3)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA CPF	0.62	1.6×10^{-6}	linearized multistage model	body surface area[2]	Based on default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation of the US EPA IRIS oral cancer potency factor of 5.7×10^{-3} per mg/kg/day.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million, where 1×10^{-6} air concentration = 1×10^{-6}/unit risk.

[2]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.

*Aniline is a new priority contaminant and this is a new fact sheet. Aniline was not identified as a priority contaminant in the 2006 Technical Support Document for the Development of Soil Cleanup Objectives in the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

Aniline is a toxicant that is expected to be absorbed into the body and cause systemic cancer effects after oral or inhalation exposure. The CA EPA unit risk for aniline is the only available value from an authoritative body listed in item 5 (below). This value was derived from a cancer potency factor using a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day. However, the NYS DEC cancer potency factor (3.4×10^{-3} per mg/kg/day) rather than the CA EPA cancer potency factor (5.7×10^{-3} per mg/kg/day) was recommended as the toxicity value for use in the derivation of an oral cancer-based soil cleanup objective for aniline (see Oral Cancer Toxicity Value Documentation for Aniline). A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day was used to derive a unit risk from the recommended cancer potency factor. Therefore, the unit risk of 9.7×10^{-7} per mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for aniline. The aniline risk specific concentration calculated from this toxicity value is 1.0 mcg/m^3.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/25/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/25/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Anthracene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Anthracene (CAS Number 120-12-7)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA ODW (2002) ♦ US EPA HEAST (1997)	0.3	1,000	NOEL	3000	Based on a lack of treatment-related effects in male and female mice in a 90-day gavage study. The NOEL was assigned to the highest dose tested.
RIVM (2001)	0.04	NA	NA	NA	Based on RIVM's evaluation of total petroleum hydrocarbons and its designation of anthracene as a non-carcinogenic aromatic containing 9 to 16 carbons.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; UF: uncertainty factor; NA: not applicable.

2. Recommendation and Rationale

The US EPA reference dose is based on chemical-specific toxicity information for anthracene and is derived using methods that reflect general consistency with current risk assessment practice. The RIVM value is based on a generic approach for petroleum related chemicals and is not derived from a chemical-specific evaluation. Therefore the US EPA reference dose (0.3 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for anthracene.

3. Review Dates

Summary table completion: February, 2004; no revision January, 2018
Toxicity value recommendation: March, 2004; no revision January, 2018

4. References for Summary Table

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001.

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 (97-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2002. Office of Drinking Water, Drinking Water Standards and Health Advisories. Washington, DC. EPA 822-R-02-038.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/16/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Anthracene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Anthracene (CAS Number 120-12-7)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1995)	--	--	--	--	Human data are not available. Cancer effects were not observed in several limited or inadequate studies in animals exposed orally, dermally, and by lung implantation.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for anthracene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: March, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. Toxicological Profile for Polycyclic Aromatic Hydrocarbons. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Anthracene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Anthracene (CAS Number 120-12-7)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for anthracene is not available from the authoritative bodies listed in item number 5 (below). Anthracene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for anthracene is 0.3 mg/kg/day. Therefore, a reference concentration of 1000 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for anthracene.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Anthracene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Anthracene (CAS Number 120-12-7)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for anthracene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Arsenic
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Inorganic Arsenic

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: • US EPA ODW • US EPA RSL • US EPA HEAST (1997)	3×10^{-4}	8×10^{-4}	NOEL[2]	3	Based on hyperpigmentation, keratosis and possible vascular complications in a Taiwanese population chronically exposed via drinking water.
ATSDR (2000)	3×10^{-4}	8×10^{-4}	NOEL	3	Based on same study and analysis as US EPA IRIS.
CA EPA PHG	3.9×10^{-4} [3]	1.17×10^{-2}	LED_{01} [4]	30	Based on the incidence (LED_{01}[4]) of cerebrovascular disease in a Taiwanese population chronically exposed via drinking water.
RIVM (2001)	0.001	2.1×10^{-3}	NOEL	2	Based on critical effects on the skin in humans and derived from the World Health Organization PTWI[3] for arsenic of 0.015 mg/kg/week for adults of 70 kg of body weight. The daily equivalent (0.0021 mg/kg/day) was considered a NOEL by the Health Council of the Netherlands.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]The NOEL of 0.009 mg/L and LOEL of 0.17 mg/L (reported in a later study of the same cohort by the same investigators) were adjusted to 8×10^{-4} mg/kg/day and 0.014 mg/kg/day, respectively, assuming a 55-kg adult drinks 4.5 L water/day.

[3]A reference dose was not derived. CA EPA applied a total UF of 10 to the LED_{01} and assumed an exposure duration of 70 years and relative source contribution of 20% for arsenic from drinking water to calculate a health-protective value (HPV) of 0.0009 mg/L (i.e., 0.00086 mg/L = [3 (mg/L)yr x 0.2]/[70 years x /10 UF].) A C_{DWEL} (a lifetime exposure concentration protective of non-cancer health effects assuming all exposure comes from drinking water) can be calculated from the HPV by eliminating the relative source contribution factor of 0.2 from the above equation (i.e., 0.00043 mg/L = [3 (mg/L)yr]/[70 years x /10 UF]. A reference dose of 3.9×10^{-4} mg/kg/day can be calculated from the C_{DWEL} (0.0043 mg/L) using US EPA IRIS assumptions on the water consumption rates and dietary intakes for Taiwanese populations (i.e., where daily intake from water = C_{DWEL} x 4.5 L/day =0.0194 mg/person-day) and is exposed to 0.002 mg/day arsenic from dietary exposure (i.e., (0.0194 + 0.002 mg)/55 kg/day = 3.9×10^{-4} mg/kg/day).

[4]LED_{01}: The 95% lower confidence limit on the cumulative dose [i.e., 3 (mg/L)yr] associated with a 1% increase (relative to controls) in cerebrovascular disease in the exposed population.

NOEL: no- observed-effect level; LOEL: lowest- observed-effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The basis for the US EPA IRIS, ATSDR, and RIVM reference doses for arsenic is skin effects in human populations chronically exposed to elevated arsenic in drinking water. There is limited documentation of the specific data providing the basis of the RIVM reference dose, and RIVM chose to apply an uncertainty factor of 2 to the NOEL point of departure, while US EPA and ATSDR applied an uncertainty factor of 3. The US EPA notes that an uncertainty factor of 3 accounts for the lack of data addressing reproductive toxicity as well as human variation. An uncertainty factor of 3 is considered more consistent with accepted risk assessment practices of United States health agencies.

CA EPA based their reference dose on the LED_{01} for cerebrovascular disease in the human populations chronically exposed to elevated arsenic in drinking water. CA EPA applied a total uncertainty factor (UF) of 10 to the LED_{01} to compensate for human variation (3) and to extrapolate to a level of negligible risks (3).

The reference dose derived by US EPA and ATSDR or estimated from the CA EPA toxicity value for non-oncogenic skin or vascular effects are similar (3×10^{-4} mg/kg/day and 3.9×10^{-4} mg/kg/day, respectively). Moreover, the available data strongly support the conclusion that oral exposures to arsenic are strong risk factors for both skin and vascular diseases. Lastly, both derivations are based on good epidemiological studies. Although the US EPA/ATSDR derivation is based on ecological studies, the cohort size was large and the derivation was based on exposure parameters specific to the population. CA EPA used the study that was strengthened by the use of estimated individual cumulative arsenic exposures and linkage to disease outcome. The study accounted for potential confounding factors (i.e., age, gender, hypertension, diabetes mellitus, cigarette smoking, and alcohol consumption), which strengthens confidence in the dose-response relationship between cumulative arsenic exposure and the incidence of cerebrovascular disease. The differences in quality between the two studies and derivations are too small to support a clear choice of one value over the other. Although the use of a benchmark dose is generally preferred over a NOEL as a point of departure, the CA EPA use of an uncertainty factor of 3 with the use of a LED_{01} may be overly conservative. Therefore, the US EPA/ATSDR reference dose (3×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for arsenic.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed 01/21/2018) at http://www.atsdr.cdc.gov/toxpro2.html, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/21/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/21/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/21/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/21/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/21/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/21/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

6. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Arsenic
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Arsenic

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA HEAST (1997)	6.7×10^{-7}	1.5	linearized multistage model (time and dose related formulation)	--	Estimated from increased incidence of skin cancer observed in Taiwanese populations consuming drinking water with elevated levels of inorganic arsenic.
HC PSAP (TERA)	3.6×10^{-7}	-- [2]	linear extrap. from TD_{05} [2]	--	Based on same data as US EPA IRIS, incorporating background rates of skin cancer for Canadians.
CA PHG *	5.3×10^{-8}	-- [3]	linear relative-risk analysis of combined cancer mortality data	--	Based on lung cancer and urinary bladder cancer mortality data in epidemiology studies from Taiwan, Chile and Argentina and background cancer mortality rates in the US.

HC DWQ *	6.2×10^{-7} to 4.4×10^{-6}	--[4]	Poisson relative-risk model fit to mortality data for each tumor site (a range of unit risks was reported for the different tumor sites)	--	Based on lung, liver and urinary bladder cancer mortality data from Taiwan, including some of the same populations as in the study used by US EPA IRIS.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]No cancer potency factor was derived. The risk specific dose was obtained by linear extrapolation from the modeled TD_{05} (= 0.84 mg/L in drinking water, assuming 1.5 L/d water consumption and 70 kg adult body weight), the dose associated with a 5% increase in mean tumor incidence (not a lower-bound estimate; TERA, 2004)
[3]No cancer potency factor was derived. The risk specific dose was obtained from the drinking water unit risk of 5.4×10^{-4} per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day. (The original unit risk is expressed as 2.7×10^{-4} per microgram per liter for a unit drinking water consumption rate of 1 liter per day, and so was adjusted to reflect a default 2 liter per day drinking water intake.)
[4]No cancer potency factor was derived. The risk specific dose range was obtained from the upper-bound drinking water unit risk range of 6.49×10^{-6} to 4.64×10^{-5} per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day.

*Agency's toxicity value added or revised during an update of fact sheets to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA IRIS and HC PSAP cancer potency factors are based on increased incidence of skin tumors among Taiwanese populations consuming drinking water containing elevated levels of inorganic arsenic. Both agencies used a time and dose-related formulation of the multistage model, but differed in assumptions regarding background skin cancer rates. The US EPA IRIS value is based on the upper-bound estimate of the modeled dose-response slope at low doses, while the HC PSAP value is a linear extrapolation to the low dose region from a maximum likelihood estimate of the dose at 5% incremental risk. Although the difference between the two values is relatively small, the use of Canadian background skin cancer rates may be less appropriate than those assumed for the US population. The HC PSAP approach of extrapolation from a central tendency estimate instead of from a statistical lower bound is also less consistent with generally-accepted risk-assessment practice.

HC DWQ and CA EPA PHG derived drinking water unit risk estimates for inorganic arsenic based on tumor mortality data from multiple tumor sites including lung, liver and urinary bladder. HC DWQ based its estimates on data that include at least some of the same Taiwan populations as used by US EPA. CA EPA PHG included Taiwan data along with other cancer data from studies in Chile and Argentina. HC DWQ reported a range of unit risks based on excess mortality modeled separately for each tumor site (lung, liver or bladder), while CA EPA PHG estimated cancer risk based on cancer mortality data for lung and bladder tumors combined. Both HC DWQ and CA EPA report their results as drinking water unit risks, without providing a cancer potency factor estimate.

The US EPA, HC DWQ and CA EPA derivations are all similar in applying some form of non-threshold relative risk model to epidemiologic data that relates tumor incidence or cancer mortality to arsenic drinking water concentrations. Information on the mode-of-action by which inorganic arsenic causes cancer is inadequate to clearly indicate whether any of the different modeling approaches used in the three assessments is preferred. The HC DWQ assessment presents a range of unit risk estimates for different tumor sites. The most potent unit risk estimate (lung tumor data) results in a risk-specific dose roughly equal to the US EPA IRIS risk-specific dose based on skin cancer incidence. The CA EPA assessment includes epidemiologic data from other cohorts in addition to the Taiwan study populations. Including these additional data could result in more robust relative-risk estimates. The CA EPA assessment also accounts for the increased risk of mortality from tumors in multiple tissues associated with arsenic exposure by combining the two tumor sites (lung and bladder) that account for most of the excess cancer mortality observed in studies they used. However, a number of uncertainties are introduced into the CA EPA unit risk analysis that raise questions about its reliability as the basis of a soil cleanup objective. In general, epidemiologic analysis based on tumor incidence is preferred over mortality data for risk assessment, since incidence is a less-severe outcome. Although the CA EPA assessment attempted to address the combined risk of two significant tumor types (lung and bladder), they applied a combined excess mortality rate for the two sites to background lung cancer rates, rather than applying tumor-specific rates to tumor-specific background rates and then combining the results. If the relative background rates for lung and bladder cancer mortality differed significantly in the study populations and the US population to which the observed relative risks were applied, this approach could introduce a significant bias in the combined analysis. The CA EPA assessment appears to obtain mean unit risk estimates rather than upper-bound estimates, which are preferred, and they average together male and female unit risks without weighting these for the relative number of total excess deaths for males and females. The CA EPA assessment also applies common drinking-water consumption rates for males and females, based on South American studies, to all the study populations in the analysis. Other analyses of the Taiwan cancer data apply a significantly larger daily water consumption rate for males in that population. These uncertainties in the CA EPA assessment may tend to overestimate cancer risk in some cases, and underestimate risk in others. The overall effect on the CA EPA unit risk estimate of these various analysis uncertainties is unknown and, therefore, confidence in the assessment is reduced. Therefore, the US EPA IRIS cancer potency factor (1.5 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for inorganic arsenic. The arsenic risk specific dose calculated from this toxicity value is 6.7×10^{-7} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/17/2018) at https://www.canada.ca/en/health-canada/services/environmental-workplace-health/water-quality/drinking-water/canadian-drinking-water-guidelines.html

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/17/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/17/2018) at http://www.tera.org/iter/

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/17/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Arsenic
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Inorganic Arsenic

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
CA EPA REL	0.015	0.46	LOEL	30	Based on decreases in intellectual function and adverse effects on neurobehavioral development in 201 children (10 years of age) exposed each day via drinking water for 9.5 to 10.5 years. A study NOEL was not identified.
US EPA RSL	0.015	--	--	--	US EPA RSL adopted the CA EPA REL reference concentration.
RIVM (2001)	1.0	10	LOEL	10	RIVM decided the most critical effect after chronic inhalation exposure of humans is lung cancer. Study LOEL = 10 mcg/m^3, based on the incidence of lung cancer in smelter workers.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level

LOEL: lowest-observed-effect level; UF: uncertainty factor.

2. Recommendation and Rationale

CA EPA derived their reference concentrations using a LOEL based on decreases in intellectual function and adverse effects on neurobehavioral development in 10-year-old children. The LOEL was identified as a drinking water concentration of arsenic (2.27 mcg/L). CA EPA assumed a water intake of 1 liter/day, essentially complete intestinal absorption, and converted the water concentration to an arsenic absorbed dose of 2.3 mcg/child/day (i.e., 2.3 mcg/child/day = 2.27 mcg/L x 1 L/child/day). CA EPA then converted the daily oral absorbed dose to an equivalent air concentration (0.46 mcg/m^3) assuming a 10-year old boy inhales 9.9 m^3/day and absorbs 50% of the inhaled arsenic (i.e., 0.46 mcg/m^3 = [2.3 mcg/child/day/9.9 m^3/child/day/0.5). CA EPA applied a total uncertainty factor of 30 to compensate for the use of a LOEL (3) and human variation (10) to derive a reference concentration of 0.015 mcg/m^3. The RIVM value is based on a carcinogenic endpoint, which is not relevant in the current context since cancer and non-cancer endpoints are being evaluated separately. Therefore, the CA EPA reference concentration (0.015 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for arsenic.

3. Review Dates

Summary table completion: November, 2004; revised January, 2018
Toxicity value recommendation: December, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/18/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/18/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Arsenic
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Arsenic

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2004)	2.3×10^{-4}	4.3×10^{-3}	Absolute-risk linear model	--	Based on the incidence of lung cancer in males occupationally exposed to arsenic at two different smelters. A geometric mean was estimated for each smelter cohort from 2 or 3 calculated unit risks. The final estimate is the geometric mean of these two values. The increase in age-specific lung cancer mortality rate was assumed to be a function only of cumulative exposure.
Cal EPA (2002)	3.0×10^{-4}	3.3×10^{-3}	Relative risk model	--	Based on lung tumor incidence from human occupational exposure (one of the cohorts used in US EPA IRIS (2004)) and adjusted for interaction with tobacco smoking.
Health Canada (1993)	7.8 reported as TC_{05} [2]; linear equivalent risk specific concentration $= 1.6 \times 10^{-4}$	-- [3]	--	--	Estimated from the standardized mortality ratios for respiratory cancer from one of the same study cohorts as US EPA IRIS (2004).

WHO (2000)	6.6×10^{-4}	1.5×10^{-3}	linearized multistage model	--	WHO reviewed available literature of the incidence of lung cancer in smelter workers and decided that a safe level for inhalation exposure cannot be recommended. At an air concentration of 1 mcg/m^3, an estimate of lifetime risk is 1.5×10^{-3} (based on pooling several unit risk estimates from the cohorts used by US EPA as well as an additional cohort).

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

[2] TC_{05} = The concentration in air (expressed in mcg/m^3) associated with a 5% increase in incidence or mortality due to tumors.

[3] The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported, but would be equal to 1×10^{-6} divided by the 10^{-6} risk-specific concentration.

2. Recommendation and Rationale

The inhalation unit risks and risk specific air concentrations derived by authoritative bodies are all based on increased incidence of lung cancer among workers exposed to arsenic from smelters. All of the estimates fall into a fairly narrow range, with the high and low values differing only by a factor of less than three. Health Canada calculated a TC_{05} which was generated directly from the dose response curve, and is not based on a lower confidence limit. Consequently, the risk specific air concentration derived from this value is not directly comparable to the other risk specific concentrations, which are based on the 95% lower bound air concentrations. The WHO, US EPA and Cal EPA estimates of potency are similar, however, the WHO analysis represents a more updated analysis of previously studied cohorts and includes an additional cohort not used by the US EPA and Cal EPA. Since this value considers a greater amount of the available human data, the WHO unit risk (1.5×10^{-3} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for arsenic. The arsenic risk specific air concentration calculated form this toxicity value is 6.6×10^{-4} mcg/m^3.

3. Review Dates

Summary table completion: November, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2002. Technical Support Document for Describing Available Cancer Potency Factors, December. Sacramento, CA: Office of Environmental Health Hazard Assessment, Air Toxicology and Epidemiology Section, California Environmental Protection Agency.

https://oehha.ca.gov/media/downloads/crnr/tsdcancerpotency.pdf

Health Canada. 1993. Priority Substances List Assessment Report: Arsenic and its compounds: Environment Canada, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/psl1-lsp1/arsenic_comp/index-eng.php#a0

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2000. Air Quality Guidelines (2nd Ed.), Chapter 6.1, Arsenic. World Health Organization, Copenhagen, Denmark. http://www.euro.who.int/__data/assets/pdf_file/0005/74732/E71922.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Barium
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Inorganic Barium

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL* ♦ US EPA ODW*	0.2	63	$BMDL_{05}$ [2]	300	Based on increased incidence of renal lesions in mice exposed each day via drinking water in a 2-year study.
CA EPA PHG	0.07	0.2	NOEL	3	Based on the absence of cardiovascular effects (age-specific mean systolic and diastolic blood pressures, prevalence rates for stroke, heart disease)in an epidemiological study of human populations from two cites with different barium concentrations in the drinking water.
RIVM (2001)	0.02	0.2	NOEL	10	Based on the same study used by CA EPA PHG.
HC DWQ	0.02 [3]	0.2 [3]	NOEL	10	Based on the same study used by CA EPA PHG.
WHO (2011)*	0.02 [4]	0.2 [4]	NOEL	10	Based on the same study used by CA EPA PHG.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2] $BMDL_{05}$: The lower 95% confidence limit on the benchmark dose associated with a 5% increase (above control mean) in the incidence of mice with renal lesions.

[3]A reference dose was not derived. The point of departure and the reference dose were derived from a water concentration assuming a 70 kg person drinks 2 liters of water/day.

[4]A reference dose was not derived. The point of departure and the reference dose were derived from a water concentration assuming a 60 kg person drinks 2 liters of water/day.

NOEL: no-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the various reference doses for barium (except for the US EPA reference dose) is essentially identical with respect to choice of study, species, potential adverse effect, and identification of the point of departure (NOEL = 0.2 mg/kg/day). The NOEL is based on the absence of cardiovascular effects in people drinking water containing barium at approximately 7.3 mg/L. Recently, US EPA IRIS re-evaluated the scientific quality of the study and rejected its use as the basis for their reference dose. US EPA noted that human epidemiological studies have not found evidence of hypertensive effect even at the highest exposure concentrations measured. Thus, US EPA concluded that epidemiological studies do not provide sufficient data to support or refute the hypothesis that chronic barium exposure causes hypertension. In the absence of dose-response data for barium-induced hypertension, US EPA did not consider it scientifically sound to base the reference dose on this effect. All five peer-reviewers of the US EPA reference dose derivation agreed with US EPA decision.

US EPA based their reference dose on the increased incidence of renal lesions in mice exposed via drinking water each day for 2 years. The study was well designed and conducted, and was peer reviewed. The derivation was peer-reviewed, well documented and is consistent with generally accepted risk assessment practices, including the use of benchmark dose modeling and appropriate uncertainty factors to compensate for animal-to-human extrapolation (10), human variation (10), and database deficiencies (3). Therefore, the US EPA reference dose (0.2 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for inorganic barium.

3. Review Dates

Summary table completion: August, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/13/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/13/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/13/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/13/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/13/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/13/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/10/2018) at https://www.who.int/water_sanitation_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Barium
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Barium

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	The absence of carcinogenic effects in several animal studies suggests that barium is not likely to cause cancer in humans.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for barium is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: August, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Division of Drinking Water and Environmental Management

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Barium
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Inorganic Barium

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA HEAST (1997) Also used by: ♦ US EPA Region 3 (2004)	0.5	500 [2]	NOEL	1000	Based on fetotoxicity in rats exposed by inhalation for 4 months. Details on derivation not available.
RIVM (2001)	1	110	NOEL	100	Based on cardiovascular effects in rats exposed via inhalation to insoluble barium carbonate dust for 4 hours per day, 6 days per week, for 4 months. Study LOEL not provided in documentation.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
[2]US EPA HEAST (1997) lists 800 mcg/m^3 as an experimental NOEL but provides no detail on the derivation of the assumed point of departure as implied by the reference concentration and the value of the uncertainty factor.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

Documentation for the derivation of reference concentrations for barium derived by authoritative bodies from the list in item 5 (below) is limited. The available reference concentrations are based on fetotoxicity and cardiac toxicity in subchronic studies in rats, with NOELs being identified for each endpoint. Neither derivation used pharmacokinetic modeling to obtain a human equivalent concentration. Each study was conducted for four months, and the NOEL for fetotoxic effects is about four times higher than the NOEL for cardiac effects. RIVM uses uncertainty factors of 10 each for interspecies and intraspecies extrapolation. Although not clearly documented, the US EPA apparently uses uncertainty factors of 10 each for inter- and intraspecies extrapolation, but also uses an additional uncertainty factor of 10 to extrapolate from a subchronic to a chronic study. The US EPA's use of the subchronic uncertainty factor is consistent with current risk assessment practice and is supported by the

fact that both studies are four months, which is considerably less than lifetime for rats. In addition, due to limited documentation, there is uncertainty about whether the US EPA NOEL is lower than the RIVM LOEL, which would suggest a lower reference concentration that offers a larger margin of exposure against effect levels should be chosen. Therefore, the US EPA reference concentration (0.5 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for barium.

3. Review Dates

Summary table completion: November, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Barium
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Barium

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA (2004)	--	--	--	--	No data on humans and subchronic inhalation studies in animals do not provide evidence of carcinogenicity

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An inhalation unit risk for barium is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: November, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Benz[a]anthracene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Benz[a]anthracene (CAS Number 56-55-3)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
--	--	--	--	--	A reference dose for benz[a]anthracene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

2. Recommendation and Rationale

Benz[a]anthracene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). Reference doses derived from chemical-specific toxicity data are available for six polycyclic aromatic hydrocarbons identified as priority contaminants in the Brownfield Cleanup Program (acenaphthene, anthracene, benzo[a]pyrene, fluoranthene, fluorene, and pyrene, see NYS, 2006). Benz[a]anthracene is chemically similar to each of these six listed polycyclic aromatic hydrocarbons. Each of these six priority contaminants could be used to represent the noncancer toxicity of benz[a]anthracene. Similarity of chemical structure cannot be used as a basis of choosing a chemical surrogate for benz[a]anthracene because toxicity data are insufficient to accurately describe the relationship between the chemical structure and non-cancer toxicity of polycyclic aromatic hydrocarbons. The recommended reference dose for benzo[a]pyrene is lower than that of the other five polycyclic aromatic hydrocarbons. Without data on which of these six polycyclic aromatic hydrocarbons would be the best surrogate for benz[a]anthracene, the recommended reference dose for benzo[a]pyrene (3×10^{-4} mg/kg/day, see Oral Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for benz[a]anthracene.

3. Review Dates

Summary table completion: February, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System
Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
Health Effects Assessment Summary Tables
Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Benz[a]anthracene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Benz[a]anthracene (CAS Number 56-55-3)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ◆ NYS DEC (2017)	1×10^{-5}	0.1	--	--	Based on a relative potency factor of 0.1 applied to the US EPA IRIS benzo[a]pyrene cancer potency factor of 1 $(mg/kg/day)^{-1}$.
CA EPA CPF	8.3×10^{-7}	1.2	--	--	Based on a potency equivalency factor of 0.1 applied to the CA EPA CPF benzo[a]pyrene cancer potency factor of 12 $(mg/kg/day)^{-1}$.
RIVM (2001)	5.0×10^{-5}	0.02 (2)	--	--	Based on a relative potency factor of 0.1 applied to the RIVM benzo[a]pyrene cancer potency factor[2] of 0.2 $(mg/kg/day)^{-1}$.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2]A cancer potency factor was not reported. The derivation directly extrapolates from an experimental dose with significant increased tumor incidence above background to the environmental dose associated with a one-in-ten-thousand risk level; the risk-specific dose is not a lower-bound estimate.

2. Recommendation and Rationale

Benz[a]anthracene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). The cancer potency factors for benz[a]anthracene available from the authoritative bodies listed in item 5 (below) are based on a cancer potency factor for benzo[a]pyrene (also a polycyclic aromatic hydrocarbon) and the application of a relative potency factor for benz[a]anthracene (see Chapter 5.1.5 of NYS (2006) for discussion of relative potency factors). The recommended cancer potency factor for benzo[a]pyrene is 1 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for Benzo[a]pyrene). The benzo[a]pyrene cancer potency factor is multiplied by the recommended relative potency factor of 0.1 for benz[a]anthracene (NYS 2006) to obtain a cancer potency factor of 0.1 per mg/kg/day. This is the toxicity value recommended for

use in the derivation of an oral cancer-based soil cleanup objective for benz[a]anthracene. The benz[a]anthracene risk specific dose calculated from this toxicity value is 1×10^{-5} mg/kg/day.

3. Review Dates

Summary table completion: February, 2004; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (02/13/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (02/13/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (02/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

NYS DEC (New York State Department of Environmental Conservation). 2017. Draft Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Benz[a]anthracene. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (02/13/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benz[a]anthracene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Benz[a]anthracene (CAS Number 56-55-3)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for benz[a]anthracene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Benz[a]anthracene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). A reference concentration based on chemical-specific inhalation toxicity data for benz[a]anthracene is not available from the authoritative bodies listed in item 5 (below).

Benzo[a]pyrene is the only polycyclic aromatic hydrocarbon identified as a priority contaminant in the Brownfield Cleanup Program for which a reference concentration is available. Benzo[a]pyrene is chemically similar to benz[a]anthracene and can be used to represent its noncancer inhalation toxicity (see Inhalation Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene). Therefore, based on using benzo[a]pyrene as a chemical surrogate, a reference concentration of 2×10^{-3} mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benz[a]anthracene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (02/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry

California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benz[a]anthracene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Benz[a]anthracene (CAS Number 56-55-3)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2009)	9.1×10^{-3}	1.1×10^{-4}	--	--	Based on the CA EPA unit risk for benzo[a]pyrene (which is derived from the increased incidence of respiratory tract tumors in hamsters exposed by inhalation) and application of a potency equivalency factor of 0.1.
US EPA IRIS	1.6×10^{-2}	6×10^{-5}	--	--	Based on application of a relative potency factor of 0.1 to the US EPA IRIS unit risk for benzo[a]pyrene, which is derived from the same study used by CA EPA

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} air concentration), where 1×10^{-6} concentration = 1×10^{-6} / inhalation unit risk.

2. Recommendation and Rationale

The unit risk values for benz[a]anthracene are based on benzo[a]pyrene and the application of relative potency factors. The recommended unit risk value for benzo[a]pyrene is 6×10^{-4} per mcg/m^3 (see Inhalation Cancer Toxicity Value Documentation for benzo[a]pyrene). Application of the recommended relative potency factor (0.1) for benz[a]anthracene to the unit risk for benzo[a]pyrene yields a unit risk of 6×10^{-5} per mcg/m^3, which is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for benz[a]anthracene (see Chapter 5.1.5 of technical support document [NYS 2006] for discussion of recommended relative potency factors). The benz[a]anthracene risk specific air concentration calculated from this toxicity value is 1.6×10^{-2} mcg/m^3.

3. Review Dates

Summary table completion: November, 2004; revised January, 2018
Toxicity value recommendation: December, 2004; revised January, 2018

4. References for Summary Table

CA EPA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2009. Technical Support Document for Cancer Potency Factors 2009. Appendix B: Chemical-Specific Summaries of the Information Used to Derive Unit Risk and Cancer Potency Values. Last accessed (02/9/2018) at http://oehha.ca.gov/air/crnr/technical-support-document-cancer-potency-factors-2009.

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (02/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (02/13/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System
Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
    Health Effects Assessment Summary Tables
    Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Benzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Benzene (CAS Number 71-43-2)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW	4×10^{-3}	1.2	$BMDL_{1sd}$	300	Based on route-to-route extrapolation of the results of benchmark dose modeling of decreased lymphocyte counts in male and female workers exposed by inhalation for an average of 6.4 years. Study LOEL = 1.2 mg/kg/day (adjusted for continuous exposure and route extrapolation).
NYS DEC (1997)	7.1×10^{-4}	0.71	NOEL	1000	Based on hematological effects (leukopenia and erythrocytopenia) in female rats in a six month gavage study. Study LOEL = 35.7 mg/kg/day.
ATSDR*	5×10^{-4}	0.014	$BMDL_{0.25sd}$	30	Based on route-to-route extrapolation of the results of benchmark dose modeling of decreased B-cell counts in male and female workers exposed by inhalation for an average of 6.1 years. Study LOEL = 0.074 mg/kg/day (adjusted for continuous exposure and route extrapolation).
CA EPA PHG*	8.7×10^{-3}	0.087	NOEL	10	Based on route-to-route extrapolation of air monitoring data for workers exposed by inhalation for up to 21 years without signs of blood cell effects or increased leukemia mortality.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.

$BMDL_{xsd}$: 95% lower confidence limit on dose corresponding to an "x" standard deviation change from the mean background response; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during an update of fact sheets to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The NYS DEC derived its reference dose based on hematological effects in a subchronic gavage study in rats, while the US EPA and ATSDR derived reference doses based on route-to-route extrapolation of air concentrations resulting in blood changes in humans exposed by inhalation in the workplace. The CA EPA PHG assessment was also based on route-to-route extrapolation of an occupational exposure study. The CA EPA study used retrospective analysis of routine worker surveillance data, rather than prospective monitoring, and the reported NOEL is higher than the LOEL air level observed in the prospective ATSDR study. Therefore, the CA EPA PHG study is not preferred as the basis for the reference dose. The US EPA and ATSDR derivations use benchmark dose modeling that is consistent with current risk assessment practice. In addition, the US EPA and ATSDR values are based on high-quality human data which is preferred in this case, even though the animal data are route specific. The ATSDR assessment is based on higher quality occupational epidemiology data than the US EPA IRIS assessment, as the ATSDR study assessed workplace exposure with multiple air samples collected over 16 months and had an exposed study population size of 250. The US EPA IRIS study involved workplace air sampling over a two-week period and had an exposed population size of 44. The ATSDR study observed a lower LOEL exposure level than did the study used by US EPA IRIS, suggesting that a more sensitive endpoint was used for the ATSDR assessment. The resulting ATSDR point of departure is lower than the US EPA IRIS point of departure, despite ATSDR's use of a somewhat less conservative benchmark response (0.25 sd below the control mean, rather than 1 sd). ATSDR noted that, at the benchmark response of 0.25 sd below the control mean, the benchmark dose was slightly below the mean exposure level in the lowest exposure group, making this an appropriate choice. US EPA IRIS applied a total uncertainty factor to the BMDL of 300, including 10-fold to account for human variability, and 3-fold each to account for use of a benchmark dose considered equivalent to a minimal LOEL, a subchronic mean exposure duration and database deficiencies due to the lack of a 2-generation reproductive study and lack of developmental toxicity studies. ATSDR applied a total uncertainty factor of 30, including 10-fold to account for human variability and 3-fold to account for uncertainty due to route-to-route extrapolation. The two assessments are of similar quality, but the ATSDR assessment is based on a more sensitive study with a much larger study population. Therefore, the ATSDR reference dose (5×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer soil cleanup objective for benzene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: April, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/12/2018) at https://www.atsdr.cdc.gov/mrls/index.asp, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/12/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Benzene. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/12/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/12/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/12/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Benzene (CAS Number 71-43-2)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS* Also used by: ♦ US EPA RSL	1.8×10^{-5} to 6.7×10^{-5}	0.015 to 0.055	linear extrapolation models, based on maximum likelihood relative risks with cumulative dose	--	Benzene is a known human carcinogen based on epidemiology studies that provide clear evidence of a causal association between benzene exposure in the workplace and acute nonlymphocytic leukemia. The cancer potency factors were derived from a range of inhalation unit risks derived from a study of occupationally exposed workers by assuming an inhalation rate of 20 m^3/day, an adult body weight of 70 kg, and 50% and 100% absorption via inhalation and ingestion, respectively. The range reflects different exposure assessments and dose-response models applied to data from one cohort study.
NYS DEC (1997)	3.4×10^{-5}	0.029	linear extrapolation models, based on maximum likelihood relative risks with cumulative dose	--	The cancer potency factor is derived from the geometric mean of the high and low maximum likelihood estimates of cancer potency from US EPA IRIS.

CA EPA PHG	1×10^{-5}	0.1	weighted cumulative dose relative risk model and lifetable analysis	--	Based on the mean of upper-bound risk estimates from two occupational inhalation cohort studies, including the same study used by US EPA IRIS, but using a different model to estimate unit risks The cancer potency factor was derived by assuming an inhalation rate of 20 m3/day, an adult body weight of 70 kg, and 50% and 100% absorption via inhalation and ingestion, respectively.
HC DWQ*	7.9×10^{-6} to 1.0×10^{-5}	--[2]	--	--	A range of drinking-water unit risks was reported based on the CA EPA PHG assessment and using 3.5 L per day drinking water equivalent exposure from all routes.
WHO (2011)*	2.9×10^{-5}	--[3]	--	--	Based on the inhalation unit risk for leukemia from occupational studies. Details of assessment are not provided, but the reported drinking water risk-specific guideline concentrations are the same as the risk-specific concentrations in US EPA IRIS that reflect the upper-end of the cancer potency factor range.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

[2]No cancer potency factor was derived. The range of risk specific doses was obtained from the drinking water unit risks of 4.8×10^{-6} to 6.3×10^{-6} per microgram per liter, assuming a 70 kg person has exposure from all routes equivalent to drinking 3.5 liters of water per day.

[3]No cancer potency factor was derived. The risk specific dose was obtained from the drinking water unit risk of 1×10^{-6} per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day.

*Agency's toxicity value added or revised during an update of fact sheets to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The various oral cancer potency factors for benzene are all based on the increased incidence of leukemia in occupationally exposed workers breathing benzene, and on a route-to-route extrapolation from inhalation unit risk values derived from the occupational studies. The US EPA IRIS and CA EPA PHG each derived inhalation unit risks from separate analyses of occupational inhalation data and then

calculated oral cancer potency factors by assuming an inhalation rate of 20 m^3/day, an adult body weight of 70 kg, and 50% and 100% absorption via inhalation and ingestion, respectively. The other assessments in the table above are either based directly on, or are equivalent to, the US EPA IRIS assessment (NYS DEC, WHO) or are based directly on the CA EPA PHG assessment (HC DWQ).

The CA EPA PHG assessment of the inhalation unit risk for benzene was preferred over the US EPA IRIS assessment due to the use by CA EPA of more data from a second, much larger occupational cohort (in addition to the cohort used by US EPA), the modeling of leukemia incidence in the entire general population rather than mortality only in a sub-set of the general population, and by the use of upper-bound estimates of cancer risk from the dose-response models, rather than maximum-likelihood values. The CA EPA PHG oral cancer potency factor obtained by route-to-route extrapolation from the CA EPA PHG inhalation unit risk is therefore also preferred. The CA EPA PHG cancer potency factor ($0.1\ (mg/kg/day)^{-1}$) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for benzene. The benzene risk-specific dose calculated from this toxicity value is 1×10^{-5} mg/kg/day.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: May, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (06/10/2015) at http://www.oehha.ca.gov/water/phg/allphgs.html.

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (06/10/2015) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Benzene. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (06/10/2015) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (06/10/20151) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (06/10/2015) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html, with supporting documentation at http://www.who.int/water_sanitation_health/dwq/chemicals/en/index.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
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New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Benzene (CAS Number 71-43-2)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL	30	8.2×10^3	$BMCL_{ADJ-1SD}$	300	Based on decreased B-lymphocyte cell count in a human study of 44 exposed workers and 44 matched controls where exposure duration ranged from 0.7 to 16 years (mean = 6.3 years). $LOEL_{ADJ}$ = 24,300 mcg/m^3 ($LOEL_{OCCUP}$) x 10 $m^3/20\ m^3$ x 5 days/7 days = 8700 mg/m^3.
ATSDR*	10**	96	$BMCL_{ADJ-0.25SD}$	10	Based on decreased B-lymphocyte counts in a study of 250 male and female workers exposed by inhalation for an average of 6.1 years and 140 matched controls. $LOEL_{ADJ}$ = 1820 mcg/m^3 ($LOEL_{OCCUP}$) x 8 hours/24 hours x 6 days/7 days = 520 mg/m^3.
CA EPA REL*	3	652	$BMCL_{ADJ-0.5SD}$	200	Based on same study and effects as ATSDR. $LOEL_{ADJ}$ = 1820 mcg/m^3 ($LOEL_{OCCUP}$) x 10 $m^3/day/20\ m^3/day$ x 6 days/7 days = 780 mcg/m^3.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

ppm: parts per million in air (1 ppm benzene = 3190 mcg/m^3); $BMCL_{ADJ-xsd}$: 95% lower confidence limit on adjusted concentration corresponding to an "x" standard deviation change from the mean background response; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

**The ATSDR value is reported as 0.003 parts per million (ppm). For benzene, 1 ppm = 3.19 mg/m^3.

2. Recommendation and Rationale

The reference concentrations for benzene derived by authoritative bodies from the list in item 5 (below) are based on hematological effects in studies of workers exposed to benzene. The US EPA IRIS estimated a lower bound on a benchmark concentration associated with a one standard-deviation reduction below the control mean absolute lymphocyte count in a two-week study of 44 exposed workers. The ATSDR and CA EPA estimated lower bounds on benchmark air concentrations associated with a 0.25 and 0.5 standard-deviation reduction, respectively, on the control mean B-lymphocyte count in a study of 250 exposed workers. The ATSDR and CA EPA assessments are based on higher quality occupational epidemiology data than the US EPA IRIS assessment. The study used by ATSDR and CA EPA assessed workplace exposure with multiple air samples collected over a longer period of time (16 months compared to two weeks) and had a larger exposed study population size (250 compared to 44) than the study used by US EPA IRIS The study used by ATSDR and CA EPA also observed effects at a lower benzene air concentration than did the study used by US EPA IRIS, suggesting a more sensitive toxicological endpoint. Therefore, the US EPA derivation will not be considered further.

The difference between the points of departure for the ATSDR and CA EPA derivations is the choice of a BMCL associated with a 0.25 or 0.5 standard-deviation reduction, respectively, of the control mean B-lymphocyte counts. Using the BMCL based on the 0.25 standard-deviation reduction is a somewhat more conservative approach since it characterizes a smaller change from the mean as an adverse effect. The ATSDR and CA EPA derivations also apply different uncertainty factors to the points of departure to obtain their reference concentrations. ATSDR used a total uncertainty factor of 10 to account for human variability, but did not use an uncertainty factor to account for the use of a less than lifetime study in humans (i.e., an average of 6.1 years of exposure out of a 70-year lifetime). We disagree with this decision, and note that both US EPA and CA EPA used and uncertainty factor to compensate for a less-than-lifetime exposure. CA EPA applied a total uncertainty factor of 200 to its point of departure, including a factor of 3 for use of a less than lifetime study, and a combined intraspecies (human variability) uncertainty factor of 60. CA EPA supported their uncertainty factor with benzene-specific toxicity data. The primary reasons given for the intraspecies uncertainty factor were 1) evidence for significant benzene toxicokinetic variation in the adult human population, 2) uncertainties related to toxicokinetic differences between adults (the subjects of the critical study) and children, and 3) uncertainties related to toxicodynamic differences between adults and children. A specific rationale for the value of 60 was not provided, other than to state it is twice the default intraspecies uncertainty factor used by CA EPA's Office of Environment Health Hazard Assessment. The two assessments are of similar quality, although we have more confidence in the magnitude of uncertainty factor used by CA EPA than by ATSDR. We also noted that reference concentration derived by CA EPA is slightly lower (and more health protective) than that derived by ATSDR. Therefore, the CA EPA reference concentration (3 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer soil cleanup objective for benzene.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/21/2018) https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Appendix D. Individual Acute, 8-Hour, and Chronic Reference Exposure Level Summaries Last accessed (01/10/2018) at http://oehha.ca.gov/air/hot_spots/2008/AppendixD1_final.pdf.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/10/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/10/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Benzene (CAS Number 71-43-2)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ♦ US EPA RSL	0.13 to 0.45	2.2×10^{-6} to 7.8×10^{-6}	low-dose linearity	--	Based on the incidence of leukemia in several studies of the Pliofilm occupational cohort. Unit risks are maximum likelihood estimates and based on several estimates of benzene exposure.
CA EPA PHG * Also used by: ♦ CA EPA (2011) [2]	0.064 [(3)]	1.6×10^{-5} (0.05/ppm)	weighted cumulative dose relative risk model & lifetable analysis	--	Based on the mean of upper-bound risk estimates from the Pliofilm and Chinese Worker cohorts. CA EPA PHG used a different model than US EPA IRIS to estimate unit risks from each occupational cohort.
CA EPA CPF	0.03	2.9×10^{-5} [(4)]	linear non-threshold model for human data; linearized multistage model for animal data	--	Selected from a range of values based on human occupational studies a (including the same data used by US EPA IRIS) and oral and inhalation animal bioassay data. The selected value is an upper bound estimate from human data.
WHO (2000)	0.17	6.0×10^{-6}	multiplicative risk model, cumulative exposure	--	Based on the geometric mean of several estimates of the excess lifetime risk of leukemia at an air concentration of 1 mcg/m^3 derived from two studies of the Pliofilm occupational cohort.

RIVM (2001)	0.2	-- [5]	--	--	Based on direct adoption of the lower end of the range of risk-specific concentrations developed by the EU Working Group evaluation for ambient air. This value is also the WHO risk-specific concentration rounded to one significant digit. Limited derivation information available.
HC PSAP	1.5×10^4 reported as a TC_{05}; linear equivalent risk specific concentration = 0.3	-- [5]	--	--	The Health Canada TC_{05} estimate was based on a study of the Pliofilm cohort in which the observed and expected numbers of deaths due to leukemia were small and for which there were few actual measurements of benzene concentrations in the workplace.

[1] The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2] CA EPA (2011) gives the "safe harbor" inhalation intake at 10^{-5} lifetime risk as 13 mcg/d, which results in an inhalation unit risk of 1.54×10^{-5} $(mcg/m^3)^{-1}$. The slight difference is due to rounding.

[3] Applying an assumption of 50% absorption by inhalation to this value would make it equivalent to the CA EPA CPF risk-specific concentration.

[4] The unit risk is presented as equivalent to a cancer potency factor obtained via route-to-route extrapolation of 0.1 $(mg/kg/d)^{-1}$. This implies that the relative bioavailabilities by the oral and inhalation routes were assumed to both be 100%. Other assessments (including more recent CA EPA assessments) assume inhalation bioavailability is 50% of oral bioavailability.

[5] The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported but would be equal to 1×10^{-6} divided by the 10^{-6} risk-specific concentration.

ppm: parts per million in air (1 ppm benzene = 3190 mcg/m^3); TC_{05} = The concentration in air (expressed in mcg/m^3) associated with a 5% increase in incidence or mortality due to tumors (the TC_{05} represents a maximum likelihood estimate rather than a lower-bound estimate).

*Agency's toxicity value added or revised during an update of fact sheets to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The unit risks and/or risk-specific concentrations derived by authoritative bodies are largely based on the increased incidence of leukemia in human occupational studies. One of the CA EPA derivations also included risk-specific concentrations based on increased incidence of tumors at several anatomical sites (including leukemias) in mice and rats exposed orally or by inhalation. All the analyses apply some form of linear-low dose extrapolation model to the dose-response data, assuming a non-threshold mode of action for the cancers observed in the occupational cohorts and in animal studies. The range of unit risk estimates based on human studies stems from differences in the exact form of the selected high-to-low dose extrapolation model and in the assumptions used to estimate occupational exposures.

US EPA IRIS obtained a range of unit risk values based on a published assessment of an occupational cohort (the "Pliofilm" cohort) that derived 96 separate unit risk estimates reflecting differences in disease endpoints, dose-response modeling assumptions, and different published exposure assessments for the cohort. Based on limited understanding of the mode of action for benzene-induced hematopoietic tumors (e.g., leukemias), US EPA restricted the analysis to results from linear models to obtain the range of unit risks reported in IRIS. The US EPA IRIS unit risks are maximum-likelihood estimates and are based on lifetable analysis of leukemia mortality rates for the U.S. population.

CA EPA PHG derived an inhalation unit risk from Pliofilm cohort data using some of the same exposure assessment data used by US EPA IRIS and similar dose-response modeling approaches. However, the CA EPA PHG analysis estimated upper-bound unit risks, rather than the maximum-likelihood estimates. CA EPA PHG also obtained an upper-bound unit risk estimate from a second larger occupational cohort (the "Chinese Worker" cohort). The CA EPA PHG analysis applied leukemia incidence rates from both cohorts to life-table analysis based on the entire California population (all races and both sexes) to estimate population-wide excess risk of developing leukemia from low-level benzene exposure. CA EPA PHG states that this approach differs from nearly all previous assessments (including the US EPA IRIS assessment) that used white males as the target population for lifetable analysis.

The CA EPA CPF value is the upper 95% confidence bound estimate from the analysis of human data (the Pliofilm occupational cohort) considered most credible by US EPA IRIS, and was recommended as the unit risk (originally equated to an inhalation cancer potency factor of 0.1 per mg/kg/d for the California Proposition 65 program in 1988. More recent values from the Proposition 65 program for the benzene inhalation cancer potency and corresponding benzene inhalation unit risk (CA EPA 2011) are reduced by a factor of about two from the earlier CA EPA CPF value. Although the difference is not clearly documented, recent US EPA and CA EPA assessments of benzene absorption by different exposure routes indicate that the inhalation absorption fraction is approximately 50% (rather than 100% as assumed by CA EPA CPF). This different absorption fraction would account for the lower unit risk in CA EPA (2011) and, if applied to the CA EPA CPF unit risk value, would make it essentially equal to the CA EPA PHG unit risk value.

The WHO value is the geometric mean of a range of unit risks based on two studies of the Pliofilm occupational cohort. The RIVM risk-specific concentration was selected from the lower end of a range of risk-specific concentration values derived by the EU Working Group, but details of the derivation are not available. HC PSAP's value is based on the Pliofilm cohort and is a TC_{05} maximum likelihood value that, when extrapolated linearly to 1×10^{-6} lifetime risk, would results in a risk-specific concentration within the range reported by US EPA IRIS.

US EPA IRIS noted that all epidemiological studies considered in its benzene assessment have some methodological limitations such as confounding exposures. US EPA IRIS asserts that limitations in all studies (including the Chinese Worker cohort) but one (i.e., the Pliofilm cohort) preclude their use in quantitative cancer risk assessment. CA EPA PHG noted limitations with use of the "Chinese Worker" cohort data for dose-response modeling and chose to focus on a cohort subset with more reliable exposure information. Despite these limitations, the unit risks derived by CA EPA PHG based on the data from the two cohorts are fairly close (0.044 and 0.056 ppm^{-1}; equivalent to 1.4×10^{-5} and 1.8×10^{-5} per mcg/m^3, respectively) and their recommended unit risk is the mean of the two unit risks.

The US EPA IRIS and CA EPA PHG assessments are both based on robust analyses of occupational cohort data that have been extensively investigated by multiple authors in the peer-reviewed literature.

They are thus preferred over the CA EPA CPF, WHO, RIVM and HC PSAP assessments. The CA EPA PHG assessment improves on the US EPA assessment by incorporating more data from a second, much larger occupational cohort, by modeling leukemia incidence in the entire general population rather than mortality only in a subset of the general population, and by using upper-bound estimates of cancer risk from the dose-response models, rather than maximum-likelihood values. Therefore, the CA EPA PHG unit risk (1.6×10^{-5} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for benzene. The benzene risk specific air concentration calculated from this toxicity value is 0.064 mcg/m^3.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2011. Proposition 65 Safe Harbor Levels: no significant risk levels for carcinogens and maximum allowable dose levels for chemicals causing reproductive toxicity, September 2011. Last accessed (06/15/2015) at. http://oehha.ca.gov/prop65/pdf/Sept2011Status.pdf

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Adoption of the Revised Air Toxics Hot Spots Program Technical Support Document for Cancer Potency Factors. Last accessed (06/15/2015) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (06/15/2015) at http://www.oehha.ca.gov/water/phg/allphgs.html.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (06/15/2015) at http://www.hc-sc.gc.ca/ewh-semt/contaminants/existsub/eval-prior/index-eng.php

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (06/15/2015) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (06/15/2015) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (06/15/2015) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

WHO (World Health Organization). 2000. Air Quality Guidelines for Europe. Last accessed (06/15/2015) at http://www.euro.who.int/en/what-we-publish/abstracts/air-quality-guidelines-for-europe.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
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- Office of Superfund Remediation and Technology Innovation
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  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[a]pyrene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Benzo[a]pyrene (CAS Number 50-32-8)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
CA EPA PHG*	1.7×10^{-3}	5	LOEL	3000	Based on increased kidney abnormalities (e.g., tubular casts) in male rats exposed via the diet in a 90-day study at the lowest dose tested.
US EPA IRIS ◆ Also used by: NYS DEC (2017)	3×10^{-4}	0.092	$BMDL_{1SD}$ [3]	300	Based on neurobehavioral changes in rats exposed by gavage on postnatal days 5 to 11. Study NOEL = 0.2 mg/kg/day; Study LOEL = 2 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.
[2]The HED_{LOEL} is the human equivalent dose at which the human internal dose equals the rat internal dose at the rat lowest-observed-effect level. The human equivalent dose was obtained from the lowest-observed-effect level through [body weight]$^{3/4}$ interspecies scaling. The lowest-observed-effect level was adjusted by a factor of $(0.18 \text{ kg}/80 \text{ kg})^{0.25}$, or 0.22.
[3]The $BMDL_{1SD}$ is the 95% lower confidence limit on benchmark dose (BMD) corresponding to a change in the mean equal to one standard deviation (SD) of the control mean.
LOEL: lowest-observed-effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The available reference doses for benzo(a)pyrene are derived by the CA EPA and the US EPA. The CA EPA reference dose for benzo[a]pyrene is based on kidney effects in a 90-day dietary study in rats. CA EPA used a LOEL as the point of departure, and applied a total uncertainty factor of 3000, which is the maximum uncertainty factor used by the agency, although the assigned individual uncertainty factors (10 each for use of a LOEL, use of a subchronic study, inter- and intraspecies extrapolation) resulted in a total uncertainty factor of 10,000. The US EPA IRIS based its reference dose on a study that reported developmental effects (neurobehavioral changes persisting into adulthood as indicated by altered responses in three behavioral tests) in rats exposed by gavage on postnatal days 5 to 11. A total uncertainty factor of 300 (10 each for inter- and intraspecies extrapolation and 3 for database deficiencies) was applied to a benchmark response level (a $BMDL_{1SD}$) to obtain the reference dose. The US EPA IRIS did not use body weight scaling to account for pharmacokinetic interspecies differences based on concerns that this scaling, which is derived from data in adult animals, may not be valid when extrapolating doses in neonatal animals.

The US EPA IRIS derivation used a study that reported statistically significant neurodevelopmental effects at a lower effect level (0.02 mg/kg-day) than the LOAEL for kidney effects (5 mg/kg-day), which was the basis of CA EPA's reference dose. US EPA also selected a benchmark dose, rather than a LOAEL, as the point of departure. Both choices (i.e., selection of the lowest effect level from available studies and use of benchmark doses rather than point estimates, when possible) are generally preferred risk assessment practices. The study used by the US EPA evaluated a sensitive toxicological endpoint in rats exposed during a critical stage of development, and the relevance of such effects to humans is supported by several epidemiology studies that associate PAH exposure with reduced growth and development. Therefore, the US EPA IRIS reference dose (3×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for benzo[a]pyrene.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/13/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

NYS DEC (New York State Department of Environmental Conservation). 2017. Draft New York State Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Benzo(a)pyrene. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/13/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary) Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[a]pyrene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Benzo[a]pyrene (CAS Number 50-32-8)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ◆ NYS DEC (2017)	1×10^{-6}	1	time-to-tumor model (multistage Weibull model)	$BW^{3/4}$ (2)	Based on the increased incidence of tumors of the forestomach, esophagus, tongue and larynx in female mice exposed in the diet for two years
CA EPA CPF	8.3×10^{-8}	12	linearized multistage model	not specified, but parallel inhalation analysis used body surface area[3] scaling	Based on increased incidence of squamous cell papillomas and carcinomas of the forestomach in mice exposed in the diet for varying lengths of time ranging from 70 to 197 days.
WHO (2011)	2.2×10^{-6}	0.46	two-stage birth-death mutation model	body weight[4]	Based on increased incidence of forestomach tumors in the same feeding study in mice used by CA EPA CPF
CA EPA PHG	5.9×10^{-7}	2.9 (5) (1.7)	time-to-tumor model (multistage-in-dose Weibull-in-time model)	$BW^{¾}$ (2)	Based on the increased combined incidence of tumors of the esophagus, forestomach or tongue in mice from the same two-year study used by US EPA IRIS.
RIVM (2001)	5.0×10^{-6}	--[6]	linear extrapolation from the TD_{LO}(7)	body weight[4]	Based on tumor development in a variety of organs and tissues in an oral (gavage) rat study (limited methodology information available).

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10^{-6} dose), where 1 x 10^{-6} dose = 1 x 10^{-6}/cancer potency factor.
[2]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$.
[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.
[4]Factor for dose adjustment from animals to humans is 1.
[5]The CA EPA PHG recommended cancer potency factor is 2.9 (mg/kg/day)$^{-1}$, which reflected the use of age-dependent adjustment factors to compensate for the increased sensitivity of children to the carcinogenic effects of benzo[a]pyrene. It was calculated by multiplying the standard cancer potency factor (1.7 (mg/kg/day)$^{-1}$) by a CA EPA calculated adjustment factor of 1.7 [i.e., 1.7 (mg/kg/day)$^{-1}$ x 1.7 = 2.9 (mg/kg/day)$^{-1}$)]. In the Brownfields Cleanup Program, however, this adjustment is made using a different approach, which uses the standard cancer potency factor. Thus, we used 1.7 (mg/kg/day)$^{-1}$ instead of 2.9 (mg/kg/day)$^{-1}$ as the cancer potency factor for CA EPA PHG, and to calculate the risk specific dose.
[6]A cancer potency factor was not reported. The derivation directly extrapolates from an experimental dose with significant increased tumor incidence above background to the environmental dose associated with a one-in-one million risk level; the risk-specific dose is not a lower-bound estimate.
[7]TD_{LO} = The lowest experimental (toxic) dose that produces a significant increase in tumor incidence above background incidence.

2. Recommendation and Rationale

The cancer potency factors for benzo[a]pyrene derived by the CA EPA CPF and WHO are based on a mouse dietary study that is clearly inferior in design to more recent studies on which the cancer potency factors derived by US EPA IRIS, CA EPA PHG, and RIVM are based. Major limitations of the study included the use of groups composed of both males and females, variable group sizes, benzo[a]pyrene administration beginning at different ages for different groups, and variable treatment (and less-than-chronic) dosing periods. The RIVM derivation was based on a chronic gavage study in rats, and it is likely that the pharmacokinetics and pharmacodynamics of mutagenic carcinogens such as benzo[a]pyrene differ greatly between dietary doses and gavage doses, particularly when the site of contact is the site of cancer. Since dietary doses are more likely to mimic human oral exposures at Brownfield sites than gavage doses, they are preferable to use as a basis to derive soil cleanup objectives for benzo[a]pyrene. Moreover, RIVM's derivation procedure does not produce a lower-bound estimate on the risk-specific dose and is not consistent with generally accepted risk assessment practice for animal-to-human extrapolations.

The US EPA IRIS and CA EPA PHG derivations are based on a two-year mouse dietary study, and are consistent with generally accepted risk assessment practice. Both use the currently recommended animal-to-human extrapolation method ($BW^{3/4}$) and a time-to-tumor model to obtain the lower confidence limit on a 10% benchmark response. The resulting potency values from the benchmark responses are numerically similar (1.4 per mg/kg/day and 1.7 per mg/kg/day for US EPA IRIS and CA EPA PHG, respectively). The US EPA IRIS derivation includes larynx tumors (in addition to tumors of the forestomach, esophagus and tongue), while the CA EPA PHG derivation does not. Accordingly, the US EPA IRIS derivation may represent a slightly more robust evaluation of the carcinogenic potential of benzo[a]pyrene on the alimentary canal since it includes additional relevant tumor sites. Further, the documentation for US EPA IRIS derivation is peer-reviewed by independent expert scientists, and is extensively documented, which facilitates evaluation of the methods used. Therefore, the US EPA IRIS cancer potency factor, 1 per mg/kg/day, is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for benzo[a]pyrene. The benzo[a]pyrene risk specific dose calculated from this toxicity value is 1 x 10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/19/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/19/2018) at http://www.oehha.ca.gov/water/phg/allphgs.html.

NYS DEC (New York State Department of Environmental Conservation). 2017. Draft Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Benzo[a]pyrene (BaP). Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/19/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/19/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html, with supporting documentation at http://www.who.int/water_sanitation_health/dwq/chemicals/en/index.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
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- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[a]pyrene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Benzo[a]pyrene (CAS Number 50-32-8)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS	2×10^{-3}	4.6	HEC_{LOEL}[2]	3000	Based on decreased fetal survival in rats exposed by inhalation for 4 hours per day on gestation days 11 to 20.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

[2]The HEC_{LOEL} is the human equivalent air concentration at which the human internal dose equals the rat internal dose at the rat lowest-observed-effect level. The human equivalent air concentration was obtained from the lowest-observed-effect level (25 mcg/m^3) by multiplying it by an adjustment factor for non-continuous exposure (0.17) and by a dosimetric adjustment factor of 1.1 (see text below).

LOEL: lowest-observed-effect level; UF: uncertainty factor

2. Recommendation and Rationale

The US EPA reference concentration for benzo(a)pyrene is the only available value from an authoritative body listed in item 5 (below). The reference concentration is based on decreased fetal survival in the offspring of rats exposed during gestation. The lowest experimental exposure level (25 mcg/m^3) was identified as the LOEL. A human equivalent air concentration was obtained from the experimental exposure by a two-step process. First, the non-continuous experimental exposure level was converted to a continuous environmental exposure level (4.2 mg/m^3) using time weighting (25 mcg/m^3 x 4 hours exposure per day/24 hours per day = 4.2 mg/m^3). Then, a human equivalent concentration (4.6 mc/m^3) was calculated by multiplying the animal time-weight-average level by a regional deposited dose ratio of 1.1, which represent an animal-to-human dosimetric adjustment factor for the extra-respiratory (i.e., systemic) effects of benzo[a]pyrene (4.2 mcg/m^3 x 1.1 = 4.6 mcg/m^3) (US EPA 1994). A total uncertainty factor of 3000 (10 for use of a LOEL, 3 for interspecies extrapolation, 10 for interspecies extrapolation, and 10 for database deficiencies) was applied to the human equivalent concentration to obtain the reference concentration. The derivation is well-documented and peer-reviewed and is consistent with generally accepted risk assessment practices for high to low dose and animal to human extrapolations. Therefore, the US EPA reference concentration (2×10^{-3} mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benzo(a)pyrene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table

US EPA (United States Environmental Protection Agency). 1994. Methods for derivation of inhalation reference concentrations and application of inhalation dosimetry [EPA Report] (pp. 1-409). (EPA/600/8-90/066F). Research Triangle Park, NC: U.S. Environmental Protection Agency, Office of Research and Development, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office. Last accessed (01/19/2018) at https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=71993&CFID=51174829&CFTOKEN=25006317.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
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  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[a]pyrene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Benzo[a]pyrene (CAS Number 50-32-8)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
WHO (2000)	1.12×10^{-5}	8.7×10^{-2}	linearized multistage model, extra risk	--	Based on the increased incidence of lung cancer in workers exposed to coke-oven emissions, assuming the benzo(a)pyrene content of coke oven emissions is 0.71%.
Health Canada (1994) (see also TERA, 2004)	1.6×10^3 reported as TC_{05} [2]; linear equivalent risk specific concentration = 0.032	-- [3]	linearized multistage model, extra risk	not specified	Based the increased incidence of respiratory tract tumors in hamsters exposed by inhalation for 4.5 hours per week, for 7 days a week for the first 10 weeks, then 3 hours per day for the remaining 96 weeks.
Cal EPA (2009)	9.1×10^{-4}	1.1×10^{-3}	linearized multistage model, extra risk	body surface area[4]	Based on the same inhalation study used by Health Canada (1994)
NYS DOH (1990)	1.7×10^{-3}	6×10^{-4}	linearized multistage model, extra risk	body surface area[4]	Based digestive tract and respiratory tract tumors in hamsters in the same inhalation study used by Health Canada (1994).
US EPA IRIS	1.6×10^{-3}	6×10^{-4}	multistage time to tumor Weibull model	equal risk assumed at equal air concentrations	Based on the same inhalation study used by Health Canada (1994).

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10^{-6} air concentration), where 1 x 10^{-6} concentration = 1 x 10^{-6} / inhalation unit risk.
[2] TC_{05} = The concentration in air (expressed in mcg/m^3) associated with a 5% increase in incidence or mortality due to tumors.
[3]No cancer potency factor was derived. The risk specific air concentration was obtained by linear extrapolation from the modeled TC_{05} (TERA, 2004).
[4] Factor for dose adjustment from animal to human is (human body weight/animal body weight)$^{0.33}$.

2. Recommendation and Rationale

The inhalation unit risks derived by authoritative bodies from the list in item 5 (below) are based on increased incidence of lung, respiratory tract, and digestive tract tumors observed in animal and human studies.

The WHO unit risk is based on the incidence of lung cancer in an epidemiology study of workers exposed to coke-oven emissions, assuming 0.71% of the content was benzo[a]pyrene. However, coke oven emissions are a complex mixture of chemicals, and the contribution of the chemicals other than benzo(a)pyrene to the observed increased incidence in lung cancer is not known. Thus, this study is not chosen for deriving a quantitative estimate of cancer potency for benzo[a]pyrene.

Health Canada, Cal EPA, NYS DOH and the US EPA IRIS base their values on the same inhalation study in hamsters. Health Canada derived a $TC_{05,}$ which cannot be directly compared to the other estimates because it represents the maximum likelihood estimate on the risk-specific air concentration rather than a 95% lower bound, and therefore this value was not considered further.

The unit risk estimates derived by the Cal EPA, NYS DOH and US EPA IRIS are numerically similar. The Cal EPA and NYS DOH derivations omit results from the highest exposure group due to a high incidence of mortality and use body surface area to scale the animal doses to human doses. The US EPA IRIS derivation uses a time to tumor model to help account for competing risks associated with decreased survival times and other causes of death. The US EPA IRIS also assumed, in the absence of data to inform a basis for extrapolation to humans, that equal risk for all species would be associated with equal benzo[a]pyrene air concentrations at anticipated environmental concentrations, as would be the case for a soluble gas. The US EPA IRIS derivation uses a more robust model to account for the early deaths of study animals, is peer-reviewed by independent expert scientists, and is extensively documented, which facilitates evaluation of the methods used. Therefore, the US EPA IRIS unit risk (6 x 10^{-4} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for benzo[a]pyrene. The benzo[a]pyrene risk specific air concentration calculated from this toxicity value is 1.6 x 10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: November, 2004; revised January, 2018
Toxicity value recommendation: December, 2004; revised January, 2018

4. References for Summary Table

CA EPA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2009. Technical Support Document for Cancer Potency Factors 2009. Appendix B: Chemical-Specific Summaries of the Information Used to Derive Unit Risk and Cancer Potency Values.

Last accessed (01/19/2018) at http://oehha.ca.gov/air/crnr/technical-support-document-cancer-potency-factors-2009.

Health Canada. 1994. Priority Substances List Assessment Report: Polycyclic Aromatic Hydrocarbons. Ottawa: Environment Canada, Ministry of Public Works and Government Services. Last accessed (01/19/2018) at http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/contaminants/psl1-lsp1/hydrocarb_aromat_polycycl/hydrocarbons-hydrocarbures-eng.pdf

TERA (Toxicology Excellence for Risk Assessment). 2004. International toxicity estimates for risk database. Last accessed (01/19/2018) at http://www.tera.org/iter/

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

WHO (World Health Organization). 2000. Air Quality Guidelines for Europe. Last accessed (01/19/2018) at http://www.euro.who.int/en/what-we-publish/abstracts/air-quality-guidelines-for-europe.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[b]fluoranthene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Benzo[b]fluoranthene (CAS Number 205-99-2)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
-	-	-	-	-	A reference dose for benzo[b]fluoranthene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

2. Recommendation and Rationale

Benzo[b]fluoranthene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). Reference doses derived from chemical-specific toxicity data are available for six polycyclic aromatic hydrocarbons identified as priority contaminants in the Brownfield Cleanup Program (acenaphthene, anthracene, benzo[a]pyrene, fluoranthene, fluorene, and pyrene, see NYS, 2006). Benzo[b]fluoranthene is chemically similar to each of these six listed polycyclic aromatic hydrocarbons. Each of these six priority contaminants could be used to represent the noncancer toxicity of benzo[b]fluoranthene. Similarity of chemical structure cannot be used as a basis of choosing a chemical surrogate for benzo[b]fluoranthene because toxicity data are insufficient to accurately describe the relationship between the chemical structure and non-cancer toxicity of polycyclic aromatic hydrocarbons. The recommended reference dose for benzo[a]pyrene is lower than that of the other five polycyclic aromatic hydrocarbons. Without data on which of these six polycyclic aromatic hydrocarbons would be the best surrogate for benzo[b]fluoranthene, the recommended reference dose for benzo[a]pyrene (3×10^{-4} mg/kg/day, see Oral Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for benzo[b]fluoranthene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (2/13/2017) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
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  - Health Effects Assessment Summary Tables
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- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[b]fluoranthene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Benzo[b]fluoranthene (CAS Number 205-99-2)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ◆ NYS DEC (2017)	1×10^{-5}	0.1	--	--	Based on a relative potency factor of 0.1 applied to the US EPA IRIS benzo[a]pyrene cancer potency factor of 1 $(mg/kg/day)^{-1}$.
CA EPA CPF	8.3×10^{-7}	1.2	--	--	Based on a potency equivalency factor of 0.1 applied to the CA EPA CPF benzo[a]pyrene cancer potency factor of 12 $(mg/kg/day)^{-1}$.
RIVM (2001)	5.0×10^{-5}	0.02 (2)	--	--	Based on a relative potency factor of 0.1 applied to the RIVM benzo[a]pyrene cancer potency factor[2] of 0.2 $(mg/kg/day)^{-1}$.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2]A cancer potency factor was not reported. The derivation directly extrapolates from an experimental dose with significant increased tumor incidence above background to the environmental dose associated with a one-in-one million risk level; the risk-specific dose is not a lower-bound estimate.

2. Recommendation and Rationale

Benzo[b]fluoranthene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). The cancer potency factors for benzo[b]fluoranthene available from the authoritative bodies listed in item 5 (below) are based on a cancer potency factor for benzo[a]pyrene (also a polycyclic aromatic hydrocarbon) and the application of a relative potency factor for benzo[b]fluoranthene (see Chapter 5.1.5 of NYS (2006) for discussion of relative potency factors). The recommended cancer potency factor for benzo[a]pyrene is 1 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for Benzo[a]pyrene). The benzo[a]pyrene cancer potency factor is multiplied by the recommended relative potency factor of 0.1 for benzo[b]fluoranthene (NYS 2006) to obtain a cancer potency factor of 0.1 per mg/kg/day. This is the

toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for benzo[b]fluoranthene. The benzo[b]fluoranthene risk specific dose calculated from this toxicity value is 1×10^{-5} mg/kg/day.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/19/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/19/2018) at http://www.dec.ny.gov/chemical/34189.html

NYS DEC (New York State Department of Environmental Conservation). 2017. Draft Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Benzo[b]fluoranthene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/19/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
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- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[b]fluoranthene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Benzo[b]fluoranthene (CAS Number 205-99-2)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for benzo[b]fluoranthene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Benzo[b]fluoranthene is a polycyclic aromatic hydrocarbon (i.e. a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). A reference concentration based on chemical-specific inhalation toxicity data for benzo[b]fluoranthene is not available from the authoritative bodies listed in item 5 (below).

Benzo[a]pyrene is the only polycyclic aromatic hydrocarbon identified as a priority contaminant in the Brownfield Cleanup Program for which a reference concentration is available. Benzo[a]pyrene is chemically similar to benzo[b]fluoranthene and can be used to represent its noncancer inhalation toxicity (see Inhalation Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene). Therefore, based on using benzo[a]pyrene as a chemical surrogate, a reference concentration of 2×10^{-3} mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benzo[b]fluoranthene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/19/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment

Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Benzo[b]fluoranthene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Benzo[b]fluoranthene (CAS Number 205-99-2)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2009)	9.1×10^{-3}	1.1×10^{-4}	--	--	Based on the CA EPA unit risk for benzo[a]pyrene (which is derived from the increased incidence of respiratory tract tumors in hamsters exposed by inhalation) and application of a potency equivalency factor of 0.1.
Health Canada (1994)	2.7×10^{4} reported as TC_{05} [(2)]; linear equivalent specific concentration = 0.53	-- [3]	--	--	Based on reported TC_{05} for benzo[a]pyrene (derived from the increased incidence of respiratory tract tumors in hamsters exposed by inhalation) and application of a relative potency factor of 0.06. The relative potency factor for benzo[b]fluoranthene is based on its ability (relative to benzo[a]pyrene) to induce lung tumors in rats exposed by lung implantation.

US EPA IRIS	1.6×10^{-2}	6×10^{-5}	--	--	Based on application of a relative potency factor of 0.1 to the US EPA IRIS unit risk for benzo[a]pyrene, which is derived from the same study used by CA EPA and Health Canada.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} air concentration), where 1×10^{-6} concentration = 1×10^{-6} / inhalation unit risk.

[2]TC_{05} = The concentration in air (expressed in mcg/m^3) associated with a 5% increase in incidence or mortality due to tumors.

[3]No cancer potency factor was derived. The risk specific air concentration was obtained by linear extrapolation from the modeled TC_{05}.

2. Recommendation and Rationale

The unit risk values for benzo[b]fluoranthene are based on benzo[a]pyrene and the application of relative potency factors. The recommended unit risk value for benzo[a]pyrene is 6×10^{-4} per mcg/m^3 (see Inhalation Cancer Toxicity Value Documentation for benzo[a]pyrene). Application of the recommended relative potency factor (0.1) for benzo[b]fluoranthene to the unit risk for benzo[a]pyrene yields a unit risk of 6×10^{-5} per mcg/m^3, which is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for benzo[b]fluoranthene (see Chapter 5.1.5 of technical support document [NYS 2006] for discussion of recommended relative potency factors). The benzo[b]fluoranthene risk specific air concentration calculated from this toxicity value is 1.6×10^{-2} mcg/m^3.

3. Review Dates

Summary table completion: November, 2004; revised January, 2018
Toxicity value recommendation: December, 2004; revised January, 2018

4. References for Summary Table

CA EPA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2009. Technical Support Document for Cancer Potency Factors 2009. Appendix B: Chemical-Specific Summaries of the Information Used to Derive Unit Risk and Cancer Potency Values. Last accessed (01/19/2018) at http://oehha.ca.gov/air/crnr/technical-support-document-cancer-potency-factors-2009.

Health Canada. 1994. Priority Substances List Assessment Report Polycyclic Aromatic Hydrocarbons:. Ottawa: Environment Canada, Ministry of Public Works and Government Services. https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/canadian-environmental-protection-act-priority-substances-list-assessment-report-polycyclic-aromatic-hydrocarbons.html

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/19/2018) at http://www.dec.ny.gov/chemical/34189.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System
Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
    Health Effects Assessment Summary Tables
    Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Benzo[g,h,i]perylene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Benzo[g,h,i]perylene (CAS Number 191-24-2)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
RIVM (2001)	0.03	--	--	--	Based on kidney effects (renal tubular pathology, decreased kidney weights) in mice exposed to pyrene via gavage each day in a 13-week study.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

2. Recommendation and Rationale

Chemical-specific reference doses for benzo[g,h,i]perylene have not been derived by the authoritative bodies listed in item 5 (see below). RIVM derived a reference dose for benzo[g,h,i]perylene based on a chemical surrogate. Benzo[g,h,i]perylene is an aromatic hydrocarbon and can be placed in a specific fraction of total petroleum hydrocarbons (i.e., non-carcinogenic aromatic hydrocarbon with an equivalent carbon (EC) number in the $>EC_{16}$ to EC_{35} range)[1]. The RIVM reference dose for this fraction of total petroleum hydrocarbons is the US EPA IRIS reference dose for pyrene (0.03 mg/kg/day), and is the RIVM reference dose for benzo[g,h,i]perylene.

Benzo[g,h,i]perylene also is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). Reference doses derived from chemical-specific toxicity data are available for six polycyclic aromatic hydrocarbons identified as priority contaminants in the Brownfield Cleanup Program (acenaphthene, anthracene, benzo[a]pyrene, fluoranthene, fluorene, and pyrene, see NYS [2006]). Benzo[g,h,i]perylene is chemically similar to each of these six listed polycyclic aromatic hydrocarbons. Each of these six priority contaminants could be used to represent the noncancer toxicity of benzo[g,h,i]perylene. Similarity of chemical structure cannot be used as a basis of choosing a chemical surrogate for benzo[g,h,i]perylene because toxicity data are insufficient to accurately describe the relationship between the chemical structure and non-cancer toxicity of polycyclic aromatic hydrocarbons. The recommended reference dose for benzo[a]pyrene is lower than that of the other five polycyclic aromatic hydrocarbons. Without data on which of these six polycyclic aromatic hydrocarbons would be the best surrogate for benzo[g,h,i]perylene, the recommended reference dose for benzo[a]pyrene (3×10^{-4} mg/kg/day, see Oral Non-Cancer Toxicity

[1] Equivalent carbon (EC) number is an index based on the boiling point of a chemical normalized to the boiling point of *n*-alkanes or its retention time in a boiling point gas chromatographic column (GC). In other words, the EC number of compound X represents the number of carbon atoms that an imaginary *n*-alkane should have in order to present exactly the same boiling point as compound X.

Value Documentation for Benzo[a]pyrene) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for benzo[g,h,i]perylene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendations and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/19/2018) at http://www.dec.ny.gov/chemical/34189.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/19/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[g,h,i]perylene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Benzo[g,h,i]perylene (CAS Number 191-24-2)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1995)	--	--	--	--	Human data are not available. Data from lung implant, skin-painting and subcutaneous injection studies in animals do not provide convincing evidence for carcinogenicity.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for benzo[g,h,i]perylene is not available. *

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. Toxicological Profile for Polycyclic Aromatic Hydrocarbons. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. Last accessed (01/18/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Benzo[g,h,i]perylene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Benzo[g,h,i]perylene (CAS Number 191-24-2)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for benzo[g,h,i]perylene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Benzo[g,h,i]perylene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). A reference concentration based on chemical-specific inhalation toxicity data for benzo[g,h,i]perylene is not available from the authoritative bodies listed in item 5 (below).

Benzo[a]pyrene is the only polycyclic aromatic hydrocarbon identified as a priority contaminant in the Brownfield Cleanup Program for which a reference concentration is available. Benzo[a]pyrene is chemically similar to benzo[g,h,i]perylene and can be used to represent its noncancer inhalation toxicity (see Inhalation Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene). Therefore, based on using benzo[a]pyrene as a chemical surrogate, a reference concentration of 2×10^{-3} mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benzo[g,h,i]perylene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/17/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment

Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[g,h,i]perylene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Benzo[g,h,i]perylene (CAS Number 191-24-2)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for benzo[g,h,i]perylene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Benzo[k]fluoranthene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Benzo[k]fluoranthene (CAS Number 207-08-9)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
--	--	--	--	--	A reference dose for benzo[k]fluoranthene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

2. Recommendation and Rationale

Benzo[k]fluoranthene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). Reference doses derived from chemical-specific toxicity data are available for six polycyclic aromatic hydrocarbons identified as priority contaminants in the Brownfield Cleanup Program (acenaphthene, anthracene, benzo[a]pyrene, fluoranthene, fluorene, and pyrene, see NYS, 2006). Benzo[k]fluoranthene is chemically similar to each of these six listed polycyclic aromatic hydrocarbons. Each of these six priority contaminants could be used to represent the noncancer toxicity of benzo[k]fluoranthene. Similarity of chemical structure cannot be used as a basis of choosing a chemical surrogate for benzo[k]fluoranthene because toxicity data are insufficient to accurately describe the relationship between the chemical structure and non-cancer toxicity of polycyclic aromatic hydrocarbons. The recommended reference dose for benzo[a]pyrene is lower than that of the other five polycyclic aromatic hydrocarbons. Without data on which of these six polycyclic aromatic hydrocarbons would be the best surrogate for benzo[k]fluoranthene, the recommended reference dose for benzo[a]pyrene (3×10^{-4} mg/kg/day, see Oral Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for benzo[k]fluoranthene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[k]fluoranthene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Benzo[k]fluoranthene (CAS Number 207-08-9)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ◆ NYS DEC (2017)	1×10^{-4}	0.01	--	--	Based on a relative potency factor of 0.01 applied to the US EPA IRIS benzo[a]pyrene cancer potency factor of 1 $(mg/kg/day)^{-1}$.
CA EPA CPF	8.3×10^{-7}	1.2	--	--	Based on a potency equivalency factor of 0.1 applied to the CA EPA CPF benzo[a]pyrene cancer potency factor of 12 $(mg/kg/day)^{-1}$.
RIVM (2001)	5.0×10^{-5}	0.2 (2)	--	--	Based on a relative potency factor of 0.1 applied to the RIVM benzo[a]pyrene cancer potency factor[2] of 0.2 $(mg/kg/day)^{-1}$.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2]A cancer potency factor was not reported. The derivation directly extrapolates from an experimental dose with significant increased tumor incidence above background to the environmental dose associated with a one-in-one million risk level; the risk-specific dose is not a lower-bound estimate.

2. Recommendation and Rationale

Benzo[k]fluoranthene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). The cancer potency factors for benzo[k]fluoranthene available from the authoritative bodies listed in item 5 (below) are based on a cancer potency factor for benzo[a]pyrene (also a polycyclic aromatic hydrocarbon) and the application of a relative potency factor for benzo[k]fluoranthene (see Chapter 5.1.5 of NYS (2006) for discussion of relative potency factors). The recommended cancer potency factor for benzo[a]pyrene is 1 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for Benzo[a]pyrene). The benzo[a]pyrene cancer potency factor is multiplied by the recommended relative potency factor of 0.01 for benzo[k]fluoranthene (NYS 2006) to obtain a cancer potency factor of 0.01 per mg/kg/day. This is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for

benzo[k]fluoranthene. The benzo[k]fluoranthene risk specific dose calculated from this toxicity value is 1×10^{-4} mg/kg/day.

3. Review Dates

Summary table completion: February, 2004; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/13/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

NYS DEC (New York State Department of Environmental Conservation). 2017. Draft Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Benzo[k]fluoranthene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/13/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/13/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Benzo[k]fluoranthene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Benzo[k]fluoranthene (CAS Number 207-08-9)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for benzo[k]fluoranthene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Benzo[k]fluoranthene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). A reference concentration based on chemical-specific inhalation toxicity data for benzo[k]fluoranthene is not available from the authoritative bodies listed in item 5 (below).

Benzo[a]pyrene is the only polycyclic aromatic hydrocarbon identified as a priority contaminant in the Brownfield Cleanup Program for which a reference concentration is available. Benzo[a]pyrene is chemically similar to benzo[k]fluoranthene and can be used to represent its noncancer inhalation toxicity (see Inhalation Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene). Therefore, based on using benzo[a]pyrene as a chemical surrogate, a reference concentration of 2×10^{-3} mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benzo[k]fluoranthene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (2/13/2017) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry

California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Benzo[k]fluoranthene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Benzo[k]fluoranthene (CAS Number 207-08-9)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2009)	9.1×10^{-3}	1.1×10^{-4}	--	--	Based on the CA EPA unit risk for benzo[a]pyrene (which is derived from the increased incidence of respiratory tract tumors in hamsters exposed by inhalation) and application of a potency equivalency factor of 0.1.
Health Canada (1994)	4.0×10^4 reported as TC_{05} [(2)]; linear equivalent specific concentration = 0.8	-- [3]	--	--	Based on reported TC_{05} for benzo[a]pyrene (derived from the increased incidence of respiratory tract tumors in hamsters exposed by inhalation) and application of a relative potency factor of 0.04. The relative potency factor for benzo[k]fluoranthene is based on its ability (relative to benzo[a]pyrene) to induce lung tumors in rats exposed by lung implantation.
US EPA IRIS	0.16	6×10^{-6}	--	--	Based on application of a relative potency factor of 0.01 to the US EPA IRIS unit risk for benzo[a]pyrene, which is derived from the same study used by CA

					EPA and Health Canada.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10^{-6} air concentration), where 1 x 10^{-6} concentration = 1 x 10^{-6} / inhalation unit risk.
[2]TC_{05} = The concentration in air (expressed in mcg/m^3) associated with a 5% increase in incidence or mortality due to tumors.
[3]No cancer potency factor was derived. The risk specific air concentration was obtained by linear extrapolation from the modeled TC_{05}.

2. Recommendation and Rationale

The unit risk values for benzo[k]fluoranthene are based on benzo[a]pyrene and the application of relative potency factors. The recommended unit risk value for benzo[a]pyrene is 6 x 10^{-4} per mcg/m^3 (see Inhalation Cancer Toxicity Value Documentation for benzo[a]pyrene). Application of the recommended relative potency factor (0.01) for benzo[k]fluoranthene to the unit risk for benzo[a]pyrene yields a unit risk of 6 x 10^{-6} per mcg/m^3, which is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for benzo[k]fluoranthene (see Chapter 5.1.5 of technical support document [NYS 2006] for discussion of recommended relative potency factors). The benzo[k]fluoranthene risk specific air concentration calculated from this toxicity value is 0.16 mcg/m^3.

3. Review Dates

Summary table completion: November, 2004; revised January, 2018
Toxicity value recommendation: December, 2004; revised January, 2018

4. References for Summary Table

CA EPA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2009. Technical Support Document for Cancer Potency Factors 2009. Appendix B: Chemical-Specific Summaries of the Information Used to Derive Unit Risk and Cancer Potency Values. Last accessed (01/13/2018) at http://oehha.ca.gov/air/crnr/technical-support-document-cancer-potency-factors-2009.

Health Canada. 1994. Priority Substances List Assessment Report Polycyclic Aromatic Hydrocarbons:. Ottawa: Environment Canada, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm.

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/13/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment

Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System
Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
    Health Effects Assessment Summary Tables
    Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Beryllium
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Inorganic Beryllium

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2004) • US EPA ODW (2004) • US EPA HEAST (1997)	2×10^{-3}	0.46	$BMDL_{10}$ [2]	300	Based on small intestinal lesions in dogs in a 172-week dietary study.
ATSDR (2002)	2×10^{-3}	0.56	$BMDL_{10}$ [2]	300	Based on the same study used by US EPA (2004).
Cal EPA (2003)	1.5×10^{-4} -- 2×10^{-4}	1.5 -- 0.2	NOEL -- $BMDL_{05}$ [2]	1000	Based on the same study used by US EPA (2004).

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; UF: uncertainty factor.
[2]$BMDL_x$ = The 95% lower confidence bound on the modeled benchmark dose associated with an excess lifetime risk of the observed effect of X%.

2. Recommendation and Rationale

The basis for the various reference doses for inorganic beryllium is essentially identical with respect to choice of study, species and adverse effect. The US EPA IRIS, ATSDR and one of the Cal EPA derivations used a benchmark dose approach to estimate a lower-bound point of departure associated with either a 5 or 10% excess lifetime risk of the observed effect (intestinal lesions). The Cal EPA also identified a NOEL point of departure from the same study. In the principal study, dogs were exposed via the diet to one of four non-zero doses. The Cal EPA identified the second-lowest dose level in females as the NOEL. However, there were no statistically significant effects observed in dogs of either sex at the next highest dose (1.1 mg/kg/day in males, 1.3 mg/kg/day in females), so that the choice of the

next-lower dose as the NOEL is questionable. Both Cal EPA derivations apply a total uncertainty factor of 1000, including a factor of 10 to account for intraspecies variability, a factor of 3 to account for interspecies variability (based on the site-of-contact nature of the lesions, therefore not requiring an adjustment for pharmacokinetic variability), a factor of 3 to account for database deficiencies and an additional factor of 10 to address uncertainties regarding the carcinogenicity of beryllium via ingestion. The additional 10-fold factor for carcinogenicity is not applicable in the current context as cancer and non-cancer effects are being addressed separately. The US EPA IRIS and ATSDR derivations are essentially equivalent, although the estimates of the $BMDL_{10}$ differ slightly. Both apply the same total uncertainty factor of 300 (10-fold each to account for intraspecies and interspecies variability and an additional 3-fold to account for database deficiencies). Therefore, the US EPA reference dose (2×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for inorganic beryllium.

3. Review Dates

Summary table completion: August, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological profile for beryllium. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. https://www.atsdr.cdc.gov/toxprofiledocs/index.html

Cal EPA (California Environmental Protection Agency). 2003. Public Health Goal for beryllium and beryllium compounds in Drinking Water. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (Office of Drinking Water). 2004. 2004 Edition of the Drinking Water Standards and Health Advisories. EPA 822-R-04-005 Office of Water. U.S. Environmental Protection Agency. Washington, DC. Last accessed (01/17/2018) at http://www.epa.gov/waterscience/drinking/

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System

- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Division of Drinking Water and Environmental Management

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Beryllium
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Beryllium

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
Cal EPA (2004)	1.4×10^{-7}	7	--	--	Oral cancer potency factor for beryllium oxide based on human occupational exposure. Very limited documentation available.
Cal EPA (2004)	3.3×10^{-10}	3000	--	--	Oral cancer potency factor for beryllium sulfate. Very limited documentation available.
US EPA IRIS (2004)	--	--	--	--	Based on limited animal studies, data were considered inadequate to derive an oral cancer potency value.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

The two cancer potency factors derived by Cal EPA are reported on the Toxicity Criteria Database for specific beryllium compounds (beryllium oxide and beryllium sulfate). Both values are derived by Cal EPA by reference to a 1987 health assessment of beryllium prepared by the US EPA (US EPA, 1987). The Cal EPA only provides a table extracted from that document as the basis for their values. An oral cancer potency factor that was previously published on US EPA IRIS was based on a lifetime study of rats exposed to beryllium sulfate in drinking water. This may have been the same value cited by Cal EPA for beryllium sulfate (3000 per mg/kg/d), but the value on IRIS was withdrawn because the tumor incidence did not differ significantly between control and exposed animals and because adequate data to develop a quantitative oral assessment were not available. Neither of the Cal EPA values is chosen for use in the derivation of a soil cleanup objective for several reasons including the lack of documentation

explaining the basis of the two Cal EPA compound-specific cancer potency factors, the current US EPA assessment concluding that data are inadequate to derive an oral cancer potency factor and the large difference in potency between beryllium sulfate and beryllium oxide suggesting that an assessment of oral cancer potency should be compound specific. The Cal EPA drinking water program has published another beryllium cancer potency factor for use in deriving a public health goal for drinking water (Cal EPA, 2003). However, that value is an inhalation cancer potency factor that is only applied to estimate the cancer risk associated with inhaling aerosols from drinking water containing beryllium, not the risk associated with beryllium ingestion. That value is therefore not chosen as an oral cancer potency factor for use in the derivation of a soil cleanup objective. Therefore, an oral cancer potency factor for oral beryllium exposure is not available.

3. Review Dates

Summary table completion: August, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2003. Public Health Goals for Chemicals in Drinking Water. Beryllium and Beryllium Compounds. Office of Environmental Health Hazard Assessment. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

Cal EPA (California Environmental Protection Agency). 2004. Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. https://oehha.ca.gov/chemicals

US EPA (United States Environmental Protection Agency). 1987. Health Assessment Document for Beryllium. Office of Health and Environmental Assessment. Washington DC. EPA/600/8-84/026F

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Division of Drinking Water and Environmental Management

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Beryllium
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Inorganic Beryllium

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2004)	0.02	0.2	LOEL	10	Based on beryllium sensitization in workers and progression to chronic beryllium disease.
Cal EPA (2001)	7×10^{-3}	0.2	LOEL	30	Based on the same study as US EPA IRIS (2004).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
LOEL: lowest observed effect level; UF: uncertainty factor

2. Recommendation and Rationale

The reference concentrations for beryllium derived by authoritative bodies from the list in item 5 (below) are both based on the same occupational study which documented beryllium sensitization (an immune response) and progression to chronic beryllium disease (a chronic inflammatory lung lesion) among workers exposed occupationally by inhalation for an average of six years. The reference concentrations are based on the same point of departure, but differ in the choice of the uncertainty factors. The US EPA applied an uncertainty factor of 3 (rather than a full 10) to account for the use of a LOEL, based on the sensitive nature of the subclinical effect (beryllium sensitization). The US EPA also used an uncertainty factor of 3 for database deficiencies, citing the poor quality of the monitoring data in the principal study, and did not use an intraspecies uncertainty factor based on the conclusion that 1 to 5% of the population is susceptible to chronic beryllium disease and that the workers in the principal study constituted the most sensitive subpopulation. The Cal EPA used a full uncertainty factor of 10 for use of a LOEL and also applied an uncertainty factor of 3 for intraspecies variation, based on their conclusion that even though a sensitive population (i.e., beryllium-sensitized workers) may have been identified by the principal study, additional factors may also determine beryllium sensitivity. Given that chronic beryllium disease (which is made more likely by beryllium

sensitization) is a debilitating and irreversible condition, retention of an uncertainty factor of at least 3 for intraspecies variation and 10 for use of a LOEL are more consistent with current risk assessment practices. Therefore, the Cal EPA reference concentration (7×10^{-3} mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for beryllium.

3. Review Dates

Summary table completion: November, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2004. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Beryllium and Beryllium Compounds. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Beryllium
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Beryllium

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2004) ♦ Cal EPA (2002)	4.2×10^{-4}	2.4×10^{-3}	relative risk	--	Based on the incidence of lung cancer in males occupationally exposed to beryllium.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

The US EPA unit risk is the only available value from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the US EPA unit risk (2.4×10^{-3} per mcg/m^3) is the toxicity value recommended for use in the derivation of a inhalation cancer-based soil cleanup objective for beryllium. The beryllium risk specific air concentration calculated from this toxicity value is 4.2×10^{-4} mcg/m^3.

3. Review Dates

Summary table completion: November, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2002. Technical Support Document for Describing Available Cancer Potency Factors, December. Sacramento, CA: Office of Environmental Health Hazard Assessment, Air Toxicology and Epidemiology Section, California Environmental Protection Agency

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). Risk-based Concentration Table. Superfund Technical Support Section. 2004. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *n*-Butylbenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for *n*-Butylbenzene (CAS Number 104-51-8)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA OSRTI* Also used by: ♦ US EPA RSL	0.05	137	$BMDL_{10}$	3000	Based on liver effects in parental male rats exposed by olive oil gavage every day for a total of 16 to 18 weeks in a two-generation reproductive study. The BMR was an increased incidence in hepatocellular hypertrophy. Study NOEL = 100 mg/kg/day. Study LOEL = 300 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

BMR: benchmark response; $BMDL_{10}$: 95% lower limit on benchmark dose associated with 10% incidence above background; NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.
*Agency's toxicity value added or revised during an update of fact sheets to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA OSRTI value is the only available reference dose for *n*-butylbenzene from an authoritative body listed in item 5 (below), and is derived using methods that reflect consistency with generally accepted risk assessment practices. Therefore, the US EPA OSRTI reference dose (0.05 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *n*-butylbenzene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; revised January, 2018

4. References for Summary Table

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund. Last accessed (01/22/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/22/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *n*-Butylbenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for *n*-Butylbenzene (CAS Number 104-51-8)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	No information available.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for *n*-butylbenzene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *n*-Butylbenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for *n*-Butylbenzene (CAS Number 104-51-8)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

n-Butylbenzene is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the recommended reference dose based on systemic effects (0.05 mg/kg/day; see Oral Non-Cancer Toxicity Value Documentation). Therefore, a reference concentration of 180 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *n*-butylbenzene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values

Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: *n*-Butylbenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for *n*-Butylbenzene (CAS Number 104-51-8)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for *n*-butylbenzene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *sec*-Butylbenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for *sec*-Butylbenzene (CAS Number 135-98-8)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
CA EPA NL*	0.037	--	--	--	Based on toxicity data for cumene (isopropylbenzene).
US EPA OSRTI Also used by: ♦ US EPA RSL	0.1	--	--	--	Based on toxicity data for cumene (isopropylbenzene).

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

UF: uncertainty factor.

*Agency's toxicity value added or revised during an update of fact sheets to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The CA EPA and US EPA OSRTI values for *sec*-butylbenzene use cumene (isopropylbenzene) as a surrogate chemical, as both chemicals are branched, short-chain alkylbenzenes which are structurally similar. The structural chemical similarity between the two chemicals provides a basis for using toxicity data for cumene to represent *sec*-butylbenzene. The CA EPA and US EPA OSRTI oral reference doses for cumene are both based on an adjusted NOAEL of 110 mg/kg/day for increased average kidney weights in female rats exposed by gavage 139 times over a 194-day period. Each agency used uncertainty factors of 10 to account for animal-to-human extrapolation, 10 to account for human variation, and 3 for the use of a subchronic study. The CA EPA derivation used an uncertainty factor of 10 for database deficiencies, while the US EPA OSRTI derivation used a database uncertainty factor of 3. A full uncertainty factor of 10 is preferable in light of the fact that the cumene database lacks oral studies to evaluate reproductive and developmental toxicity, as well as chronic two year cancer bioassays by any route of exposure. Therefore, the CA EPA reference dose for cumene (0.037 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *sec*-butylbenzene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA NL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Notification Levels for Chemicals in Drinking Water. Last accessed (01/14/2018) at https://oehha.ca.gov/water/notification-levels-chemicals-drinking-water

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund . Last accessed (01/14/2018) at https://www.epa.gov/pprtv/provisional-peer-reviewed-toxicity-values-pprtvs-assessments

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *sec*-Butylbenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for *sec*-Butylbenzene (CAS Number 135-98-8)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	No information available.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for *sec*-butylbenzene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *sec*-Butylbenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for *sec*-Butylbenzene (CAS Number 135-98-8)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Reference concentrations based on chemical-specific inhalation toxicity data for *sec*-butylbenzene or its potential chemical surrogates are not available from the authoritative bodies listed in item 5 (below). *sec*-Butylbenzene is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. The recommended oral toxicity value for *sec*-butylbenzene is based on cumene (isopropylbenzene) as a surrogate chemical, and the similarity between the two chemicals provides a basis for using toxicity data for cumene to represent *sec*-butylbenzene. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration for *sec*-butylbenzene from the recommended reference dose for the chemical surrogate cumene. Therefore, based on the chemical surrogate and exposure route extrapolation, a reference concentration of 130 mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *sec*-butylbenzene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; January, 2018

4. References for Summary Table and Recommendation and Rationale

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency

Integrated Risk Information System
Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
Health Effects Assessment Summary Tables
Provisional Peer Reviewed Toxicity Values
Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: *sec*-Butylbenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for *sec*-Butylbenzene (CAS Number 135-98-8)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for *sec*-butylbenzene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *tert*-Butylbenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for *tert*-Butylbenzene (CAS Number 98-06-6)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
CA EPA NL*	0.037	--	--	--	Based on toxicity data for cumene (isopropylbenzene).
US EPA OSRTI Also used by: ♦ US EPA RSL	0.1	--	--	--	Based on toxicity data for cumene (isopropylbenzene).

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

UF: uncertainty factor.

*Agency's toxicity value added or revised during an update of fact sheets to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The CA EPA and US EPA OSRTI values for *tert*-butylbenzene use cumene (isopropylbenzene) as a surrogate chemical, as both chemicals are branched, short-chain alkylbenzenes which are structurally similar. The structural chemical similarity between the two chemicals provides a basis for using toxicity data for cumene to represent *tert*-butylbenzene. The CA EPA and US EPA OSRTI oral reference doses for cumene are both based on an adjusted NOAEL of 110 mg/kg/day for increased average kidney weights in female rats exposed by gavage 139 times over a 194-day period. Each agency used uncertainty factors of 10 to account for animal-to-human extrapolation, 10 to account for human variation, and 3 for the use of a subchronic study. The CA EPA derivation used an uncertainty factor of 10 for database deficiencies, while the US EPA OSRTI derivation used a database uncertainty factor of 3. A full uncertainty factor of 10 is preferable in light of the fact that the cumene database lacks oral studies to evaluate reproductive and developmental toxicity, as well as chronic two year cancer bioassays by any route of exposure. Therefore, the CA EPA reference dose for cumene (0.037 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *tert*-butylbenzene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA NL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Notification Levels for Chemicals in Drinking Water. Last accessed (01/15/2018) at https://oehha.ca.gov/water/notification-levels-chemicals-drinking-water

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund. Last accessed (01/15/2018) at https://www.epa.gov/pprtv/provisional-peer-reviewed-toxicity-values-pprtvs-assessments

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *tert*-Butylbenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for *tert*-Butylbenzene (CAS Number 98-06-6)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	No information available.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for *tert*-butylbenzene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water

Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *tert*-Butylbenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for *tert*-Butylbenzene (CAS Number 98-06-6)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Reference concentrations based on chemical-specific inhalation toxicity data for *tert*-butylbenzene or its potential chemical surrogates are not available from the authoritative bodies listed in item 5 (below). *tert*-Butylbenzene is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. The recommended oral toxicity value for *tert*-butylbenzene is based on cumene (isopropylbenzene) as a surrogate chemical, and the similarity between the two chemicals provides a basis for using toxicity data for cumene to represent *tert*-butylbenzene. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration for *tert*-butylbenzene from the recommended reference dose for the chemical surrogate cumene. Therefore, based on the chemical surrogate and exposure route extrapolation, a reference concentration of 130 mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *tert*-butylbenzene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation

New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *tert*-Butylbenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for *tert*-Butylbenzene (CAS Number 98-06-6)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for *tert*-butylbenzene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Cadmium
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Inorganic Cadmium

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
General Population					
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW	5×10^{-4} (water) 1×10^{-3} (food)	0.005 0.01	NOEL NOEL	10 10	Based on the highest level of cadmium in the human renal cortex not associated with significant proteinuria, obtained from many studies on the toxicity of cadmium in both humans and animals.
ATSDR*	1.0×10^{-4}	0.00033 (females) 0.0007 (males)	$UCDL_{10}$	3	Based on a meta-analysis of seven studies reporting 11 total dose-response relationships between urinary cadmium levels and biomarkers of kidney effects in humans. Study results were partitioned geographically, and a statistical lower-bound on lowest urinary cadmium level associated with a 10% increase in kidney function biomarkers among the three geographic data sets was chosen as the point of departure.
EFSA (2009)*	3.6×10^{-4}	0.00036	$BMDL_{05}$ (adjusted)	-- [2]	Based on a meta-analysis of 35 studies reporting associations between urinary cadmium concentrations a biomarker of kidney toxicity in humans. The point of departure was estimated as the average daily dietary intake that would result in 95% of the exposed population having a urinary

					cadmium concentration not exceeding the adjusted $BMDL_{05}$ of 0.001 mg Cd/g creatinine in urine.
CA EPA PHG*	6.3×10^{-6}	0.0003	NOEL	50	Based on estimates of daily oral cadmium intake that limit daily cadmium excretion in urine to 0.001 mg/g creatinine, thereby preventing renal toxicity.
RIVM (2001)	5.0×10^{-4}	0.001	LOEL	2	RIVM concluded that human data demonstrated that kidney damage will be prevented if cadmium levels in the renal cortex and urine are below 50 mg/kg and 0.0025 mg/g creatinine, respectively, and that these cadmium levels are likely to be reached following a lifetime exposure to a dose of 0.001 mg/kg/day.
WHO (2011)*	8.6×10^{-4}	0.0008	NOEL	-- [3]	Based on identification of a daily dietary cadmium intake of 0.0008 mg/kg as resulting in a daily urinary cadmium concentration of 0.00524 mg/g creatinine, a urinary level below which urinary biomarkers of kidney toxicity are not elevated. Documentation of this reference dose is limited and only provides the point of departure and an associated drinking water guideline value based on a 10% relative source contribution attributed to drinking water.
NYS DEC (1997)	7.0×10^{-4}	--	--	--	The reference dose is the average of 5 values derived by NYS DOH (0.0007 mg/kg/day), US EPA (0.0005 mg/kg/day), US FDA (0.0008 mg/kg/day), WHO (0.0010 mg/kg/day) and ATSDR (0.0007 mg/kg/day).

HC DWQ	6×10^{-4} to 7×10^{-4} (4)	--	--	--	Based on multi-compartmental model for cadmium distribution in the body and the conclusion that a daily intake of 0.04 to 0.05 mg would lead to only 0.1 percent of the population reaching the critical cadmium concentration of 0.2 mg/g in the renal cortex after 50 years. Documentation on actual derivation is limited.
Child-Specific Reference Dose (chRD)					
CA EPA chRD*	1.1×10^{-5}	1.0×10^{-3}	LOEL	90	Child-specific reference dose based on tubular damage indicated by the appearance of small proteins in the urine in an epidemiological study of a cross sectional sample of the adult Belgian population.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.
[2]Application of a default UF was not reported. The $BMDL_{05}$ was obtained from a statistical model relating outcome and exposure biomarkers based on group means, rather than individual-level data. An adjustment factor of 3.9 was applied to the resulting $BMDL_{05}$ to estimate expected variation in urinary cadmium clearance in the absence of individual-level data. The adjustment factor assumes urinary cadmium is log-normally distributed with inter-individual coefficient of variation = 100%. EFSA considered this value to be a chemical-specific adjustment factor that resulted in an adjusted $BMDL_{05}$.
[3] The documentation does not provide an uncertainty factor that what used to derive the reference dose, and a reference dose was not reported. The reference dose value was obtained from the drinking water guideline of 0.003 mg/L, assuming a 70 kg adult body weight and the relative source contribution of 10% used by WHO (2011). Based on the reported NOEL point of departure and the resulting reference dose based on the drinking water guideline, the effective UF would be approximately 1.
[4]A reference dose was not calculated. The range of reference doses was obtained from the daily intakes of 0.04 to 0.05 mg/day assuming a 70 kg adult body weight.

NOEL: no observed effect level; LOEL: lowest observed effect level; $UCDL_{10}$: 95% lower confidence limit on the urinary cadmium dose associated with a 10% increase in kidney biomarker levels above background; $BMDL_{05}$: 95% lower confidence limit on the benchmark dose associated with a 5% increase in kidney biomarker levels above background;
chRD: child-specific reference dose; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the various cadmium reference doses is dietary exposure associated with kidney toxicity in humans. All of the derivations are based on relationships between oral cadmium intake, urinary cadmium levels or cadmium levels in the renal cortex, and biomarkers of kidney toxicity. The specific

human data and assumptions used to derive a reference dose value differ among the authoritative bodies.

The NYS DEC obtained their reference dose by averaging values from other authoritative bodies, including some values that have subsequently been revised by those authorities. The derivations from WHO and HC do not provide complete information to assess the assumptions used as the basis of the reference dose values. The NYS DEC, WHO and HC values are not considered further.

The US EPA IRIS values (separate values for food and drinking water based on assumed differences in cadmium absorption) and several of the values that were averaged to derive the NYS DEC value are based on a critical concentration of 0.2 mg cadmium/g of human kidney cortex that is associated with minimal renal tubule dysfunction (initially manifested clinically as proteinuria) in the general population. A cadmium pharmacokinetic model predicts the chronic cadmium intake that will result in a specific cadmium level in the kidney cortex. This cadmium concentration in kidney cortex reflects data from many older studies on cadmium exposure and kidney toxicity in human populations and laboratory animals, and has been considered a NOEL body burden by many authoritative bodies. The CA EPA chRD and RIVM reference dose derivations are similar, except that 0.05 mg/g in the kidney cortex is considered a critical level, one that RIVM states is associated with about 4% incidence of renal toxicity.

The ATSDR, CA EPA and EFSA (2009) reference dose values are based on observed relationships in human between urinary cadmium levels and sensitive urinary biomarkers of kidney toxicity, rather than on an assumed critical cadmium level in kidney cortex and pharmacokinetic modeling. The ATSDR reference dose is based on a meta-analysis of human epidemiology studies relating urinary cadmium levels to urinary biomarkers of kidney damage (beta-2-microglobulin). Based on separate analyses for studies grouped geographically, ATSDR identified the point of departure as the lowest estimate of the 95% lower bound on the urinary cadmium concentration associated with a 10% increase in the excess risk of urinary low-molecular-weight proteinuria. Although the population-based studies used as the basis of the point of departure likely included sensitive subpopulations, an uncertainty factor of 3 was applied to the point of departure to account for additional human variability, particularly as diabetics may be especially sensitive to cadmium renal toxicity and diabetics were excluded from a number of the studies.

The CA EPA reference dose is based on a level of urinary cadmium assumed to not result in increased excretion of urinary protein biomarkers that are very sensitive indicators of the onset of renal toxicity. CA EPA points to data from a large number of human studies (including some also used by ATSDR) relating urinary cadmium and renal toxicity biomarker levels as the basis of their point of departure. However, no clear quantitative or narrative analysis is presented that supports the specific value chosen for the point of departure. CA EPA applied a total uncertainty factor of 50 to their NOEL point of departure, including a factor of 5 to account for human variability, particularly uncertainties due to limited information on the toxicokinetics of cadmium, and an additional factor of 10 to account for the carcinogenicity of cadmium by the oral route.

The EFSA (2009) reference dose is based on a meta-analysis of 35 studies reporting associations between urinary cadmium concentrations and beta-2-microglobulin in humans. The $BMDL_{05}$ was adjusted with a chemical-specific adjustment factor to account for variation in urinary cadmium clearance. Using a one-compartment pharmacokinetic model, a point of departure was estimated as the average daily dietary intake that would result in 95% of the exposed population having a urinary cadmium concentration not exceeding the adjusted $BMDL_{05}$ of 0.001 mg Cd/g creatinine in urine.

Although several assessments of chronic kidney toxicity due to cadmium ingestion have been based on a cadmium level in kidney cortex of 0.2 mg/g as a NOEL, CA EPA and RIVM both noted more recent studies that have found indicators of kidney toxicity can be detected in a small percentage of the population at levels as low as 0.05 mg cadmium/g kidney cortex. The RIVM assessment is less robust than either the ATSDR, EFSA (2009) or CA EPA derivations, as it is based on a single study. In addition, the RIVM application of a total uncertainty factor of 2 to a LOEL point of departure (even if a minimal LOEL) is not clearly justified and does not appear to adequately account for uncertainties regarding human variability. The CA EPA, ATSDR and EFSA (2009) reference doses are all based on robust analyses of a number of human studies that include direct observation of cadmium biomarkers and sensitive biomarkers of the onset of kidney toxicity. However, the CA EPA reference dose includes an additional 10-fold uncertainty factor accounting for cadmium carcinogenicity by the oral route. This is not relevant in this context as carcinogenicity is considered separately in the brownfields program.

The EFSA (2009) and ATSDR derivations were peer-reviewed, are well-documented, and are similar in their overall analytical approach, that is, the use of a pooled analysis of multiple human biomarker data sets and the use of benchmark dose analysis and pharmacokinetic modeling to estimate a point of departure. The EFSA derivation is based on a larger total sample of data sets, but the pooled analysis was conducted using study group means, requiring a statistical adjustment to the estimated $BMDL_{05}$ to account for assumed inter-individual variance in urinary cadmium excretion. The ATSDR derivation involved fewer total data sets, but individual study-participant data were modeled from each data set, the results were stratified geographically and then were pooled in order to choose the most sensitive geographic sub-group to derive a point of departure. Pharmacokinetic extrapolation to an oral point of departure at the BMDL was accomplished with a one-compartment classical kinetic model in the EFSA derivation, while the ATSDR derivation used a multi-compartment biokinetic model. Although overall study quality is similar for the two derivations, ATSDR's use of individual study-participant data for dose-response modeling in their pooled assessment and the use of a multi-compartment biokinetic model to obtain an oral point of departure are slightly preferred analytical approaches. Therefore, the ATSDR reference dose (1×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for cadmium in scenarios involving only adult exposure.

CA EPA has developed a program to derive reference doses for evaluating childhood exposures to contaminants in and around schools. This program stems from the possibility that children may be more sensitive than adults to contaminant exposures. CA EPA derived a child-specific reference dose (chRD) based on a 50-year oral intake (1 microgram/kg/day in Belgian subjects) that corresponds to a mean renal cortex concentration of 0.05 mg cadmium/g kidney cortex and a risk of renal effects at or above a urinary excretion rate of 2 micrograms cadmium in 24 hours. A total uncertainty factor of 90 was applied to the LOEL (10 for intra-human variability, 3 for use of a LOEL based on a minimal effect, and 3 to account for differences in GI absorption among children and adults) to obtain the chRD. The CA EPA chRD (1.1×10^{-5} mg/kg/day) is the only child-specific toxicity value derived by an authoritative body in item 5 (below), and is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for cadmium in scenarios involving child exposure.

3. Review Dates

Summary table completion: February, 2012; revised January 2018
Toxicity value recommendation: February, 2012; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/10/2018) at http://www.atsdr.cdc.gov/mrls/index.asp, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/10/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

CA EPA chRD (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Child-Specific Reference Doses. Last accessed (01/10/2018) at http://www.oehha.ca.gov/public_info/public/kids/chrds.html.

EFSA (European Food Safety Authority). 2009. Cadmium in Food. Scientific Opinion of the Panel on Contaminants in the Food Chain. Question No EFSA-Q-2007-138. EFSA J. 980:1-139. Last accessed (01/10/2018) at https://www.efsa.europa.eu/en/efsajournal/pub/980.

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/10/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Cadmium. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/10/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/10/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2012 Edition of the Drinking Water Standards and Health Advisories. EPA 822-S-12-001. Last accessed (01/10/2018) at http://water.epa.gov/drink/standards/hascience.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/10/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/10/2018) at https://www.who.int/water_sanitation_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Cadmium
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Cadmium

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
NYS DEC (2014)	1.5×10^{-5}	0.067	linear extrapolation from $BMDL_{10}$ (2) estimated using a multistage model	$BW^{3/4}$ (3)	Based on a marginally dose-related increase in testicular tumors (i.e., interstitial-cell or Leydig cell tumors) in male rats exposed to cadmium in the diet for 77 weeks.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

[2]$BMDL_{10}$: The lower 95% confidence limit on the benchmark dose associated with a 10% increase (relative to controls) in the incidence of tumors.

[3]Factor for dose adjustment from animals to humans is (animal body weight (0.4 kg)/human body weight (80 kg)$^{0.25}$, where 80 kg is the mean adult human body weight recommended in US EPA (2011), and human LED_{10} = rat LED_{10} x (0.4 kg / 80 kg)$^{1/4}$.

2. Recommendation and Rationale

The NYS DEC cancer potency factor is the only available factor from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. The NYS DEC cancer potency factor (0.067 per mg/kg/day) is therefore the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for cadmium. The cadmium risk specific dose calculated from this toxicity value is 1.5×10^{-5} mg/kg/day.

3. Review Dates

Summary table completion: August, 2014; no revision January, 2018
Toxicity value recommendation: August, 2014; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS DEC (New York State Department of Environmental Conservation). 2014. Draft Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Cadmium. Albany, NY: Division of Water.

US EPA (U.S. Environmental Protection Agency). 2011b. Exposure Factors Handbook. 2011 Edition. EPA/600/R-09/052F. Last accessed (01/16/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=20563.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Cadmium
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Inorganic Cadmium

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
ATSDR * Also used by: US EPA RSL *	0.01	0.1 [2]	$UCDL_{10}$	10	Based on a modeled human inhalation exposure that, when combined with background oral cadmium exposure, would result in a urinary cadmium concentration of 0.5 mcg/g creatinine. This is a statistical lower-bound on the lowest urinary cadmium level associated with a 10% increase in biomarkers of kidney damage among three sets of human (nonworker) exposure-response data.
CA EPA REL	0.02	0.5	NOEL	30	Based on kidney and respiratory toxicity in workers exposed to cadmium by inhalation. The NOEL (1.4 mcg/m^3) was adjusted to a human equivalent concentration that accounts for occupational ventilation rates and continuous exposure. Study LOEL = 21 mcg/m^3.

NYS DOH (1990)	0.02	200 mcg cadmium/gram kidney cortex; biokinetic modeling relates this body burden to total daily intake of 14.3 mcg cadmium[3]	LOEL	5	Based on a collective evaluation of epidemiologic evidence for kidney toxicity in workers exposed to cadmium and modeled data that suggests 40 mcg cadmium/gram is associated with a 0.1% risk of renal dysfunction.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

[2] The point-of-departure air concentration was estimated using cadmium biokinetic modeling of a continuous inhalation exposure combined with an average background oral cadmium intake to obtain a urinary cadmium concentration equal to 0.5 microgram per gram creatinine.

[3]The same model predicts an acceptable level of 40 mcg cadmium/g kidney cortex would result from a daily intake of 2.9 mcg/day from all routes of exposure. NYS DOH corrected this intake for the cadmium intake from food and water (1.7 mcg/day) and used an allocation factor 15% to account for cadmium exposure in air. The resulting intake from air (0.18 mcg/day) was converted to an air concentration of 0.02 mcg/m^3 assuming an inhalation rate of 20 m^3/day and that 50% of the inhaled dose is absorbed.

NOEL: no observed effect level; LOEL: lowest observed effect level; $UCDL_{10}$: 95% lower-bound on the urinary cadmium dose (expressed as microgram cadmium per gram creatinine excreted) associated with a 10% increase in kidney biomarker levels above background; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. **Recommendation and Rationale**

The reference concentrations for cadmium derived by authoritative bodies from the list in item 5 (below) are all based on kidney toxicity (and in one case also respiratory toxicity) in humans. The ATSDR reference concentration is based on the most sensitive point of departure for kidney toxicity from a meta-analysis of 11 datasets from seven studies of people exposed to cadmium occupationally and in the general population. The ATSDR used a pharmacokinetic model to estimate the cadmium air concentration that would result in a urinary cadmium concentration of 0.5 microgram per gram creatinine, assuming continuous inhalation exposure and taking background oral cadmium exposure into account. This urinary cadmium concentration is associated with a 10% increase in beta2-microglobulin, a sensitive biomarker for kidney damage. An uncertainty factor of 3 for human variability and a modifying factor of 3 for lack of adequate human data to compare the relative sensitivities of the respiratory tract and kidneys were applied to the point of departure. The Cal EPA derivation is based on estimated air exposure levels that caused kidney effects (proteinuria) and respiratory toxicity (reduced spirometry parameters) in workers exposed to cadmium for an average of 4.1 years. A total uncertainty factor of 30 (3 for use of a subchronic study and 10 for human variability) was applied to the time-weighted NOEL to obtain the reference concentration. The NYS DOH value is based on pharmacokinetic modeling and the weight of epidemiologic evidence

suggesting that subtle kidney toxicity effects are associated with kidney Cd levels of 200 mcg/g kidney cortex. The air concentration is set at a level that is predicted to result in a kidney level of 40 mcg/g by age 50, or a 5-fold lower level than the kidney concentration thought to be associated with effects.

The ATSDR reference concentration is preferred because it is based on a robust analysis of three population-based studies (rather than only workers in a single study, as in the CA EPA derivation) and it uses observed relationships between urinary cadmium levels and a sensitive urinary biomarker of kidney toxicity, rather than the assumed critical cadmium level in kidney cortex (as in the NYS DOH derivation). Furthermore, recent studies have found that indicators of kidney toxicity can be detected in a small percentage of the population at levels as low as 50 mcg cadmium/g kidney cortex, suggesting the 200 mcg/g point of departure used for the NYSDOH derivation may not be adequately protective. Therefore, the ATSDR reference concentration (0.01 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for cadmium.

3. Review Dates

Summary table completion: December, 2013; no revision January, 2018
Toxicity value recommendation: December, 2013; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/12/2018) at http://www.atsdr.cdc.gov/mrls/index.asp, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/12/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

NYS DOH (New York State Department of Health). 1990. Ambient Air Criteria Document: Cadmium. Albany, NY: Bureau of Toxic Substance Assessment.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/12/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System

Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
Health Effects Assessment Summary Tables
Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Cadmium
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Cadmium

Agency	Risk Specific Concentration[1] (mcg/m^3)	Cancer Potency Factor $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2004)	5.6×10^{-4}	1.8×10^{-3}	two stage model, extra risk	--	Based on evidence of lung, tracheal, and bronchus cancer deaths in workers exposed to cadmium by inhalation.
Cal EPA (2002)	2.4×10^{-4}	4.2×10^{-3}	poisson regression model and life table analysis	--	Based on the same study used by US EPA IRIS (2004).
Health Canada (1994)	5.1 reported as a TC_{05} [2]; linear equivalent risk specific concentration $= 1.0 \times 10^{-4}$	--[3]	linearized multistage model, extra risk	scaled based on default breathing rates and body weights of rats and humans	Based on an increased incidence of lung tumors in rats exposed by inhalation 23 hours per day for 18 months.
NYS DOH (1990)	5×10^{-4}	2.0×10^{-3}	linear average relative risk model	---	Based on the same study used by US EPA IRIS (2004).

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} concentration = 1×10^{-6} / cancer potency factor.

[2] TC_{05} = The concentration in air (expressed in mcg/m^3) associated with a 5% increase in incidence or mortality due to tumors. The TC_{05} represents a maximum likelihood estimate rather than a lower-bound estimate.

[3] The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported, but would be equal to 1×10^{-6} divided by the 10^{-6} risk-specific concentration.

2. Recommendation and Rationale

The inhalation unit risks derived by authoritative bodies from the list in item 5 (below) are based on increased incidence of lung tumors in human occupational studies or in rats exposed by inhalation for 18 months. Health Canada derived an inhalation risk-specific concentration from the rat study, but only reported a maximum likelihood TC_{05} that does not provide a lower-bound estimate on the risk specific concentration. The Health Canada derivation also used an interspecies scaling procedure based on inhaled dose and body weight scaling which is not consistent with currently-accepted risk assessment practice.

The US EPA, Cal EPA and NYS DOH derivations are all based on the same occupational lung cancer data for cadmium smelter workers. Small differences in the unit risks are due to use of different dose-response models. The Cal EPA derivation accounts for the influence of a healthy-worker effect on expected lung-cancer mortality, while the US EPA and NYS DOH derivations do not. Therefore, the Cal EPA unit risk (4.2×10^{-3} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for cadmium. The cadmium risk specific air concentration calculated from this toxicity value is 2.4×10^{-4} mcg/m^3.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency), 2002. Office of Environmental Health Hazard Assessment. Air Toxics Hot Spot Program Risk Assessment Guideline. Part II. Technical Support Documentation for Describing Available Cancer Potency Factors. Available at http://www.oehha.ca.gov/air/cancer_guide/TSD2.html.

Health Canada. 1994. Priority Substances List Assessment Report: Cadmium and its Compounds. Ottawa: Environment Canada, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

NYSDOH (New York State Department of Health) 1990. Ambient Air Criteria Document: Cadmium. Albany, NY: Bureau of Toxic Substance Assessment.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System

- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Division of Drinking Water and Environmental Management

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Carbon Tetrachloride
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Carbon Tetrachloride (CAS Number 56-23-5)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW	4×10^{-3}	3.9	BMDL	1000	Based on liver effect in rats exposed by corn oil gavage 5 days/week for 12 weeks. Study LOEL = 7.1 mg/kg/day. The BMR was a 2-fold increase in serum SDH activity above the control mean, time weighted to daily exposure.
RIVM (2001)	4×10^{-3}	1	NOEL	250	Based on same study, species, and effects as used by US EPA IRIS.
WHO (2011)	1.4×10^{-3}	0.71	NOEL	500	Based on same study, species, and effects as used by US EPA IRIS.
CA EPA PHG	7×10^{-4}	0.71	NOEL	1000	Based on same study, species, and effects as used by US EPA IRIS.
HC DWQ	7×10^{-4}	0.71	NOEL	1000	Based on same study, species, and effects as used by US EPA IRIS.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

BMR: benchmark response; BMDL: 95% lower limit on benchmark dose; NOEL: no-observed-effect level; UF: uncertainty factor; SDR: sorbitol dehydrogenase

2. Recommendation and Rationale

The basis for the various reference doses for carbon tetrachloride is essentially identical with respect to choice of study, species and adverse effect. Agencies differ in their identification of the point of departure (a NOEL of 1.0 mg/kg/day, 5 days per week or a BMDL). The RIVM value does not time-weight the NOEL dose for the 5 days per week dosing scheme and reduces the uncertainty factor for a subchronic study from 10 to 2.5 without clearly documenting a justification for that choice. The WHO, HC DWQ and CA EPA PHG values were almost identically derived, except WHO chose to reduce the

total uncertainty factor applied to the NOEL by a factor of 2 due to the use of bolus gavage dosing. The WHO did not provide sufficient justification for reduction of the uncertainty factor. The US EPA IRIS derived a BMDL based on a specific marker of liver toxicity (increased serum sorbitol dehydrogenase activity). The US EPA IRIS derivation is more consistent with generally accepted risk assessment practices by using a benchmark-dose approach for the point of departure and applying 10-fold uncertainty factors to account for animal-to-human extrapolation and human variation, and 3-fold uncertainty factors to account for the use of a subchronic study and for database deficiencies. Therefore, the US EPA IRIS reference dose (4×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for carbon tetrachloride.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; revised January, 2018

4. References for Summary Table

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/18/2018) at http://www.oehha.ca.gov/water/phg/allphgs.html.

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/18/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/18/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/18/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/18/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/18/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html, with supporting documentation at http://www.who.int/water_sanitation_health/dwq/chemicals/en/index.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment

Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Carbon Tetrachloride
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Carbon Tetrachloride (CAS Number 56-23-5)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ♦ US EPA RSL	1.4×10^{-5}	0.07	multistage model with linear extrapolation from the point of departure	metabolized dose based on PBPK[2] modeling	Based on hepatocellular carcinomas and adenomas in mice exposed for 6 hours/day, 5 days/week for 104 weeks by inhalation. Pharmacokinetic models were used to perform a $route_{Inhalation}$-to-$route_{Oral}$ extrapolation.
HC DWQ	2.9×10^{-6} to 8.6×10^{-5}	--[3]	--	--	Based on hepatocellular carcinomas in rats and mice in two studies, including the same study used by US EPA IRIS
CA EPA PHG	5.6×10^{-6}	0.18	linearized multistage model	--	Based on hepatomas in male and female mice exposed by gavage two to three times per weeks for a total of 46 treatments (about 4 months) and then observed for about another 3 months.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2]Dose adjustment from animals to humans were based on physiologically-based pharmacokinetic models.

[3]A cancer potency factor was not derived. The range of risk specific doses was obtained from the drinking water unit risk range of 3.3×10^{-7} to 1.0×10^{-5} per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day. It is not clear whether these estimates represent maximum likelihood or upper-bound risk values.

2. Recommendation and Rationale

The US EPA IRIS and CA EPA PHG cancer potency factors and the HC DWQ risk-specific doses for carbon tetrachloride are based on liver tumors in animals. They differ in the specific animal dose response data sets chosen for the derivations and the methods used to derive cancer potency factors or risk-specific doses. HC DWQ reports drinking water unit risk values (cancer risk per unit concentration in drinking water), does not specify whether the values are maximum likelihood or upper-bound risk estimates and provides very little detail documenting how the drinking water unit risks were derived. The CA EPA PHG cancer potency factor is based on rodent data from a relatively short-duration study and the documentation does not fully describe how the value was derived. The US EPA IRIS derivation is more transparent, uses data from a full-lifetime duration study, and is more consistent with generally accepted risk assessment practices. Therefore, the US EPA IRIS cancer potency factor (0.07 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for carbon tetrachloride. The carbon tetrachloride risk specific dose calculated from this toxicity value is 1.4×10^{-5} mg/kg/day.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: November, 2004; revised January, 2018

4. References for Summary Table

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/18/2018) at https://oehha.ca.gov/air/air-toxics-hot-spots

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/18/2018) at http://www.oehha.ca.gov/water/phg/allphgs.html.

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/18/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/18/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System

Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
Health Effects Assessment Summary T) Tables
Provisional Peer Reviewed Toxicity Values
Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Carbon Tetrachloride
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Carbon Tetrachloride (CAS Number 56-23-5)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL	100	1.43×10^4 (HEC)	BMDL (internal dose metric)	100	Based on liver toxicity in male and female rats exposed via inhalation for 6 hours/day, 5 days/week for 104 weeks. Time-weighted-continuous study NOEL = 5.6×10^3 mcg/m^3 (0.9 ppm); LOEL = 2.8×10^4 mcg/m^3 (4.5 ppm). BMR was a 10% increase (above controls) in incidence of rats with fatty changes in the liver. HEC derived using PBPK models for rats and humans.
ATSDR	180 (0.03 ppm)	5.6×10^3 (0.9 ppm) (HEC)	NOEL	30	Based on the same study used by US EPA IRIS. HEC derived using default systemic gas dosimetric adjustment.
CA EPA REL	40	1.1×10^4 (1.7 ppm)	LOEL	300	Based on increased relative liver weight in female guinea pigs exposed via inhalation for 7 hours/day, 5 days/week for 6 months. No effects were observed in males.
RIVM (2001)	60	6.4×10^3	NOEL	100	Based on liver toxicity in male and female rats in a 200-day inhalation study. Study LOEL = 1.3×10^4 mcg/m^3.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

BMR: benchmark response; BMDL: 95% lower limit on benchmark dose; HEC: human equivalent concentration; NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The reference concentrations for carbon tetrachloride derived by authoritative bodies listed in item 5 (below) are all based on liver toxicity observed in rats or guinea pigs exposed via inhalation, as well as kidney and spleen toxicity observed in rats in one study. A LOEL was observed in the subchronic guinea pig study that, on a time-weighted continuous basis, was between the rat LOELs and the rat NOELs (one of which was from a chronic study). Although this might suggest that guinea pigs could be a more sensitive species than rats for carbon tetrachloride liver toxicity, CA EPA REL considered the response observed in guinea pigs a minimal LOEL, since effects were only seen in one sex (females, not males) and the increase in relative liver weight, although statistically significant, was only about 10%. Therefore, the lowest dose in the guinea pig study appears to be close to a subchronic NOEL. The well-conducted chronic inhalation study in rats is preferred to the subchronic guinea pig or the subchronic rat study as the basis for a chronic reference concentration. The US EPA IRIS used a full physiologically-based pharmacokinetic modeling approach, combined with benchmark dose modeling to derive a point of departure from the chronic rat study. US EPA IRIS applied a total uncertainty factor of 100 to the point of departure, including 10 for human intraspecies variability, a reduced interspecies uncertainty factor of 3 based on the use of models to account for species differences in pharmacokinetics and an additional database uncertainty factor of 3 (given the lack of a multi-generation reproductive toxicity study). The ATSDR chronic minimal risk level was derived by using the study NOEL as the point of departure and applying a total uncertainty factor of 30 to the point of departure. The ATSDR uncertainty factors included 10 for intraspecies variability and a reduced value of 3 for interspecies variation based on a default interspecies pharmacokinetic extrapolation for a systemic gas. Overall, the US EPA reference concentration derivation is more consistent with generally accepted risk assessment practices. Therefore, the US EPA IRIS reference concentration (100 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for carbon tetrachloride.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/19/2018) at http://www.atsdr.cdc.gov/toxpro2.html, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/19/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/19/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/19/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Carbon Tetrachloride
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for Carbon Tetrachloride (CAS Number 56-23-5)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ♦ US EPA RSL	0.17	6×10^{-6}	linear extrapolation from a point of departure based on benchmark concentration modeling	average blood level of parent and associated air level based on PBPK[2] modeling	Based on adrenal pheochromocytomas in mice exposed for 6 hours/day, 5 days/week for 104 weeks by inhalation. Increased liver tumor incidences were also observed in mice and rats in the same study. Adrenal tumors in mice gave highest potency estimate.
US EPA HEAST	0.07	1.5×10^{-5}	linearized multistage model	body surface area[3]	Unit risks were estimated based on $route_{Oral}$-to-$route_{Inhalation}$ extrapolation of data from four studies where increased incidence of liver tumors was observed in mice, rats, and hamsters exposed via gavage for varying less-than-lifetime durations. Extrapolation assumed 70 kg adult body weight, 20 m^3/day continuous inhalation and 40% human absorption via inhalation. The unit risk value is the geometric mean of the results from the four studies.

CA EPA CPF	0.024	4.2×10^{-5}	linearized multistage model	body surface area[3]	Based on three of the same studies and reviews used by US EPA HEAST (rat data were excluded). $Route_{Oral}$-to-$route_{Inhalation}$ extrapolation assumed 60 kg adult body weight, continuous exposure, daily inhalation rate of 18 m^3/day, and 50% human absorption via inhalation. The unit risk value is the middle estimate of the results from the three studies.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million, where 1×10^{-6} air concentration = 1×10^{-6}/unit risk.
[2]Dose adjustment from animals to humans were based on physiologically-based pharmacokinetic models.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.

2. Recommendation and Rationale

The inhalation unit risks for carbon tetrachloride derived by authoritative bodies are based on increased incidence of pheochromocytomas in mice exposed by inhalation (US EPA IRIS) or by route-to-route extrapolation of data showing increased liver tumor incidence in rats, mice and hamsters exposed via gavage (US EPA HEAST, CA EPA CPF). In the absence of other study deficiencies, assessment based on data from a study using the relevant route of exposure (i.e., inhalation) is preferable to assessment based on route extrapolation. The data used by US EPA IRIS are from a well-conducted, lifetime inhalation study in mice and rats and so are preferred both because they represent response via the relevant exposure route and for full lifetime exposure, unlike the gavage studies. The US EPA IRIS derivation based on pharmacokinetic modeling to estimate a human equivalent benchmark concentration is also more consistent with generally accepted risk assessment practices. Therefore, the US EPA IRIS unit risk (6×10^{-6} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for carbon tetrachloride. The carbon tetrachloride risk specific air concentration calculated from this toxicity value is 0.17 mcg/m^3.

3. Review Dates

Summary table completion: July 2004; revised January, 2018
Toxicity value recommendation: November, 2004; revised January, 2018

4. References for Summary Table

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/18/2018) at https://oehha.ca.gov/air/air-toxics-hot-spots.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/18/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/18/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System
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Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
    Health Effects Assessment Summary T) Tables
    Provisional Peer Reviewed Toxicity Values
Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Chlordane
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Chlordane (CAS Number 12789-03-6)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
General Population					
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW	5×10^{-4}	0.15	NOEL	300	Based on hepatic necrosis in mice exposed via the diet in a 104-week study.
US HEAST	6×10^{-5}	0.055	NOEL	1000	Based on liver hypertrophy in female rats exposed via the diet in a 130-week study.
NYS DEC (1997)	5.5×10^{-5}	0.055	NOEL	1000	Based on same study, species, sex, and effects as US EPA HEAST (1997).
ATSDR	6×10^{-4}	0.055	NOEL	100	Based on same study, species, sex, and effects as US EPA HEAST (1997).
WHO (2011)	5×10^{-4}	0.05	NOEL	100	Based on same study, species, sex, and effects as US EPA HEAST (1997).
Child-Specific Reference Dose (chRD)					
CA EPA chRD*	3.3×10^{-5}	0.1	LOEL	3000	Based on alterations of sex steroid mediated behaviors of male and female rats exposed during gestation and lactation (day 4 of gestation through day 21 of lactation) and directly via gavage from postnatal day 22 to postnatal day 80. Both dams and pups were dosed (0.1 mg/kg/day) with technical chlordane. The study did not identify a NOEL.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.
NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the US EPA IRIS chlordane reference dose is liver necrosis in mice chronically exposed to chlordane via the diet. The basis for the reference doses derived by the other four agencies (US HEAST, NY DEC, ATSDR and WHO) is liver hypertrophy in female rats chronically exposed to chlordane via the diet in a parallel experiment by the same investigators as the US EPA IRIS mouse study. Although US EPA IRIS previously based a reference dose derivation on the female rat data, the IRIS derivation discusses a re-evaluation of those data and notes that interpretation of the liver lesions is confounded by leukemia-related liver effects in some animals. The older EPA analysis (US HEAST) also included a 10-fold uncertainty factor to account for lack of an adequate reproductive toxicity study and an adequate chronic toxicity study in a second species and the generally insensitive endpoints studied. The latter two points are questionable, given the two rodent studies used as the critical studies in the two different assessments, and the large database of supporting studies indicating the liver as the primary target organ for chlordane toxicity. In the more recent US EPA IRIS derivation, an extra uncertainty factor of 3 was applied to account for the lack of an adequate reproductive study, and is more consistent with the quality of the database and accepted practice. Given the confounding of the female rat liver non-neoplastic effects by the leukemia-related effects and the database uncertainty factor used in the US EPA IRIS assessment, the US EPA IRIS reference dose (5×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for chlordane in scenarios involving only adult exposure.

CA EPA has developed a program to derive reference doses for evaluating childhood exposures to contaminants in and around schools. This program stems from the possibility that children may be more sensitive than adults to contaminant exposures. CA EPA bases child-specific reference doses (chRD), when possible, on studies in young animals or children rather than on studies based on adult animal or humans and the use of an uncertainty factor to compensate for typically unknown adult-child differences in pharmacokinetics and pharmacodynamics. CA EPA identified such studies for chlordane. CA EPA based their child-specific reference dose for chlordane on developmental neurological effects in young male rats exposed prenatally and postnatally. Although the study was published in a peer-reviewed journal, the US EPA IRIS has serious concerns about the study results, interpretation, and the identification of a LOEL. US EPA IRIS noted that "The lack of consistent dose-response relationships among the effects noted in this study, as well the uncertainty of their toxicological significance, preclude a clear interpretation of this study and assignment of any adverse effect levels." Consequently, US EPA IRIS did not use the study to derive a reference dose. CA EPA applied a total uncertainty factor of 3000 to the study LOEL to compensate for animal to human extrapolation (10), the use of a LOEL (10), human variation (10), and inadequate database for hematotoxicity, immunotoxicity, neurotoxicity, and the lack of a valid developmental study (3). The CA EPA chRD (3.3×10^{-5} mg/kg/day) is the only child-specific toxicity value derived by an authoritative body in item 5 (below), and is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for chlordane in scenarios involving child exposure.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/16 /2018) at http://www.atsdr.cdc.gov/mrls/index.asp, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA chRD (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Child-Specific Reference Doses. Last accessed (01/16 /2018) at http://www.oehha.ca.gov/public_info/public/kids/chrds.html.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Chlordane. Albany, NY: Division of Water.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/16 /2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/16 /2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/16 /2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/16 /2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/16 /2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html, with supporting documentation at http://www.who.int/water_sanitation_health/dwq/chemicals/en/index.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values

Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Chlordane
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Chlordane (CAS Number 12789-03-6)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: ♦ US EPA HEAST (1997) ♦ US EPA Region 3 (2004)	2.9×10^{-6}	0.35	linearized multistage model, extra risk	$BW^{3/4}$ [2]	Based on the geometric mean of 5 sets of dose-response data for liver tumors in mice exposed via the diet.
CA EPA (1997)	7×10^{-7}	1.3	Linear extrapo-lation from LED_{10} [3] point of departure	$BW^{3/4}$ [2]	Based on the geometric mean of 4 sets of dose-response data for liver tumors in mice exposed via the diet.
NYS DEC (1997)	1.5×10^{-6}	0.68	linearized multistage model, extra risk	$BW^{3/4}$ [2]	Based on the geometric mean of 4 sets of dose-response data for liver tumors in mice exposed via the diet.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[3]LED_{10} = The 95% lower confidence limit on the dose that causes a 10% increase in tumor incidence.

2. Recommendation and Rationale

The basis of the cancer potency factors for chlordane derived by authoritative bodies is an increased incidence of liver tumors in male and female mice chronically exposed to chlordane in the diet. In each case, the derived cancer potency factor is a geometric mean of cancer potency factors from several individual tumor-data sets. Four data sets are common to all three derivations, while the US EPA value includes data from a fifth study not represented by the other two values. All values are based on body weight interspecies dose scaling. Cal EPA derived their value based on a point-of-departure low-dose extrapolation methodology, while the NYS DEC and US EPA values are derived using the linearized multistage model extrapolation procedure. Although the Cal EPA point-of-departure method derivation is more consistent with current accepted risk assessment practices, the US EPA value reflects more extensive and more recent dose-response data. Therefore, the US EPA cancer potency factor (0.35 per

mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for chlordane. The chlordane risk specific dose calculated from this toxicity value is 2.9×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: June, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/18/2018) at http://www.oehha.ca.gov/water/phg/allphgs.html.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Chlordane. Albany, NY: Division of Water.

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/16/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/16/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Chlordane
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Chlordane (CAS Number 57-74-9)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS (2004) Also used by: ◆ US EPA Region 3 (2004)	0.7	650	NOEL	1000	Based on increased liver weights in rats exposed by inhalation 8 hours per day, 5 days per week, for 13 weeks. Study LOEL = 6500 mcg/m^3.
ATSDR (1994)	0.02	24	NOEL	1000	Based on hepatocellular hypertrophy in the same study used by US EPA IRIS (2004). Study LOEL = 240 mcg/m^3.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The available reference concentrations for chlordane derived by authoritative bodies from the list in item 5 (below) are based on the same subchronic inhalation study in rats. The ATSDR considered the lowest exposure level from this study a NOEL and the next level (the middle exposure level) a LOEL for mild liver effects (hepatocellular enlargement or vacuolization and slight changes in serum chemistry). The ATSDR applied a total uncertainty factor of 1000 to the NOEL, including 10-fold each for intraspecies variability, interspecies variability, and use of a subchronic study. The US EPA did not consider the mild liver lesions at the middle exposure level adverse, and designated this level the NOEL. The LOEL was assigned the highest exposure level for increased liver weights and changes in serum chemistry indicative hepatic functional alteration. The US EPA used dosimetric modeling for a particle extrarespiratory effect to estimate the human equivalent concentration at the NOEL, and applied a total uncertainty factor of 1000, including 3 for inter species extrapolation, 10 for intraspecies variability, 10 for the use of a subchronic study, and an additional 3-fold to account for database limitations, based on the lack of reproductive studies. Although the mild effects seen at the lowest dose in the study progressed to more pronounced effects at higher doses in rats, the same study reported no effects in monkeys at the middle exposure level. This suggests that rats may be more sensitive to the liver effects of chlordane than primates, and supports US EPA's use of the higher LOEL, as response levels in primates may be more relevant to human effect levels. The US EPA derivation also uses dosimetric

modeling to estimate the point of departure, which is more consistent with current risk assessment practices. Therefore, the US EPA reference concentration (0.7 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chlordane.

3. Review Dates

Summary table completion: December, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1994. Toxicological Profile for Chlordane Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Last accessed (01/16/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/16/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. 2004. Last accessed (01/16/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Chlordane
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for Chlordane (CAS Number 57-74-9)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ♦ US EPA RSL	0.01	1×10^{-4}	linearized multistage model	$BW^{¾}$ [2]	The unit risk was estimated from an oral cancer potency factor using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. The cancer potency factor is the geometric mean of five dose-response datasets from three chronic dietary studies in which chlordane increased the incidence of liver tumors in mice.
CA EPA TCDB (supporting documentation from CA EPA PHG, NYS DEC, 1997)	2.9×10^{-3}	3.4×10^{-4}	linearized multistage model	BW surface area [3]	The unit risk was estimated from an oral cancer potency factor using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. Chronic dietary studies showed chlordane increased the incidence of liver tumors in mice. The cancer potency factor is based on the geometric mean of four dose-response datasets from four studies.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million, where 1×10^{-6} concentration $= 1 \times 10^{-6}$ inhalation unit risk.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.

2. Recommendation and Rationale

Chlordane is a toxicant that is expected to be absorbed into the body and cause systemic cancer effects following oral or inhalation exposure. A unit risk for chlordane based on inhalation exposures is not available from the authoritative bodies listed in item number 5 (below). However, the US EPA IRIS

derived a unit risk (1×10^{-4} per mcg/m^3) from their oral cancer potency factor (0.35 per mg/kg/day) using a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day. The CA EPA derived unit risk (3.4×10^{-4} per mcg/m^3) from their oral cancer potency factor (1.2 per mg/kg/day) using the same exposure route extrapolation used by US EPA. The recommended cancer potency factor for chlordane is US EPA's value of 0.35 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for Chlordane). Therefore, a unit risk of 1×10^{-4} per mcg/m^3 based on the exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for chlordane. The risk specific air concentration calculated from this toxicity value is 0.01 mcg/m^3.

3. Review Dates

Summary table completion: December, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

CA EPA TCDB (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Toxicity Criteria Database. Last accessed (01/17/2018) at https://oehha.ca.gov/chemicals.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Cadmium. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values

Chemical Name: Chlorobenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Chlorobenzene (CAS Number 108-90-7)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA HEAST (1997) ♦ NYS DEC (1997)	0.02	19	NOEL	1000	Based on histopathologic changes in the liver of male and female dogs given chlorobenzene in capsules for 13 weeks. Study LOEL = 39 mg/kg/day
RIVM (2000)	0.2	19.5	NOEL	100	Based on the same data as the US EPA IRIS derivation.
Health Canada (1992)	0.086	43	NOEL	500	Based on histopathologic changes in liver of male rats and mice given chlorobenzene by gavage for 103 weeks.
WHO (1996)	0.086	43	NOEL	500	Based on same data as Health Canada (1991).

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The basis for the US EPA IRIS and RIVM chlorobenzene reference doses is liver histopathology effects in dogs exposed orally for 13 weeks. The basis for the Health Canada and WHO reference doses for chlorobenzene is liver neoplastic nodules in male rats chronically exposed to chlorobenzene via gavage. Although the rodent study would generally be chosen as the basis for a reference dose because animals were exposed for their entire lifetimes (rather than only sub-chronically as in the dog study), the dog study identified a LOEL dose essentially the same as the NOEL dose in the rat study, suggesting dogs may be a more sensitive species. RIVM only applied a total uncertainty factor of 100 to the dog NOEL, suggesting that an additional uncertainty factor to account for the use of sub-chronic value was unnecessary because a higher NOEL dose existed (i.e., the rat NOEL). This rationale does not account for the LOEL dose in the dog study and is not consistent with generally accepted risk assessment practice. Therefore, the US EPA reference dose (0.02 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for chlorobenzene.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1990. Toxicological Profile for Chlorobenzene. U.S. Department of Health and Human Services, Public Health Service. December. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

Health Canada. 1992. Priority substances list assessment report No. 3: Chlorobenzene. Ottawa. Ministry of Public Works and Government Services.
Last accessed (01/17/2018) at https://www.tera.org/iter/HCPSL1supportdoc.pdf

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 193-216.
Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

NYSDEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Chlorobenzene. Albany, NY: Division of Water.

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 997-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO. (World Health Organization). 1996. Monochlorobenzene.
Last accessed (01/17/2018) at https://www.who.int/water_sanitation_health/water-quality/guidelines/chemicals/monochlorobenzene/en/

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Chlorobenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Chlorobenzene (CAS Number 108-90-7)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
ATSDR (1990) Health Canada (1991) RIVM (2000) US EPA IRIS (2004)	--	--	--	--	One chronic animal bioassay showed a positive trend for carcinogenicity but had serious methodological flaws. Data are inadequate to evaluate carcinogenic potential.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for chlorobenzene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1990. Toxicological Profile for Chlorobenzene. U.S. Department of Health and Human Services, Public Health Service. December. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

Health Canada. 1992. Priority substances list assessment report: Chlorobenzene. Ottawa. Ministry of Public Works and Government Services. Last accessed (01/17/2018) at https://www.tera.org/iter/HCPSL1supportdoc.pdf

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 193-216. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Chlorobenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Chlorobenzene (CAS Number 108-90-7)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA OSRTI* Also used by: • US EPA RSL*	50	4.6×10^4 (HEC)	$BMCL_{10}$	1000	Based on liver and kidney toxicity in parental and offspring rats exposed by inhalation for 6 hours/day and 7 days/week in a multigenerational study. Study LOEL = 1.73×10^5 mcg/m^3 (time weighted).
HC PSAP modified by Health Canada (1996a, b) as cited by TERA, 2004	10	5×10^4	LOEL	5000	Based on increased absolute and relative liver weights in rats exposed by inhalation for 7 hours/day, 5 days/week for up to 24 weeks.
RIVM (2001)	500	--	--	--	Based on same study as Health Canada. Value was adopted from a third-party risk assessment without supporting documentation.
CA EPA REL	1×10^3	1.2×10^5	NOEL	100	Based on same study as US EPA OSRTI.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
HEC: human equivalent concentration; $BMCL_{10}$: 95% lower limit on benchmark concentration at 10% response above background; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The reference concentrations for chlorobenzene derived by authoritative bodies from the list in item 5 (below) are all based on liver or kidney toxicity in rats exposed via inhalation. The Health Canada and RIVM derivations are based on a subchronic LOEL for liver toxicity in rats exposed via inhalation. RIVM concluded no adequate data were available to derive a reference concentration, but chose to adopt a value derived by another organization without any supporting documentation. The Health Canada derivation is a modification of the value they derived under the priority substances program (HC PSAP). TERA (2004) reports that Health Canada indirectly scaled the exposure concentration in rats to an exposure concentration in a human child (age 5 –11) by estimating per unit body weight intake in rats and then back-calculating a human exposure concentration based on assumed inhalation rates and body weights. Despite that adjustment, Health Canada applied a 10-fold uncertainty factor for animal-to-human variability, along with 10-fold factors for human variability and use of a subchronic value. They also used a 5-fold uncertainty factor for use of a minimal LOEL, for a total uncertainty factor of 5000. The CA EPA value is derived from a NOEL in a multigenerational reproductive study where increased liver weights and kidney tubule dilation were observed in both parental and offspring male rats. US EPA OSRTI derived an RfC based on the same data by estimating the 95% lower bound on a benchmark concentration at 10% extra risk. US EPA applied a total uncertainty factor of 1000, including 10-fold to account for human variability, 3-fold with a default pharmacokinetic adjustment (equal to 1) to account for animal-to-human variability, 10-fold for the lack of a chronic inhalation study and an additional 3-fold to account for database uncertainties including lack of data on neurotoxicity and toxicity of the entire respiratory system. The CA EPA applied the same 10-fold and 3-fold uncertainty factors to account for intra- and animal-to-human variability, respectively, and included a 3-fold uncertainty factor for use of a subchronic NOEL. CA EPA used a pharmacokinetic adjustment of 2-fold to increase the human equivalent NOEL, based on the ratio of blood:air partitioning coefficients in rats and humans. Current guidance is to use a default pharmacokinetic adjustment of 1 if partitioning coefficient data are unavailable or if the animal:human ratio is greater than 1. Overall, the US EPA derivation is most consistent with generally-accepted risk assessment practice. Therefore, the US EPA reference concentration (50 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chlorobenzene.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/18/2018) at https://oehha.ca.gov/air/crnr/notice-adoption-air-toxics-hot-spots-program-technical-support-document-derivation

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/18/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

Health Canada. 1996a. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. Ottawa: Ministry of Supply and Services Canada. H46-2/96-194E.

Health Canada. 1996b. Canadian Environmental Protection Act. Priority Substances List. Supporting Documentation: Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. (unpublished). (as cited by TERA, 2004)

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/18/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

Toxicology Excellence for Risk Assessment (TERA). 2004. International toxicity estimates for risk database. Last accessed (01/18/2018) at http://www.tera.org/iter/

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund . Last accessed (01/18/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Chlorobenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Chlorobenzene (CAS Number 108-90-7)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	No human data, inadequate animal data and predominantly negative genetic toxicity data in bacterial, yeast, and mouse lymphoma cells.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An inhalation unit risk for chlorobenzene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System

National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Chloroform
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Chloroform (CAS Number 67-66-3)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS* Also used by: • US EPA RSL • US EPA OPP • US EPA ODW • US EPA HEAST (1997)	0.01 0.01	12.9 1.2	LOEL $BMDL_{10}$	1000 100	Based on moderate to marked fatty cyst formation in the liver and elevated SGPT (serum glutamate-pyruvate transaminase) in male and female dogs in a 7.5-year feeding (gelatin capsule) study. The study LOEL of 15 mg/kg/day was time-weighted based on exposure for 6 days per week. US EPA IRIS also fit a benchmark dose model to the same data, obtaining a lower point of departure, but also decreasing the total UF, resulting in the same RfD.
ATSDR	0.01	12.9	LOEL	1000	Based on the same study and review as US EPA IRIS.
RIVM (2001)	0.03	30	LOEL	1000	Based on liver toxicity in male and female mice in a chronic drinking water study (limited information available.)
WHO (2011)*	0.015	12 mg/L	LED_{05}	25	Based on the same data used by US EPA IRIS. A PBPK model was used to estimate the internal dose associated with a 5% increased incidence of hepatic cysts. The point of departure was reported as the continuous lifetime drinking water exposure level corresponding to the modeled internal dose metric at the LED_{05}.

HC DWQ*	6.2×10^{-3}	13	LOEL	2100	Based on the same data used by US EPA IRIS.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.

$BMDL_{10}$: 95% lower limit on benchmark dose associated with a 10% increased risk above background; LED_{05}: 95% lower limit on effective dose associated with a 5% increased risk above background; LOEL: lowest observed effect level; PBPK: physiologically-based pharmacokinetic model; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the US EPA IRIS, ATSDR, WHO and HC reference doses is liver toxicity in dogs chronically exposed to chloroform in gelatin capsules. The basis for the RIVM reference dose for chloroform is liver toxicity mice chronically exposed to chloroform in drinking water. A NOEL was not observed in either study. The lower LOEL in the dog study was dismissed in the RIVM derivation without a clear rationale provided in the limited documentation for that value. The dog study suggests that effects may occur at lower doses than the LOEL identified in the mouse study. HC DWQ used the same LOEL point of departure as US EPA IRIS and ATSDR (rounded to two significant figures) but applied a total uncertainty factor of 2100, including 10-fold factors for human and animal-to-human variability, a factor of 7 to account for less-than-lifetime exposure and a factor of 3 to account for the use of a LOEL. Treating data from a 7.5 year study as representing subchronic effects is not consistent with generally-accepted risk assessment practice. US EPA IRIS and ATSDR both considered the 7.5 year duration of the dog study to be a sufficient fraction of the lifetime to not require a further uncertainty factor for the use of less-than-lifetime data. Therefore, the HC DWQ value is not preferred. WHO (2011) obtained a point of departure by using a PBPK model to estimate the lower bound on the internal dose associated with a 5% increase in incidence of liver cysts, and then estimating the continuous lifetime drinking water exposure concentration corresponding to this internal dose metric. WHO then applied a total uncertainty factor of 25 to this point of departure, and assumed a 64 kg adult drinks 2 liters of water per day to obtain their RfD. The uncertainty factor included a factor of 10 to account for human variability and a factor of 2.5 (combined with a pharmacokinetic model) to account for animal-to-human variability. US EPA IRIS and ATSDR applied a total uncertainty factor of 1000 to the study LOEL, including 10-fold factors to account for human and animal-to-human variability and the use of a LOEL. US EPA IRIS also showed that obtaining a $BMDL_{10}$ from the same dose-response data and applying a total uncertainty factor of 100 to that point of departure (treating the $BMDL_{10}$ as equivalent to a NOEL), resulted in the same RfD. The WHO assessment based on pharmacokinetic modeling of a 5% effect level internal dose is consistent with generally-accepted risk assessment practices, but their use of a 2.5 animal-to-human uncertainty factor as well as a default adult body weight of 64 kg deviates somewhat from conventional practice. If conventional defaults of an animal-to-human uncertainty factor of 3 (with a pharmacokinetic model) and adult body weight of 70 kg were applied to WHO point of departure, the resulting RfD would be nearly the same as the US EPA IRIS and ATSDR value. Therefore, the US EPA IRIS and ATSDR reference dose (0.01 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for chloroform.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/16/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/16/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/16/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/16/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/16/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/16/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA OPP (United States Environmental Protection Agency, Office of Pesticide Programs). Pesticide Reregistration Status. Last accessed (01/16/2018) at http://www.epa.gov/opp00001/reregistration/status.htm.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/16/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/16/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. **Authoritative Bodies**

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation

Health Effects Assessment Summary Tables
Provisional Peer Reviewed Toxicity Values
Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Chloroform
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Cancer Potency Values for Chloroform (CAS Number 67-66-3)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS	--	--	--	--	The US EPA states there is sufficient evidence to conclude that a non-genotoxic mode of action for carcinogenicity applies to chloroform. Based on a margin of exposure analysis, the chloroform RfD is considered protective for oral cancer risk.
CA EPA (1990, 2009)	3.2×10^{-5}	0.031	linearized multistage model, extra risk	body surface area [2]	Based on the geometric mean of 11 slope factors from several studies of the incidence of liver and kidney tumors in male and female mice and rats

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.

2. Recommendation and Rationale

The CA EPA cancer potency estimate is based on the geometric mean of 11 data sets from seven studies showing an increased incidence of liver and kidney tumors in rats and mice. The US EPA does not recommend an oral cancer potency factor for chloroform because of evidence that suggests that chloroform-induced kidney and liver cancers in laboratory animals are the result of repeated cytotoxicity and regenerative cell proliferation in these target organs, and that these events occur only after high chloroform doses. Although sustained or repeated cytotoxicity with regenerative hyperplasia is probably a causal factor in animal cancers caused by chloroform, other modes of action (e.g., genotoxicity) could also contribute at lower doses, and these have not been rigorously investigated. Therefore, the CA EPA cancer potency factor (0.031 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for chloroform. The chloroform risk specific dose calculated from this toxicity value is 3.2×10^{-5} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA (California Environmental Protection Agency). 1990. Proposed Identification of Chloroform as a Toxic Air Contaminant: Part B Health Assessment. Sacramento, CA: California Air Resources Board, California Environmental Protection Agency. Last accessed (01/20/2018) at https://www.arb.ca.gov/toxics/id/summary/chloroform_B.pdf

CA EPA (California Environmental Protection Agency). 2009. Technical Support Document for Cancer Potency Factors 2009. Office of Environmental Health Hazard Assessment. Last accessed (01/20/2018) at: http://oehha.ca.gov/air/crnr/technical-support-document-cancer-potency-factors-2009

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Chloroform
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Chloroform (CAS Number 67-66-3)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
ATSDR	100*	9.8×10^3	LOEL	100	Based on liver effects in 68 workers occupationally exposed to chloroform over one to four years.
US EPA RSL**	98	9.8×10^3	LOEL	100	Based on the ATSDR RfC rounded to two significant digits.
CA EPA REL	300	7.8×10^4	LOEL	300	Based on liver and kidney toxicity in rats exposed by inhalation for 7 hours/day, 5 days/week for 6 months.
RIVM (2001) TERA	100	1.1×10^5	NOEL	1000	Based on the same study as CA EPA; limited documentation.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor; ppm: parts per million.

*The ATSDR value is reported as 0.02 parts per million (ppm). For chloroform, 1 ppm = 4.88 mg/m^3.
**Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The reference concentrations for chloroform derived by authoritative bodies from the list in item 5 (below) are based on liver toxicity observed in workers exposed to chloroform in workplace air, and liver and kidney toxicity observed in mice and rats exposed to chloroform via inhalation. The CA EPA and RIVM based their derivations on a 6-month rat inhalation study. The CA EPA considered the lowest exposure level in that study a LOEL and converted that exposure level to a human equivalent air concentration by adjusting to a time-weighted continuous exposure that was then increased by a pharmacokinetic adjustment of 3-fold representing the ratio of rat:human blood:air partitioning coefficients. RIVM cites an earlier chloroform assessment without full documentation that identified the

same exposure level in the rat study as a NOEL. The CA EPA REL documents significant increased relative kidney weight compared to controls at the lowest dose in all animals tested. Therefore, the RIVM analysis appears to be in error in this respect. RIVM equated the rat exposure level to an equivalent human exposure level without any adjustment for non-continuous exposure or pharmacokinetic variability. The CA EPA applied a total uncertainty factor of 300, including 10-fold to account for human variability, 3-fold (with a pharmacokinetic adjustment) to account for animal-to-human variability and 10-fold for use of a LOEL. The CA EPA pharmacokinetic adjustment does not following US EPA's inhalation dosimetry default guidance to use a conversion factor of 1 for category 3 gases when the animal blood:air partitioning coefficient is larger than the human partitioning coefficient. RIVM applied a total uncertainty factor of 1000 that, as cited by TERA, included 10-fold factors for intra- and animal-to-human variability and another 10-fold factor accounting for the adjustment from discontinuous to continuous exposure. Neither the CA EPA nor RIVM provided any justification for not including an uncertainty factor accounting for the use of a subchronic point of departure. In terms of estimating the human equivalent concentration and in terms of applying uncertainty factors, neither the CA EPA nor the RIVM derivation is entirely consistent with generally accepted risk assessment practice and do not clearly document the bases for judgments made.

The ATSDR based their value on a human occupational study where workers were exposed to chloroform vapors for one to four years at concentrations that varied by approximately 100-fold. They considered the lower end of this range a LOEL for liver effects and applied a total uncertainty factor of 100 to that LOEL to account for human variability and the use of a LOEL. US EPA RSL adopted ATSDR's RfC derivation, with only a slight difference in rounding. When expressed with one significant figure, the values are the same. The ATSDR and US EPA derivations are generally more consistent with currently-accepted risk assessment practice than the CA EPA and RIVM derivations and are also preferred since they are based on human data. Therefore, the ATSDR reference concentration (100 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chloroform.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/16/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/16/2018) at https://oehha.ca.gov/air/crnr/notice-adoption-air-toxics-hot-spots-program-technical-support-document-derivation.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/16/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/16/2018) at https://www.tera.org/iter/

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/16/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
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  - Health Effects Assessment Summary Tables
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- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Chloroform
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Chloroform (CAS Number 67-66-3)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2004)	0.04	2.3×10^{-5}	linearized multistage model, extra risk	body surface area[2]	Based on route-to-route extrapolation from a single data set of hepatocellular carcinoma in female mice in a two-year oral gavage study.
Cal EPA (2002)	0.2	5.3×10^{-6}	linearized multistage model, extra risk	PBPK estimate of internal dose metric or body surface area[2] depending on data set and study analysis	Based on route-to-route extrapolation of several oral cancer potency estimates from chronic oral studies in mice and rats, specifically incorporating the arithmetic average of unit risks for renal tumors in male rats from two different analyses of two different studies (four total unit risks) and the geometric mean for two different analyses of supporting data sets of renal tumors in male mice and liver tumors in female rats (an additional four total unit risks).

Health Canada (2004) and as detailed by TERA (2004)	7.4×10^5 reported as lower bound on TC_{05} [3]; linear equivalent risk specific concentration = 14.8	-- [4]	--	PBPK estimate of internal dose metric	Based on the relationship between internal dose metrics derived via PBPK modeling and kidney tumor incidence in rats exposed for their lifetimes via drinking water. Benchmark dose modeling was used to derive the equivalent rate of metabolite formation in humans associated with a 5% increase in lifetime cancer risk and then a continuous inhalation exposure associated with the benchmark rate of metabolite formation was derived as the risk-specific concentration.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.

[3] TC_{05} = The concentration in air (expressed in mcg/m^3) associated with a 5% increase in incidence or mortality due to tumors.

[4] The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported, but would be equal to 1×10^{-6} divided by the 10^{-6} risk-specific concentration.

2. Recommendation and Rationale

The inhalation unit risks derived by authoritative bodies are all based on route-to-route extrapolation from studies of rats or mice orally exposed to chloroform. Increased incidence of liver tumors in mice and kidney tumors in rats was observed in these studies. The US EPA IRIS value is derived from liver tumor data in mice exposed by gavage while the Cal EPA and Health Canada values are based on the incidence of kidney tumors in rats exposed by gavage or drinking water. The US EPA IRIS notes that their assessment, originally done in 1987, does not incorporate new data or more recent cancer risk-assessment guidelines and is currently being revised. The oral cancer risk assessment on IRIS reflects the conclusion that chloroform carcinogenicity results from a non-genotoxic mode of action involving regenerative hyperplasia following tissue necrosis. Therefore, an oral cancer potency factor is not

derived and a margin of exposure analysis is presented supporting the oral reference dose (RfD) as being protective of increased cancer risk from chloroform exposure. The Cal EPA value was derived from two combined analyses of four separate data sets. One analysis followed older default practices for animal to human dose scaling, while the other used PBPK-based scaling to develop human doses equivalent to rodent exposures in terms of an internal dose metric. Of the four data sets, two were considered as the primary dose-response data by Cal EPA and two others were considered to be supporting data. No basis is provided for this distinction, and no basis is provided for the method used to combine the data sets, which entailed taking a geometric mean of the four derivations based on the supporting data sets and then combining, via an arithmetic mean, that geometric mean with the four derivations based on the primary data sets. The Health Canada derivation is based on one of the data sets considered as primary data by Cal EPA and used PBPK modeling and a benchmark dose approach to estimate the lower bound on the air concentration associated with a 5% increased excess tumor incidence. This derivation follows currently accepted risk assessment practice, but Health Canada did not explicitly report a unit risk or a 10^{-6} risk-specific concentration based on their derivation. However, since the 95% lower bound on the TC_{05} is reported, a linear extrapolation to the 10^{-6} risk-specific concentration is implied following currently accepted risk assessment practice by dividing the lower bound on the TC_{05} by 50,000. Dividing 10^{-6} by the 10^{-6} risk-specific concentration implied by the lower bound on the TC_{05} would yield the equivalent unit risk. Therefore, the Health Canada unit risk (6.8×10^{-8} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for chloroform. The chloroform risk specific air concentration calculated from this toxicity value is 14.8 mcg/m^3.

3. **Review Dates**

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2002. Air Toxics Hot Spots Program Risk Assessment Guidelines: Part II Technical Support Document for Describing Available Cancer Potency Factors. Sacramento, CA. Last accessed (01/18/2018) at https://oehha.ca.gov/media/downloads/crnr/tsdcancerpotency.pdf

Health Canada, Environment Canada. 2004. Health Bases Guidance Values for Substances on the Second Priority Substances List. Health Canada. Last accessed (01/18/2018) at http://publications.gc.ca/collections/Collection/H49-187-2004E.pdf

TERA (Toxicology Excellence for Risk Assessment). 2004. International toxicity estimates for risk database. Last accessed (01/18/2018) at http://www.tera.org/iter/

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Chromium (III)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Inorganic Chromium (III)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA HEAST (1997)	1.5	1468	NOEL	1000	Based on the absence of toxic effects in male and female rats fed 5% Cr_2O_3 baked in bread for 600 feedings (840 days) for an average total dose of 1800 g/kg. A LOEL was not identified. The NOEL was adjusted for continuous exposure and the molar fraction contribution of chromium (III) to Cr_2O_3. This RfD is limited to metallic chromium (III) of insoluble salts.
RIVM (2001)	5×10^{-3} (water soluble chromium compounds)	2.5 0.46	NOEL	500 100	Based on two chronic feeding study in rats with chromium compounds of varying water solubility (limited information available).
	5 (insoluble chromium compounds)	--	--	--	Based on RIVM's assertion that chronic NOELs for water insoluble chromium compounds are approximately 1,000 times higher than for soluble chromium compounds.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

Both chromium (III) reference doses are based on NOELs from chronic feeding studies in rats. There is a large degree of variation in NOEL (and therefore reference dose) estimates between the US EPA and RIVM because the toxicity in rodent feeding studies apparently varies substantially with the water solubility of the particular chromium compound being tested. The US EPA reference dose is only intended for assessment of exposure to insoluble chromium (III) salts. RIVM derived a value specifically from a soluble form of chromium (III), and then extrapolated that result to a second

reference dose for insoluble chromium compounds, based on an inference from available chronic rodent NOELs that insoluble forms were approximately 1000-fold less toxic than soluble forms. If chromium (III) is present in the form of soluble salts, or if the form of chromium (III) (and, therefore, its solubility) is unknown, then the RIVM reference dose for water-soluble compounds (5×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of a non-cancer-based soil cleanup objective for chromium (III). If it is known that chromium (III) is present as insoluble salts, then the US EPA reference dose (1.5 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for insoluble chromium (III) salts.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 249-257. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 997-1.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada

Chemical Name: Chromium (III)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. **Summary of Available Oral Cancer Potency Values for Inorganic Chromium (III)**

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (2000)	--	--	--	--	Human data are not available. Negative results for rats and mice have been reported in oral, inhalation, intrapleural injection, or intrabronchial implantation laboratory studies.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for chromium (III) is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2000. Toxicological profile for chromium. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
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New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Chromium (III)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Inorganic Chromium (III)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS (2004)	--	--	--	--	Data are considered to be inadequate for development of an RfC due to the lack of a relevant toxicity study addressing respiratory effects of chromium (III).
RIVM (2001)	60	600	NOEL	10	Based on kidney effects in workers occupationally exposed to metallic chromium. The reference concentration is intended only for metallic chromium and insoluble Cr(III) salts.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
NOEL: no observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The RIVM value is the only available reference concentration for chromium (III) derived by an authoritative body from the list in item 5 (below). Therefore the RIVM reference concentration (60 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chromium(III).

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
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New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Chromium (III)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. **Summary of Available Inhalation Unit Risk Values for Inorganic Chromium (III)**

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	The data from inhalation exposures of animals to trivalent chromium do not support determination of the carcinogenicity of trivalent chromium.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for chromium (III) is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
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Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Chromium (VI)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Inorganic Chromium (VI)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW ♦ US EPA HEAST (1997)	3×10^{-3}	2.5	NOEL	900	Based on a lack of adverse effects in male and female rats exposed via drinking water each day to chromium (VI) as K_2CrO_4 in a 1-year drinking water study. A study LOEL was not identified.
RIVM (2001)	5×10^{-3}	2.5	NOEL	500	Based on the same study used by US EPA IRIS.
CA EPA PHG*	2×10^{-4}	0.2	LOEL	1000	Based on indications of mild hepatotoxicity (chronic inflammation, fatty changes) in female rats exposed via drinking water each day to chromium (VI) as $Na_2Cr_2O_7$ in a 2-year study. A study NOEL was not identified.
ATSDR*	9×10^{-4}	0.09	$BMDL_{10}$ [2]	100	Based on indications of diffuse epithelial hyperplasia of the duodenum in female mice exposed via drinking water each day to chromium (VI) as $Na_2Cr_2O_7$ in a 2-year study. A study NOEL was not identified. Study LOEL = 0.38 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]$BMDL_{10}$: The lower 95% confidence limit on the benchmark dose (BMD) associated with a 10% increase (relative to controls) in the incidence of female mice with diffuse epithelial hyperplasia of the duodenum.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The animal study used as the basis for the US EPA IRIS and RIVM reference dose of chromium (VI) did not detect any effects. This is a serious limitation of the study. CA EPA and ATSDR based their

reference doses on observed effects (chronic inflammation and fatty changes in the livers of female rats or indications of diffuse epithelial hyperplasia of the duodenum in female mice, respectively) in lifetime studies that were well-designed, well conducted/reported and peer-reviewed. The 2-year studies used by CA EPA and ATSDR are a more appropriate basis for the derivation of a reference dose. In addition, both derivations are consistent with generally accepted risk assessment practices for high-to-low dose and animal-to-human extrapolations of non-cancer effects. CA EPA identified a LOEL, and used a 1000-fold uncertainty factor to compensate for animal-to-human extrapolation (10), the use of a LOEL (10), and human variation (10). ATSDR performed benchmark dose modeling of a variety of endpoints and selected the lowest $BMDL_{10}$ as their point of departure. ATSDR used a 100-fold uncertainty factor to compensate for animal-to-human extrapolation (10) and human variation (10). In this case, where a NOEL was not identified for the species/endpoint used by each agency, the selection of a benchmark dose as the point of departure is preferred because it replaces an assumed relationship between a LOEL and NOEL (a 10-fold difference) with a procedural equivalent of the NOEL (i.e., $BMDL_{10}$) based on the actual data and a mathematical model. Therefore, the ATSDR reference dose (9×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for chromium (VI).

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/20/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/20/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/20/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/20/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/20/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/20/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
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- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Chromium (VI)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Inorganic Chromium (VI)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA PHG*	2×10^{-6}	0.5	linear extrapolation from LED_{10}[2], estimated using a multistage model	$BW^{3/4}$ (3)	Based on increased incidences of adenomas and carcinomas in the small intestine of male mice exposed via drinking water in a 2-year study.
CA EPA CPF*	2.3×10^{-6}	0.42	linearized multistage model	body surface area[4]	Based on increased incidences of benign and malignant stomach tumors (combined) in mice exposed via drinking water in a three-generation study.
NYS DEC (2017)	1.9×10^{-6}	0.53	linear extrapolation from LED_{10}[2], estimated using a multistage model	$BW^{3/4}$ (5)	Same basis as for CA EPA PHG.
US EPA IRIS[6]	--	--	--	--	No data were located in the available literature that suggests chromium (VI) is carcinogenic by the oral route of exposure.
US EPA Draft (2010)*	2×10^{-6}	0.5	linear extrapolation from $BMDL_{10}$[7], estimated using a multistage model	$BW^{3/4}$ (3)	Based on increase incidences of adenomas and carcinomas in the small intestine of male mice exposed via drinking water in a 2-year study. Same study as used by CA EPA PHG.
US EPA RSL[8] *	2×10^{-6}	0.5	linear extrapolation from $BMDL_{10}$[7], estimated using the "best-fit" quantal model	$BW^{3/4}$ (3)	Based on increased incidences of adenomas and carcinomas in the small intestine of male mice exposed via drinking water in a 2-year study. Same study as used by CA EPA PHG.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} /cancer potency factor.

[2]LED_{10} = The 95% lower confidence limit on the effective dose (LED) associated with a 10% increase (relative to controls) in the incidence of tumors.
[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$.
[4]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.
[5]Factor for dose adjustment from animals to humans is (animal body weight (0.05 kg)/human body weight (80 kg)$^{0.25}$, where 80 kg is the mean adult human body weight recommended in US EPA (2011), and human LED_{10} = mouse LED_{10} x (0.05 kg / 80 kg)$^{1/4}$.
[6]US EPA IRIS file on carcinogenicity was last updated in 09/03/1998, and animal study used by CA EPA PHG to derive a cancer potency factor was published in 2008.
[7]$BMDL_{10}$: The lower 95% confidence limit on the benchmark dose (BMD) associated with a 10% increase (relative to controls) in the incidence of tumors. It is equivalent to the LED_{10}.
[8]US EPA RSL adopted the derivation and cancer potency factor of NJ DEP (2009).

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The CA EPA CPF cancer potency factor for chromium (VI) is based on a study with several methodological problems, including a viral infection that caused substantial intercurrent mortality, a single dose level, differences in the length of survival in different generations, and other factors. Thus, both CA EPA PHG and US EPA IRIS concluded that the study was unsuitable for the assessment of the oral carcinogenicity of chromium (VI). The CA EPA PHG and US EPA RSL cancer potency factors (0.5 per mg/kg/day) are the only other available final values from an authoritative body listed in item 5 (below). Both were derived using methods that are consistent with generally accepted risk assessment practices. The draft cancer potency factor derived by the US EPA IRIS is also 0.5 per mg/kg/day. New York State derived a cancer potency factor of 0.53 per mg/kg/day based on the same study as CA EPA and US EPA RSL, but using the US EPA's most recent recommendation of 80 kg for mean adult human body weight (US EPA, 2011). This value is preferred because it is based on the agency's most recent recommendation. Therefore, the NYS DEC cancer potency factor (0.53 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for chromium (VI). The chromium (VI) risk specific dose calculated from this toxicity value is 1.9×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/15/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/15/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

NJ DEP (New Jersey Department of Environmental Protection). 2009. Derivation of Ingestion-Based Soil Remediation Criterion for Cr+6 Based on the NTP Chronic Bioassay Data for Sodium Dichromate Dihydrate. Last accessed (01/15/2018) at http://www.state.nj.us/dep/dsr/chromium/.

NYS DEC (New York State Department of Environmental Conservation). 2017. Draft Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Chromium (hexavalent). Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA Draft (United States Environmental Protection Agency Integrated Risk Information System). 2010. Toxicological Review of Hexavalent Chromium (External Review Draft). EPA/635/R-10/004A. Washington, DC: US EPA. Last accessed (01/15/2018) at http://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=221433.

US EPA (United States Environmental Protection Agency). 2011. Exposure Factors Handbook: 2011 Edition. EPA/600/R-09/052F. Last accessed (01/15/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=20563.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
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- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Chromium (VI)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Inorganic Chromium (VI)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS	8.0×10^{-3}	0.714	LOEL	90	Based on nasal septum atrophy in workers exposed in chrome plating plants. The reference concentration applies to chromic acid mists and dissolved chromium (VI) aerosols.
US EPA IRIS Also used by: ♦ US EPA RSL*	0.1	34	$BMCL_{10}$[2]	300	Based on increased lung and spleen weight and several indicators of toxic effects on the lower respiratory system in bronchioalveolar lavage fluid in rats from two studies exposed to sodium dichromate particulate aerosols for 90 days. The reference concentration applies to chromium (VI) particulates.
CA EPA REL	0.2	24.5	$BMCL_{05}$[2]	100	Based on the same rat studies as the US EPA IRIS reference concentration for chromium (VI) particulates. This reference concentration is intended to apply to soluble hexavalent chromium compounds other than chromic acid.
	2×10^{-3}	0.68	LOEL	300	Based on the same human study as the US EPA IRIS reference concentration for chromium (VI) chromic acid mists and dissolved aerosols. This reference concentration is intended to apply to chromium trioxide as chromic acid mist.

TERA (2004)	0.3	80	BMCL[2,3]	300	Based on the same rat studies as the US EPA IRIS reference concentration for chromium (VI) particulates. This reference concentration is intended to apply to chromium particulates.
ATSDR*	5×10^{-3}	0.5	LOEL	100	Based on nasal irritation, mucosal atrophy, and ulceration and decreases in spirometric parameters in workers occupationally exposed to chromic acid mist. This reference concentration applies to dissolved chromium (VI) aerosols and mists.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

[2]$BMCL_{05 \text{ or } 10}$: The lower 95% confidence limit on the benchmark concentration (BMC) associated with a 5 or 10% increase (relative to controls) in the incidence of the selected toxicity endpoint.

[3]Whether TERA's BMCL represents a level associated with a 5 or 10% incremental increase in the modeled effect is not clearly presented in their documentation, but the range of BMCL values is the same as the range presented by US EPA IRIS documentation for their $BMCL_{10}$ estimates, suggesting TERA's estimates are also $BMCL_{10}$s.

NOEL: no-observed-effect-level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The reference concentrations for chromium (VI) derived by authoritative bodies from the list in item 5 (below) are based on data from occupational studies and inhalation studies in rats. The US EPA IRIS derived separate reference concentrations for particulate chromium (VI) aerosols and for chromic acid mists and other soluble chromium (VI) aerosols. TERA's reference concentration is specifically for hexavalent chromium particulates.

The CA EPA derived two reference concentrations, based on the same rat and human studies used for the two US EPA derivations, but one is specified for chromic acid mists and the other is for other hexavalent chromium soluble compounds. Thus, the CA EPA has not derived a reference concentration specifically for evaluation of chromium (VI) particulates. However, CA EPA's derivation of the value for dissolved hexavalent chromium compounds other than chromic acid is very similar to the US EPA and TERA derivations for particulate hexavalent chromium and includes a pharmacokinetic adjustment based on relative particulate deposition in the respiratory tract of rats and humans. The particulate reference concentrations are the only values relevant to exposure scenarios involving contaminated soil. Therefore, the US EPA, CA EPA, and ATSDR reference concentrations based on exposures to chromic acid mists are not further considered as potential toxicity values for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chromium (VI).

The three remaining reference concentrations are all based on benchmark concentration estimates for a large number of quantitative endpoints associated with lower respiratory tract and immune system toxicity and increased spleen weight in rats exposed via inhalation for 90 days in two related studies. The US EPA used the lowest $BMCL_{10}$ estimate from the various endpoints as their point of departure,

and the CA EPA used a single $BMCL_{05}$ estimate for their point of departure, although whether or not this was the lowest value is unclear from their documentation. TERA based their value on the arithmetic average of all the BMCLs they estimated. TERA's documentation does not specify whether their estimates are $BMCL_{05}$s or $BMCL_{10}$s, but the reported range of BMCLs is the same as the range reported by US EPA, suggesting the TERA value is an arithmetic mean of $BMCL_{10}$s. All three derivations used the same pharmacokinetic adjustment to account for relative particulate deposition in the lower respiratory tract of rats versus humans.

The US EPA, TERA, and CA EPA all used a 10-fold uncertainty factor to account for human variation and a 3-fold factor to account for interspecies variability. The US EPA and TERA used a default 10-fold factor to account for use of a subchronic study, whereas CA EPA used its standard default 3-fold factor to account for the use of a subchronic animal study. The US EPA noted that data from one of the 90-day rat studies indicated that particles were still accumulating in the lung at the end of the study, suggesting that a longer exposure duration could achieve a critical concentration for lung effects at a lower exposure level than a shorter exposure period. The US EPA also suggested that subchronic studies may not adequately predict inflammatory effects in the lung associated with chronic exposure. These uncertainties warrant maintaining a default factor of 10 for the use of a subchronic study.

The US EPA chose to use the lowest BMCL as their point of departure, while TERA used the arithmetic mean of all the BMCL estimates. The BMCL estimates range by more than 3-fold from lowest to highest, and so, based on US EPA benchmark dose default guidance, the BMCL shows some model dependence that should be accounted for by using the lowest BMCL estimate as the point of departure. Therefore, the US EPA reference concentration (0.1 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chromium (VI).

3. Review Dates

Summary table completion: September, 2004; revised January 2018
Toxicity value recommendation: October, 2004; no revision January 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/12/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Appendix D.3 Chronic RELs and Toxicity Summaries using the Previous Version of the Hot Spots Risk Assessment Guidelines (OEHHA 1999) Last accessed (01/12/2018) at https://oehha.ca.gov/air/crnr/notice-adoption-air-toxics-hot-spots-program-technical-support-document-derivation

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/12/2018) at https://www.tera.org/iter/

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/12/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/12/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Chromium (VI)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for Inorganic Chromium (VI)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: • US EPA HEAST (1997)	8×10^{-5}	0.012	multistage model	--	Based on the incidence of lung cancer in a combined cohort of 332 workers. The original study assumed cancer mortality was due to chromium (VI), which was further assumed to be no less than $1/7^{th}$ of total chromium. However, the unit risk derivation is based on total chromium exposure.
US EPA RSL*	1.2×10^{-5}	0.084	--	--	Based on multiplying the US EPA IRIS unit risk by 7
CA EPA CPF	6.7×10^{-6}	0.15	linearized multistage model	--	Based on the same study as US EPA IRIS. CA EPA reports that their unit risk estimate is an upper bound from a multistage linearized "crude" procedure, whereas the US EPA derivation is a maximum likelihood estimated from a multistage "competing risks" analysis.
HC PSAP	1.3×10^{-5} [3]	0.66 (TC_{05}) [2,3]	--	--	Based on the same study as US EPA IRIS. The TC_{05} is derived for chromium (VI) assuming that it is $1/7^{th}$ of total chromium and assumes no competing causes of death.
NYS DOH (1990)	2×10^{-5}	0.05	linear average relative risk model	--	Based on the same study as US EPA IRIS. The unit risk is based on analytical data indicating that 21% of the total chromium in facility air was chromium (VI).

WHO (2000)	2.5×10^{-5}	0.04	--	--	Based on several occupational cohort studies of chromate workers not including the study cohort used by US EPA IRIS. The unit risk is the geometric mean of four estimates that span about 1 order of magnitude.
RIVM (2001)	2.5×10^{-5}	0.04	--	--	Based on the WHO derivation.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million, where 1×10^{-6} air concentration = 1×10^{-6}/unit risk.

[2]TC_{05} = The tumorigenic concentration in air (expressed in mcg/m^3) associated with a 5% increase in incidence or mortality due to tumors. The TC_{05} represents a maximum likelihood estimate rather than a lower-bound estimate.

[3]A unit risk was not derived. A linear extrapolation to 1×10^{-6} risk from TC_{05} would yield a risk specific concentration of 1.3×10^{-5} per mcg/m^3 (risk specific air concentration = (TC_{05} x 1×10^{-6} risk level)/0.05 risk level).

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The unit risks for chromium (VI) derived by authoritative bodies are all based on increased incidence of lung cancer in cohort studies of chromium industry workers. The US EPA IRIS and RSL, CA EPA, NYS DOH, and HC derivations are all based on the same cohort analysis but use differing procedures to derive their unit risk or risk-specific concentration values. The WHO (and RIVM) value is derived from analyses of four other occupational cohort data sets. The US EPA IRIS considered some of the studies used by the WHO as possible sources of dose-response data and concluded that there were significant deficiencies with the exposure data available from those studies, which precluded their use in deriving a unit risk. The HC value is a modeled maximum likelihood estimate of the exposure level associated with a 5% increased tumor incidence and therefore does not represent a lower-bound exposure estimate, but could be used as the basis of a linear extrapolation to a maximum likelihood 10^{-6} risk-specific air concentration. The CA EPA and the US EPA IRIS analyses differ in that the US EPA IRIS unit risk is a maximum likelihood estimate rather than an upper bound and the US EPA IRIS analysis takes competing causes of mortality into account while the CA EPA "crude" analysis assumes no competing causes of mortality. Both differences contribute to a more conservative CA EPA unit risk estimate, although US EPA IRIS showed that the difference between the crude and competing mortality derivations was small. The US EPA RSL derivation multiplied the US EPA IRIS unit risk by 7 because the IRIS unit risk was derived for total chromium even though US EPA IRIS assumed that not less than $1/7^{th}$ of the chromium was chromium (VI). The NYS DOH derivation makes use of chromium (VI) analytical data for the same chromium facility and cohort considered in the US EPA IRIS, CA EPA and HC derivations. The result is a unit risk based on empirical data specifically for the species of interest (chromium (VI)) rather than an assumption about the percentage of total chromium at the facility that was chromium (VI). Therefore, the NYS DOH unit risk (0.05 per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for chromium (VI). The chromium (VI) risk specific air concentration calculated from this toxicity value is 2×10^{-5} mcg/m^3.

3. Review Dates

Summary table completion: September, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/20/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/20/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

NYS DOH (New York State Department of Health). 1990. Ambient Air Criteria Document for Chromium. Bureau of Toxic Substance Assessment. Albany, NY: NYSDOH.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/20/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/20/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/20/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2000. Air Quality Guidelines for Europe. Last accessed (01/20/2018) at http://www.euro.who.int/en/what-we-publish/abstracts/air-quality-guidelines-for-europe.

5. **Authoritative Bodies**

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Chrysene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Chrysene (CAS Number 218-01-9)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
--	--	--	--	--	A reference dose for chrysene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

2. Recommendation and Rationale

Chrysene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). Reference doses derived from chemical-specific toxicity data are available for six polycyclic aromatic hydrocarbons identified as priority contaminants in the Brownfield Cleanup Program (acenaphthene, anthracene, benzo[a]pyrene, fluoranthene, fluorene, and pyrene, see NYS, 2006). Chrysene is chemically similar to each of these six listed polycyclic aromatic hydrocarbons. Each of these six priority contaminants could be used to represent the noncancer toxicity of chrysene. Similarity of chemical structure cannot be used as a basis of choosing a chemical surrogate for chrysene because toxicity data are insufficient to accurately describe the relationship between the chemical structure and non-cancer toxicity of polycyclic aromatic hydrocarbons. The recommended reference dose for benzo[a]pyrene is lower than that of the other five polycyclic aromatic hydrocarbons. Without data on which of these six polycyclic aromatic hydrocarbons would be the best surrogate for chrysene, the recommended reference dose for benzo[a]pyrene (3×10^{-4} mg/kg/day, see Oral Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for chrysene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Chrysene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Chrysene (CAS Number 218-01-9)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ◆ NYS DEC (2017)	1×10^{-4}	0.01	--	--	Based on a relative potency factor of 0.01 applied to the US EPA IRIS benzo[a]pyrene cancer potency factor of 1 $(mg/kg/day)^{-1}$.
CA EPA CPF	8.3×10^{-6}	0.12	--	--	Based on a potency equivalency factor of 0.01 applied to the CA EPA CPF benzo[a]pyrene cancer potency factor of 12 $(mg/kg/day)^{-1}$.
RIVM (2001)	5.0×10^{-4}	0.02 (2)	--	--	Based on a relative potency factor of 0.1 applied to the RIVM benzo[a]pyrene cancer potency factor[2] of 0.2 $(mg/kg/day)^{-1}$.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2]A cancer potency factor was not reported. The derivation directly extrapolates from an experimental dose with significant increased tumor incidence above background to the environmental dose associated with a one-in-one million risk level; the risk-specific dose is not a lower-bound estimate.

2. Recommendation and Rationale

Chrysene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). The cancer potency factors for chrysene available from the authoritative bodies listed in item 5 (below) are based on a cancer potency factor for benzo[a]pyrene (also a polycyclic aromatic hydrocarbon) and the application of a relative potency factor for chrysene (see Chapter 5.1.5 of NYS (2006) for discussion of relative potency factors). The recommended cancer potency factor for benzo[a]pyrene is 1 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for Benzo[a]pyrene). The benzo[a]pyrene cancer potency factor is multiplied by the recommended relative potency factor of 0.01 for chrysene (NYS 2006) to obtain a cancer potency factor of 0.01 per mg/kg/day. This is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for chrysene. The chrysene risk specific dose calculated from this toxicity value is 1×10^{-4} mg/kg/day.

3. Review Dates

Summary table completion: February, 2004; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/13/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

NYS DEC (New York State Department of Environmental Conservation). 2017. Draft Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Chrysene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/13/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/13/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
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- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Chrysene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Chrysene (CAS Number 218-01-9)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for chrysene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Chrysene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). A reference concentration based on chemical-specific inhalation toxicity data for chrysene is not available from the authoritative bodies listed in item 5 (below).

Benzo[a]pyrene is the only polycyclic aromatic hydrocarbon identified as a priority contaminant in the Brownfield Cleanup Program for which a reference concentration is available. Benzo[a]pyrene is chemically similar to chrysene and can be used to represent its noncancer inhalation toxicity (see Inhalation Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene). Therefore, based on using benzo[a]pyrene as a chemical surrogate, a reference concentration of 2×10^{-3} mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chrysene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry

California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Chrysene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Chrysene (CAS Number 218-01-9)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2009)	9.1×10^{-2}	1.1×10^{-5}	--	--	Based on the CA EPA unit risk for benzo[a]pyrene (which is derived from the increased incidence of respiratory tract tumors in hamsters exposed by inhalation) and application of a potency equivalency factor of 0.01.
US EPA IRIS	0.16	6×10^{-6}	--	--	Based on application of a relative potency factor of 0.01 to the US EPA IRIS unit risk for benzo[a]pyrene, which is derived from the same study used by CA EPA

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} air concentration), where 1×10^{-6} concentration = 1×10^{-6} / inhalation unit risk.

2. Recommendation and Rationale

The unit risk values for chrysene are based on benzo[a]pyrene and the application of relative potency factors. The recommended unit risk value for benzo[a]pyrene is 6×10^{-4} per mcg/m^3 (see Inhalation Cancer Toxicity Value Documentation for benzo[a]pyrene). Application of the recommended relative potency factor (0.01) for chrysene to the unit risk for benzo[a]pyrene yields a unit risk of 6×10^{-6} per mcg/m^3, which is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for chrysene (see Chapter 5.1.5 of technical support document [NYS 2006] for discussion of recommended relative potency factors). The chrysene risk specific air concentration calculated from this toxicity value is 0.16 mcg/m^3.

3. Review Dates

Summary table completion: November, 2004; revised January, 2018
Toxicity value recommendation: December, 2004; revised January, 2018

4. References for Summary Table

CA EPA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2009. Technical Support Document for Cancer Potency Factors 2009. Appendix B: Chemical-Specific Summaries of the Information Used to Derive Unit Risk and Cancer Potency Values. Last accessed (01/19/2018) at http://oehha.ca.gov/air/crnr/technical-support-document-cancer-potency-factors-2009.

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/19/2018) at http://www.dec.ny.gov/chemical/34189.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System
Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
    Health Effects Assessment Summary Tables
    Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Copper
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Inorganic Copper

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA HEAST (1997) Also used by: ◆ US EPA Region 3 (2003)	0.04	0.08	LOEL	2	Based on current US EPA action level for copper in drinking water of 1.3 mg/L, which was derived from a LOEL of 5.3 mg/person (0.08 mg/kg/day for a 70-kg person) from a single dose oral study reporting gastrointestinal irritation. The allocation of all the dose to water, and the assumption of water consumption rate of 2 L/day
RIVM (2001)	0.14	--	--	--	Equal to the RIVM derived maximum daily copper intake of the (Dutch) population.
IOM (2001)	0.14	0.14	NOEL	1	Based on absence of liver effects in 7 adults (assumed weight of 70 kg) who ingested 10 mg copper daily (as copper gluconate) during a 12-week study

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.
LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The basis for the US EPA and RIVM reference dose values are not well documented. The US EPA drinking water action level (and the HEAST reference dose) are based on a report (Wyllie, 1975) of gastrointestinal irritation in women who consumed a copper-contaminated beverage (a cocktail containing alcohol). A review of the report, however, reveals potential confounding factors and significant uncertainties in dose estimates that seriously weaken confidence in the derived reference dose. The RIVM value appears to be an exposure-based, rather than health-effect-based reference dose.

The IOM (2001) considered a large uncertainty factor unnecessary given the large international database in humans indicating no adverse effects from daily consumption of 10 to 20 mg/day of copper in foods and the rarity of observed liver damage from copper exposure in human populations with normal homeostatic mechanisms for regulation the uptake and excretion of copper. Moreover, copper is an essential element, and the routine application of traditional uncertainty factor leads to reference doses that are below those doses needed for nutritional needs (NRC, 2000). Therefore, the IOM (2001) reference dose (0.14 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for copper.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

IOM (Institute of Medicine). 2001. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington, DC: National Academy Press.

NRC (National Research Council). 2000. Copper in Drinking Water. Washington, DC: National Academy Press.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Document No. 9200.6-303 997-1. Washington, DC: Office of Research and Development, Office of Emergency and Remedial Response.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

Wyllie, J. 1957. Copper poisoning at a cocktail party. Am. J. Public Health. 47:617.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Copper
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Copper

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	There are no human data and inadequate animal data on the potential carcinogenicity of copper compounds.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for copper is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Copper
Exposure Route: Inhalation
Toxicity: Non-cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Inorganic Copper

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for copper is not available from the authoritative bodies listed in item number 5 (below). Copper is a toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for copper is 0.14 mg/kg/day. Therefore, a reference concentration of 490 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for copper.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Copper
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Copper

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for copper is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Cyanide
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

6. Summary of Oral Reference Doses for Free Cyanide (CAS Number 57-12-5)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL[3] ♦ US EPA ODW[3]	6×10^{-4}	1.9	$BMDL_{1sd}$ [2]	3000	Based on decreased cauda epididymis weight in male rats exposed via drinking water each day for 13 weeks
NYS DEC (1997)	0.022	10.8	NOEL	500	Based on the absence for absence (at any dose) of clinical and histological effects in female rats exposed via the diet (4.6 or 10.8 mg/kg/day) each day for 2 years. The identified NOEL was the highest dose tested.
US EPA HEAST (1997)	0.022	10.8	NOEL	500	Based on same study used by NYS DEC (1997).
CA EPA PHG	0.022	10.8	NOEL	500	Based on same study used by NYS DEC (1997).
RIVM (2001)	0.05	5	NOEL	100	Based on the same study used by NYS DEC (1997). The identified NOEL was 5 mg/kg/day because there was an increased concentration of cyanide metabolites in the blood of rats at the highest tested dose.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.
[2]$BMDL_{1sd}$: 95% lower confidence limit on the benchmark dose corresponding to a change in the mean response equal to 1 standard deviation (SD) from the control mean.
[3]Reported for hydrogen cyanide.

NOEL: no-observed-effect level; UF: uncertainty factor

7. Recommendation and Rationale

The basis for the NYS DEC, US EPA HEAST, CA EPA PHG, and RIVM reference doses for cyanide is identical with respect to choice of study and species, but the presence or absence of effects at the two non-zero doses in the study has been interpreted differently. There were no toxic effects observed in the study, and the NYS DEC, US EPA HEAST and CA EPA PHG considered the higher dose a NOEL. However, RIVM (based on an earlier WHO analysis) noted that increased cyanide metabolites were

observed in blood at the higher dose and considered the lower dose the NOEL. The limited RIVM documentation does not fully support this decision as the appearance of increased cyanide metabolites in the blood is a reflection of detoxification of the increased cyanide dose and would not necessarily suggest an increased risk for toxicity. The US EPA IRIS derivation is based on a well-designed, conducted, and reported 13-week study. The study identified statistically significant male reproductive effects in rats and mice that increased in severity in a dose-dependent manner. The observed effects included decreased cauda and whole epididymis weights, decreased testes weight, and altered sperm parameters. The US EPA IRIS selected decreased cauda epididymis weight as the critical effect because it was determined that this effect represents the most sensitive endpoint indicative of male reproductive toxicity. The derivation is consistent with generally accepted risk assessment practices for high-to-low dose and animal-to-human extrapolations of non-cancer effects, including the use benchmark dose models. The US EPA IRIS used a 3000-fold uncertainty factor for animal-to-human extrapolation (10), the use of a subchronic study (10), human variation (3), and deficiencies in the toxicity database (3), which included the lack of a multigenerational reproductive toxicity study and a sensitive neurodevelopmental toxicity study. Although the study used by US EPA IRIS was shorter (13 weeks) than the study used by the other agencies (2 years), the lack of observed effects in the latter study is a serious limitation. Thus, the US EPA IRIS reference dose (6×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for free cyanide.

8. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

9. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/14/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/14/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/14/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/14/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/14/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/14/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

7. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Cyanide
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Free Cyanide (CAS Number 57-12-5)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
	--	--	--	--	No values or reviews were found in any of the listed sources.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for cyanide is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Cyanide
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Free Cyanide (CAS Number 57-12-5)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL[4]	0.8 [2]	2500	$LOEL_{ADJ}$ [3]	3000	Based on statistically significantly altered rates of iodide uptake by the thyroid, thyroid enlargement, and CNS symptoms (e.g., self-reported increased incidence of headache, weakness, and sensory changes for taste and smell) in workers exposed via inhalation for 5–15 years in three electroplating factories. $\underline{LOEL_{Workplace}}$ = 7.07 mg/m^3.
RIVM (2001)	25	2500	$LOEL_{ADJ}$ [3]	100	Based on same study and effects as US EPA IRIS.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.
[2]Derived for hydrogen cyanide (HCN; CAS No. 74-90-8) but also the reference concentration for free cyanide. The reference concentration for free cyanide (CN^-; CAS No. 57-12-5) = (0.83 mcg/m^3 (reference concentration for HCN) × 26 (molecular weight for CN^-)/27 (molecular weight for HCN) = 0.80 mcg/m^3.
[3]The workplace LOEL of 7.07 mg HCN/m^3 was adjusted for daily exposure by multiplying the workplace air concentrations x 10 m^3 per workday/20 m^3 per day x 5 days per workweek/7 days per week ($LOAEL_{(ADJ)}$ = 7.07 mg/m^3 HCN × 10/20 × 5 /7 = 2.5 mg/m^3 HCN = 2500 mcg/m^3 HCN.
[4]Reported for hydrogen cyanide.

$LOEL_{ADJ}$: adjusted lowest-observed-effect level; UF: uncertainty factor.

2. Recommendation and Rationale

Both the US EPA IRIS and RIVM used the same occupational study, toxic effects, LOEL, and $LOEL_{ADJ}$ as the basis of the reference concentration. However, the US EPA IRIS used a total uncertainty factor of 3000 to compensate for human variation (10), the use of a LOEL (10), the use of a subchronic study (3), and deficiencies (lack of developmental and multigenerational reproductive toxicity studies) in the cyanide inhalation database (10). RIVM used a total uncertainty factor of 100 to compensate for human variation (10) and the use of a LOEL (10). RIVM did not use uncertainty factors for the use of a subchronic study or database deficiencies because the mechanism of cyanide toxicity is well-known, which reduces the need for additional uncertainty factors. However, RIVM appears to be focusing on the mechanism of action for neurotoxicity (chemical asphyxiation), whereas US EPA IRIS concluded that hydrogen cyanide may also cause effects by disrupting thyroid function via inhibition of iodide

uptake by the primary metabolite (thiocyanate) of hydrogen cyanide. US EPA IRIS used a subchronic uncertainty factor in the absence of information indicating the effects observed in the occupational study would not progress in incidence or severity. US EPA IRIS used a database deficiency uncertainty factor because interference with iodide uptake during pregnancy could lead subclinical hypothyroidism, with associated nervous system effects in the infants. Thus, US EPA IRIS identified the lack of developmental neurotoxicity studies or developmental studies assessing maternal and fetal thyroid function to be major database deficiencies. Finally, the US EPA IRIS derivation is well-documented, peer-reviewed and is consistent with generally accepted risk assessment practices. Therefore, the US EPA reference concentration (0.8 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for cyanide.

3. Review Dates

Summary table completion: September, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/14/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/14/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/14/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Cyanide
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Cyanide

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Cancer potency values for inhalation were not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} concentration = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An inhalation unit risk for cyanide is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Division of Drinking Water and Environmental Management
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyldichloroethane (DDD)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for p,p'-Dichlorodiphenyldichloroethane (DDD) (CAS Number 72-54-8)

Agency	Reference Value[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
RIVM (2000)	5×10^{-4}	0.05	NOEL	100	Based on liver lesions in rats fed commercial grade DDT in corn oil mixed with powdered food for 27 weeks. DDD is structurally similar to and is a metabolite of DDT. Study LOEL = 0.25 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The RIVM value is the only available reference dose for p,p'-DDD from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore the RIVM reference dose (5×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for p,p'-DDD.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 249-257. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyldichloroethane (DDD)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for p,p'-Dichlorodiphenyldichloroethane (DDD) (CAS Number 72-54-8)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • Cal EPA (2004)	4.2×10^{-5}	0.24	Linearized multistage model, extra risk	body surface area [2]	Cancer potency factor based on increased incidence of liver tumors in male mice exposed to DDD in their diets for 130 weeks.
NYS DEC (1997)	8.0×10^{-6}	0.125	Linearized multistage model, extra risk	$BW^{¾}$ [3]	Based on the same tumor incidence data as the US EPA IRIS cancer potency factor.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.

2. Recommendation and Rationale

The basis of the cancer potency factors derived by authoritative bodies is identical with respect to study, species, critical effect and tumor incidence data. The only difference between the values is the use of body surface area scaling for interspecies extrapolation by the US EPA and $BW^{3/4}$ scaling by the NYS DEC. The latter method is more consistent with currently accepted risk assessment practice. Therefore, the NYS DEC cancer potency factor (0.125 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for p,p'-DDD. The p,p'-DDD risk specific dose calculated from this toxicity value is 8.0×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: February, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2004. Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. Last accessed (01/18/2018) at https://oehha.ca.gov/chemicals

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for p,p'-DDD. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/14/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyldichloroethane (DDD)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for p,p'-Dichlorodiphenyldichloroethane (DDD) (CAS Number 72-54-8)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for p,p'-DDD is not available from the authoritative bodies listed in item number 5 (below). DDD is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for p,p'-DDD is 5×10^{-4} mg/kg/day. Therefore, a reference concentration of 1.8 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for p,p'-DDD.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'Dichlorodiphenyldichloroethane (DDD)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for p,p'Dichlorodiphenyldichloroethane (DDD) (CAS Number 72-54-8)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for p,p'-DDD is not available from the authoritative bodies listed in item number 5 (below). DDD is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral cancer potency factor based on cancer effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a unit risk from the cancer potency factor. The recommended oral cancer potency factor for p,p'-DDD is 0.125 per mg/kg/day. Therefore, a unit risk of 3.6×10^{-5} per mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for p,p'-DDD. The risk specific air concentration calculated from this toxicity value is 0.028 mcg/m^3.

2. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

3. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/14/2018) at http://www.epa.gov/iris/.

4. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyldichloroethylene (DDE)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for p,p'-Dichlorodiphenyldichloroethylene (DDE) (CAS Number 72-55-9)

Agency	Reference Value[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
RIVM (2000)	5×10^{-4}	0.05	NOEL	100	Based on liver lesions in rats fed commercial grade DDT in corn oil mixed with powdered food for 27 weeks. DDE is structurally similar to and is a metabolite of DDT. Study LOEL = 0.25 mg/kg/day.
NYS DEC (1997)	0.012	12	LOEL	1000	Based on liver effects (centrilobular necrosis) in rats in a 78-week dietary study.
ATSDR (2002)	--	--	--	--	Toxicity studies reviewed, but a chronic reference value was not derived.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The basis of the NYS DEC reference dose for p,p'-DDE is liver toxicity in a chronic rat feeding study. The RIVM value is derived based on structural similarity of p,p'-DDE to p,p'-DDT, the presumption that structurally similar chemicals have similar toxic effects, and DDE's relationship as a metabolite of DDT. The NYS DEC value is based on chemical specific information. In addition, the study used by the NYS DEC (NCI, 1978) exposed the animals for a larger portion of their lifetimes than the study used by RIVM. Therefore, the NYS DEC reference dose (0.012 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for p,p'-DDE.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: April, 2005; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological Profile for DDT, DDE and DDD. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. Last accessed (01/18/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

NCI (National Cancer Institute). 1978. Bioassays of DDT, TDE and p,p'-DDE for possible carcinogenicity. US Department of Health Education and Welfare, Public Health Service, National Institutes of Health. NCI-CG-TR-131.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for p,p'-DDE. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyldichloroethylene (DDE)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for p,p'-Dichlorodiphenyldichloroethylene (DDE) (CAS Number 72-55-9)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2003) • Cal EPA (2004)	2.9×10^{-6}	0.34	Linearized multistage model, extra risk	body surface area [2]	The cancer slope factor is the geometric mean of six slope factors from three different dietary studies. The studies observed hepatocellular carcinomas and hepatomas in both sexes of mice after 78 and 130 weeks of DDE dietary exposure, respectively, and an increase in liver neoplastic nodules in both sexes of hamsters after 128 weeks dietary exposure to DDE.
NYS DEC (1997)	5.4×10^{-6}	0.185	Linearized multistage model, extra risk	$BW^{¾}$ [3]	Slope factor based on same studies as US EPA.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.

2.Recommendation and Rationale

The basis of the cancer potency factors derived by authoritative bodies is identical with respect to study, species, critical effect and tumor incidence data. The only difference between the values is the use of body surface area scaling for interspecies extrapolation by the US EPA and $BW^{3/4}$ scaling by the NYS DEC. The latter method is more consistent with currently accepted risk assessment practice. Therefore, the NYS DEC cancer potency factor (0.185 per mg/kg/day) is the toxicity value recommended for use in

the derivation of an oral cancer-based soil cleanup objective for p,p'-DDE. The p,p'-DDE risk specific dose calculated from this toxicity value is 5.4×10^{-6} mg/kg/day.

3.Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2004. Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. Last accessed (01/18/2018) at https://oehha.ca.gov/chemicals

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for p,p'-DDE. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/14/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyldichloroethylene (DDE)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for p,p'-Dichlorodiphenyldichloroethylene (DDE) (CAS Number 72-55-9)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for p,p'-DDE is not available from the authoritative bodies listed in item number 5 (below). DDE is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for p,p'-DDE is 0.012 mg/kg/day. Therefore, a reference concentration of 42 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for p,p'-DDE.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: April, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyldichloroethylene (DDE)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for p,p'-Dichlorodiphenyldichloroethylene (DDE) (CAS Number 72-55-9)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for p,p'-DDE is not available from the authoritative bodies listed in item number 5 (below). DDE is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral cancer potency factor based on cancer effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a unit risk from the cancer potency factor. The recommended oral cancer potency factor for p,p'-DDE is 0.185 per mg/kg/day. Therefore, a unit risk of 5.3×10^{-5} per mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for p,p'-DDE. The risk specific air concentration calculated from this toxicity value is 0.019 mcg/m^3.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/14/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyltrichloroethane (DDT)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. **Summary of Available Oral Reference Doses for p,p'-Dichlorodiphenyltrichloroethane (DDT) (CAS Number 50-29-3)**

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA HEAST (1997) ♦ US EPA Region 3 (2003)	5×10^{-4}	0.05	NOEL	100	Based on liver lesions in rats fed commercial grade DDT in corn oil mixed with powdered food for 27 weeks. Study LOEL = 0.25 mg/kg/day.
NYS DEC (1997)	5×10^{-4}	0.05	NOEL	100	Based on same data used to derive US EPA IRIS value
ATSDR (2002)	5×10^{-4}	0.05	NOEL	100	Based on same data used to derive US EPA IRIS value
RIVM (2001)	5×10^{-4}	0.05	NOEL	100	Based on same data used to derive US EPA IRIS value

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. **Recommendation and Rationale**

The basis for the various reference doses for DDT (and the reference doses themselves) are identical with respect to choice of study, species, adverse effect and identification of the point of departure (0.05 mg/kg/day). Therefore, the US EPA reference dose (5×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for DDT.

3. **Review Dates**

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological Profile for DDT, DDE, DDD. U.S. Department of Health and Human Services, Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for p,p'-DDT. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 997-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/19/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyltrichloroethane (DDT)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for p,p'-Dichlorodiphenyltrichloroethane (DDT) (CAS Number 50-29-3)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: ♦ EPA Region 3 (2004) ♦ Cal EPA (2004)	2.9×10^{-6}	0.34	linearized multistage model, extra risk	body surface area[2]	Based on hepatocellular adenomas and carcinomas and malignant lung tumors in two rat and four mouse studies where animals were exposed in their diet for their lifetime or for multiple generations (two of the mouse studies). The potency factor is the geometric mean of 10 individual values.
NYS DEC (1997)	5.3×10^{-6}	0.189	linearized multistage model, extra risk	$BW^{¾}$ [3]	Value was based on same studies used by EPA IRIS.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.

2. Recommendation and Rationale

All the cancer potency factors derived by authoritative bodies are based on the same set of 10 cancer potency factors derived from six feeding studies in mice and rats showing an increased incidence of liver and lung tumors. The US EPA IRIS value is a geometric mean of the 10 individual values. The NYS DEC value differs only in applying $BW^{3/4}$ scaling rather than body surface area scaling to convert the rodent potency factor to a human potency factor. Since that methodology is more consistent with currently accepted risk assessment practice, the NYS DEC cancer potency factor

(0.189 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for DDT. The DDT risk specific dose calculated from this toxicity value is 5.3×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. Last accessed (01/18/2018) at https://oehha.ca.gov/chemicals

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for p,p'-DDT. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyltrichloroethane (DDT)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. **Summary of Available Inhalation Reference Concentrations for p,p'-Dichlorodiphenyltrichloroethane (DDT) (CAS Number 50-29-3)**

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. **Recommendation and Rationale**

An inhalation reference concentration for p,p'-DDT is not available from the authoritative bodies listed in item number 5 (below). DDT is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for p,p'-DDT is 5×10^{-4} mg/kg/day. Therefore, a reference concentration of 1.8 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for p,p'-DDT.

3. **Review Dates**

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. **References for Summary Table**

5. **Authoritative Bodies**

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: p,p'-Dichlorodiphenyltrichloroethane (DDT)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for p,p'-Dichlorodiphenyltrichloroethane (DDT) (CAS Number 50-29-3)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for p,p'-DDT is not available from the authoritative bodies listed in item number 5 (below). DDT is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral cancer potency factor based on cancer effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a unit risk from the cancer potency factor. The recommended oral cancer potency factor for p,p'-DDT is 0.189 per mg/kg/day. Therefore, a unit risk of 5.4×10^{-5} per mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for p,p'-DDT. The risk specific air concentration calculated from this toxicity value is 0.018 mcg/m^3.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Dibenz[a,h]anthracene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Dibenz[a,h]anthracene (CAS Number 53-70-3)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
--	--	--	--	--	A reference dose for dibenz[a,h]anthracene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

2. Recommendation and Rationale

Dibenz[a,h]anthracene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). Reference doses derived from chemical-specific toxicity data are available for six polycyclic aromatic hydrocarbons identified as priority contaminants in the Brownfield Cleanup Program (acenaphthene, anthracene, benzo[a]pyrene, fluoranthene, fluorene, and pyrene, see NYS, 2006). Dibenz[a,h]anthracene is chemically similar to each of these six listed polycyclic aromatic hydrocarbons. Each of these six priority contaminants could be used to represent the noncancer toxicity of dibenz[a,h]anthracene. Similarity of chemical structure cannot be used as a basis of choosing a chemical surrogate for dibenz[a,h]anthracene because toxicity data are insufficient to accurately describe the relationship between the chemical structure and non-cancer toxicity of polycyclic aromatic hydrocarbons. The recommended reference dose for benzo[a]pyrene is lower than that of the other five polycyclic aromatic hydrocarbons. Without data on which of these six polycyclic aromatic hydrocarbons would be the best surrogate for dibenz[a,h]anthracene, the recommended reference dose for benzo[a]pyrene (3×10^{-4} mg/kg/day, see Oral Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for dibenz[a,h]anthracene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendations and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Dibenz[a,h]anthracene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Dibenz[a,h]anthracene (CAS Number 53-70-3)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ◆ NYS DEC (2017)	1×10^{-6}	1	--	--	Based on a relative potency factor of 1 applied to the US EPA IRIS benzo[a]pyrene cancer potency factor of 1 $(mg/kg/day)^{-1}$.
RIVM (2001)	5.0×10^{-6}	0.2 (2)	--	--	Based on a relative potency factor of 1 applied to the RIVM benzo[a]pyrene cancer potency factor[2] of 0.2 $(mg/kg/day)^{-1}$.
CA EPA CPF	2.4×10^{-7}	4.1	linearized multistage model	body surface area[3]	Based on increased incidence of lung carcinomas in mice exposed via an aqueous olive oil emulsion.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2]A cancer potency factor was not reported. The derivation directly extrapolates from an experimental dose with significant increased tumor incidence above background to the environmental dose associated with a one-in-one million risk level; the risk-specific dose is not a lower-bound estimate.

[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.

2. Recommendation and Rationale

The CA EPA cancer potency factor for dibenz[a,h]anthracene is based on a less than lifetime study of mice given an aqueous olive-oil emulsion of dibenz[a,h]anthracene instead of drinking water. Only one dose level was used, and all the mice that were exposed for more than 200 days developed lung tumors (14 males and 13 females). The use of a single dose level, the less than lifetime study length, the small number of animals, and the 100% tumor incidence are all limitations of the study, and reduce confidence in the derived cancer potency factor. Therefore, the CA EPA cancer potency factor is not used in the derivation of an oral cancer-based soil cleanup objective for dibenz[a,h]anthracene.

Dibenz[a,h]anthracene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). The cancer potency factors for dibenz[a,h]anthracene available from the authoritative bodies other than CA EPA listed in item 5

(below) are based on a cancer potency factor for benzo[a]pyrene (also a polycyclic aromatic hydrocarbon) and the application of a relative potency factor for dibenz[a,h]anthracene (see Chapter 5.1.5 of NYS (2006) for discussion of relative potency factors). The recommended cancer potency factor for benzo[a]pyrene is 1 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for Benzo[a]pyrene). The benzo[a]pyrene cancer potency factor is multiplied by the recommended relative potency factor of 1 for dibenz[a,h]anthracene (NYS 2006) to obtain a cancer potency factor of 1per mg/kg/day. This is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for dibenz[a,h]anthracene. The dibenz[a,h]anthracene risk specific dose calculated from this toxicity value is 1×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: February, 2004; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/13/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

NYS DEC (New York State Department of Environmental Conservation). 2017. Draft Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Dibenz[a,h]anthracene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/13/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/13/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values

Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Dibenz[a,h]anthracene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. **Summary of Inhalation Reference Concentrations for Dibenz[a,h]anthracene (CAS Number 53-70-3)**

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for dibenz[a,h]anthracene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. **Recommendation and Rationale**

Dibenz[a,h]anthracene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). A reference concentration based on chemical-specific inhalation toxicity data for dibenz[a,h]anthracene is not available from the authoritative bodies listed in item 5 (below).

Benzo[a]pyrene is the only polycyclic aromatic hydrocarbon identified as a priority contaminant in the Brownfield Cleanup Program for which a reference concentration is available. Benzo[a]pyrene is chemically similar to dibenz[a,h]anthracene and can be used to represent its noncancer inhalation toxicity (see Inhalation Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene). Therefore, based on using benzo[a]pyrene as a chemical surrogate, a reference concentration of 2×10^{-3} mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for dibenz[a,h]anthracene.

3. **Review Dates**

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. **References for Summary Table and Recommendations and Rationale**

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. **Authoritative Bodies**

Agency for Toxic Substances and Disease Registry

California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Dibenz[a,h]anthracene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Dibenz[a,h]anthracene (CAS Number 53-70-3)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2009)	8.3×10^{-4}	1.2×10^{-3}	linearized multistage model, extra risk	not clearly specified	Estimated from route-to-route extrapolation of an oral cancer potency factor of 4.1 per mg/kg/day, which was based on the increased incidence of lung carcinomas in mice exposed in aqueous olive oil emulsion.
US EPA IRIS	1.6×10^{-3}	6×10^{-4}	--	--	Based on application of a relative potency factor of 1 to the US EPA IRIS unit risk for benzo[a]pyrene.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} air concentration), where 1×10^{-6} concentration = 1×10^{-6} / inhalation unit risk.

2. Recommendation and Rationale

The Cal EPA inhalation unit risk for dibenz[a,h]anthracene is based on a less than lifetime oral study in mice that used a single exposure level. The primary limitations of the study include the use of one exposure level (at which 100% of the animals tested developed lung tumors) which consequently provides no information on dose response, and the relevance of the administration in an aqueous olive oil emulsion to exposure by inhalation. The Cal EPA oral study is therefore not chosen for deriving a quantitative estimate of the inhalation unit risk.

The unit risk value for dibenz[a,h]anthracene is based on benzo[a]pyrene and the application of a relative potency factor. The recommended unit risk value for benzo[a]pyrene is 6×10^{-4} per mcg/m^3 (see Inhalation Cancer Toxicity Value Documentation for benzo[a]pyrene). Application of the recommended relative potency factor (1) for dibenz[a,h]anthracene to the unit risk for benzo[a]pyrene yields a unit risk of 6×10^{-4} per mcg/m^3, which is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for dibenz[a,h]anthracene (see Chapter 5.1.5 of technical support document [NYS 2006] for discussion of recommended relative potency factors). The

dibenz[a,h]anthracene risk specific air concentration calculated from this toxicity value is 1.6×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: November, 2004; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table

CA EPA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2009. Technical Support Document for Cancer Potency Factors 2009. Appendix B: Chemical-Specific Summaries of the Information Used to Derive Unit Risk and Cancer Potency Values. Last accessed (01/9/2018) at https://oehha.ca.gov/air/crnr/technical-support-document-cancer-potency-factors-2009

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/9/2018) at http://www.dec.ny.gov/chemical/34189.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/9/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System
Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
    Health Effects Assessment Summary Tables
    Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Dibenzofuran
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Dibenzofuran (CAS Number 132-64-9)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA OSRTI* Also used by: ♦ US EPA RSL*	1×10^{-3}	12.3	LOEL	10,000	Based on reduced body length and organ weights, and excess abdominal fat in female rats exposed via the diet in a 200-day study.
NYS DEC (2013)*	1×10^{-3}	3.1 [(2)]	LOEL	3000	Based on same study, species, sex, effects, and LOEL used by US EPA OSRTI.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]The point of departure was adjusted by a dosimetric adjustment factor [$(\text{animal BW}/\text{human BW})^{1/4}$] equal to $(0.32\ \text{kg}/80\ \text{kg})^{1/4}$.

LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the US EPA OSRTI and NYS DEC reference doses for dibenzofuran is identical with respect to choice of study, species, sex, effect and point of departure. The US EPA OSRTI applied a total uncertainty factor of 10,000 to the LOEL of 12.3 mg/kg/day to compensate for animal to human extrapolation (10), use of a minimal LOEL (3), use of a 200-day study (3), human variation (10) and deficiencies in the toxicity database (10), including the lack of developmental data and the minimal data details reported in the key study. The NYS DEC modified the point of departure using a dosimetric adjustment factor based on body weight scaling, according to US EPA recommendations (US EPA 2011). Consequently, they used an uncertainty factor of 3 (rather than 10) to account for differences in pharmacodynamics between animals and humans, and applied a total uncertainty factor of 3000 to the adjusted point of departure (3.1 mg/kg/day), rather than the 10,000-fold UF applied by the US EPA OSRTI to the unadjusted point of departure (12.3 mg/kg/day). Although the references doses are numerically equivalent, the use of an excessively large uncertainty factor (10,000) is not consistent with generally accepted risk assessment practices. Moreover, the NYS DEC provided a scientifically sound and well-documented rationale for the use of a 3000-fold uncertainty factor, and used the currently recommended method for interspecies extrapolation. Therefore, the NYS DEC reference dose (1×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for dibenzofuran.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: August, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS DEC (New York State Department of Environmental Conservation). 2013. Draft New York State Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Dibenzofuran. Albany, NY: Division of Water.

US EPA (U.S. Environmental Protection Agency). 2011. Recommended Use of Body Weight$^{3/4}$ as the Default Method in Derivation of the Oral Reference Dose. EPA/100/R11/0001. Last accessed (01/24/2018) at https://www.epa.gov/risk/recommended-use-body-weight-34-default-method-derivation-oral-reference-dose

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund. Last accessed (01/24/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/24/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation

New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Dibenzofuran
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Dibenzofuran (CAS Number 132-64-9)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	No human or animals data available.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for dibenzofuran is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: August, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Dibenzofuran
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Dibenzofuran (CAS Number 132-64-9)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for dibenzofuran is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Dibenzofuran is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects after oral or inhalation exposure. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration (4 mcg/m^3) from the recommended reference dose based on systemic effects (1×10^{-3} mg/kg/day; see Oral Non-Cancer Toxicity Value Documentation for Dibenzofuran). Therefore, a reference concentration of 4 mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for dibenzofuran.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs

Office of Superfund Remediation and Technology Innovation
Health Effects Assessment Summary Tables
Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Dibenzofuran
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Dibenzofuran (CAS Number 132-64-9)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for dibenzofuran is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,2-Dichlorobenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for 1,2-Dichlorobenzene (CAS Number 95-50-1)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA HEAST (1997) ♦ US EPA ODW ♦ NYS DEC (1997)	0.09	85.7	NOEL	1000	Based on the absence of treatment related effects in rats and mice exposed by corn oil gavage for 103 weeks.
WHO (2011)	0.429	42.9	NOEL	100	Based on tubular degeneration (*sic*) in the kidneys of the most highly exposed male mice exposed by corn oil gavage for 103 weeks.
RIVM (2001)	0.43	43	NOEL	100	Based on tubular regeneration in the kidneys of the most highly exposed male mice exposed by corn oil gavage for 103 weeks.
ATSDR*	0.3	30.74	$BMDL_{10}$	100	Based on tubular regeneration in the kidneys of the most highly exposed male mice exposed by corn oil gavage for 103 weeks.
CA EPA PHG*	0.09	89.3	NOEL	1000	Based on liver toxicity in rats exposed by corn oil gavage for 13 weeks.
HC DWQ	0.021	21	LOEL	1000	Based on increases in serum cholesterol (males), total serum protein (females) and serum glucose levels (females) in rats exposed by gavage 5 days per week for 13 weeks (same subchronic study used by CA EPA).
HC PSAP	0.43	43	NOEL	100	Based on tubular regeneration in the kidneys of the most highly exposed male mice exposed by corn oil gavage for 103 weeks.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. BMCL10: 95% lower limit on benchmark concentration at 10% response above background; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the reference doses for 1,2-dichlorobenzene derived by the US EPA, WHO, RIVM, ATSDR and HC PSAP is identical with respect to choice of study and species, but the interpretation of the critical effect or lack of effect in the study varies among the authoritative bodies. The US EPA concluded that the renal tubule regeneration observed in the high-dose male mice was of questionable significance since the effect was not observed in female mice or rats of either sex, and because the male mouse control incidence was significantly lower that those of three other approximately concurrent control groups. The US EPA therefore considered the highest dose tested a NOEL. The WHO, RIVM, ATSDR and HC PSAP considered the increasing trend in the renal tubule effect in male mice treatment related, and so chose the low dose as a NOEL. ATSDR used these data to estimate a 95% lower bound on the benchmark dose at 10% extra risk as the point of departure. The US EPA included an additional uncertainty factor of 10 to account for database deficiencies (including lack of a supporting reproductive study and inadequate chronic toxicity in a second species) that the WHO, RIVM, ATSDR and HC PSAP did not include, presumably because they considered the available chronic toxicity studies in rats and mice to be of sufficient quality. CA EPA also questioned the significance of the renal tubular regeneration in male mice at the high dose in the chronic study, but instead of considering that dose a chronic NOEL, chose a NOEL from the subchronic segment of the same study as its point of departure. CA EPA applied a total uncertainty factor of 1000 to this subchronic NOEL, 10-fold each to account for human and animal-to-human variability and10-fold for a subchronic extrapolation. Since the chronic high dose and the subchronic NOEL were nearly equal, the CA EPA RfD results in the same value as the US EPA RfD. For its Water Quality and Health program, HC DWQ derived a reference dose based on changes in serum chemistry parameters in the same subchronic rat gavage study used by CA EPA. These were observed at lower doses than the exposure level CA EPA considered a LOEL from that study. HC DWQ used uncertainty factors of 10 for use of a LOEL, 10 for use of a subchronic study and 10 for animal-to-human extrapolation to derive its reference dose. An uncertainty factor for human variation was not used on the basis that the LOEL was considered to be for a sensitive effect and at an exposure level below the NOELs in the chronic study. The serum chemistry changes observed in the subchronic segment of the NTP study were characterized as "slight", "minimal" or "relatively small" in the original NTP study report and might not be biologically significant. That no effects of clear biological significance were observed at exposure levels above this subchronic LOEL in the subsequent chronic gavage study suggests these biochemical changes were not precursors of more overt toxic responses and may only have been transient compensatory responses. The chronic gavage study was a well-conducted lifetime duration study in two rodent species and so is preferred for deriving a chronic oral RfD. Among the values based on the chronic data, the ATSDR chronic MRL derivation is most consistent with generally-accepted risk-assessment practice. Therefore 0.3 mg/kg/d is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,2-dichlorobenzene.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/18/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/18/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/18/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/18/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for 1,2-Dichlorobenzene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/18/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/18/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/18/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/18/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/18/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: 1,2-Dichlorobenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 1,2-Dichlorobenzene (CAS Number 95-50-1)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) RIVM (2000) Health Canada (1991) NYSDEC (1997)	--	--	--	--	Human data are not available. Available animal studies show both positive and negative trends for carcinogenicity

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for 1,2-dichlorobenzene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

Health Canada. 1993. Priority substances list assessment report: 1,2-dichlorobenzene. Ottawa. Ministry of Public Works and Government Services. Last accessed (01/18/2018) at https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/canadian-environmental-protection-act-priority-substances-list-report-1-2-dichlorobenzene.html

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for 1,2-Dichlorobenzene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 193-203. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies Checked for Cancer Potency Values:

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,2-Dichlorobenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for 1,2-Dichlorobenzene (CAS Number 95-50-1)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA HEAST (1997) Also used by: ♦ US EPA Region 3 (2003)	200	2×10^5	NOEL	1000	Based on decreased weight gain in rats exposed by inhalation for 7 months.
RIVM (2000)	600	6×10^4	NOEL	100	Based on decreased spleen weight in guinea pigs exposed via inhalation for 7 hours/day, 5 days/week for up to 7 months. LOEL = 5.6×10^5 mcg/m^3.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

The reference concentrations for 1,2-dichlorobenzene derived by authoritative bodies from the list in item 5 (below) are both based on subchronic inhalation studies. The US EPA reference concentration is based on decreased weight gain in rats, while the RIVM value is based on decreased spleen weight in guinea pigs. Both values are derived using default reference concentration methods, including application of 10-fold uncertainty factors to account for inter- and intraspecies variability. The US EPA derivation includes an additional 10-fold uncertainty factor for use of a subchronic study. Study durations were very similar in both cases and the additional 10-fold uncertainty factor is consistent with current risk assessment practices. Therefore, the US EPA reference concentration (200 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,2-dichlorobenzene.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,2-Dichlorobenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 1,2-Dichlorobenzene (CAS Number 95-50-1)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for 1,2-dichlorobenzene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,3-Dichlorobenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for 1,3-Dichlorobenzene (CAS Number 541-73-1)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
NYS DEC (1997)	9×10^{-3}	9	LOEL	1000	Based on biochemical indicators of liver dysfunction in male rats exposed by corn oil gavage for 90 days
US EPA Region 3 (2003[2]; 2004; Draft)	3×10^{-3}	9	LOEL	3000	Based on same study and same effects as NYS DEC reference dose.
US EPA OW (2004)	0.09	--	--	--	Information on the basis of the reference dose is unavailable.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. LOEL: lowest observed effect level; UF: uncertainty factor.

2 Value in online table is in error; correct value obtained via personal communication (US EPA Region 3, 2004)

2. Recommendation and Rationale

The basis of the US EPA Region 3 and NYS DEC reference doses is identical with respect to study, species and critical effect. The basis of the US EPA Office of Water value is unclear based on available documentation. NYS DEC applied an uncertainty factor of 1000 to the subchronic LOEL. They cited US EPA IRIS documentation noting that in a study of chronic oral exposure to a related chemical (1,4-dichlorobenzene) in rats, liver lesions in rats did not progress in severity with increasing duration of exposure, and so used a less than 10-fold uncertainty factor (unspecified, but would be UF = 1 if other conventional UF's are assumed) to account for the use of a subchronic study. The US EPA Region 3 value is based on application of a total uncertainty factor of 3000, accounting for interspecies and intraspecies variability, the use of a LOEL, the use of a subchronic study and database deficiencies. In citing the lack of progression of the rat liver lesions with chronic 1,4-dichlorobenzene exposure, the US EPA IRIS documentation for the 1,4-dichlorobenzene reference concentration reduces the sub-chronic uncertainty factor from 10 to 3, rather than 1. Therefore, the US EPA Region 3 reference dose (3×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,3-dichlorobenzene.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for 1,3-Dichlorobenzene. Albany, NY: Division of Water.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Cited as an NCEA provisional value (not peer reviewed). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Personal communication from Region 3 staff correcting error in risk-based concentration table.

US EPA Region 3 (United States Environmental Protection Agency Region 3). Draft. Risk assessment issue paper for: derivation of a provisional RfD for 1,3-dichlorobenzene (CASRN 541-73-1).

US EPA ODW (United States Environmental Protection Agency Office of Water). 2004. 2004 Edition of the Drinking Water Standards and Health Advisories. EPA 822-R-04-005. Last accessed (01/18/2018) at http://www.epa.gov/waterscience/drinking/standards/dwstandards.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,3-Dichlorobenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 1,3-Dichlorobenzene (CAS Number 541-73-1)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Human data and chronic animal bioassays are not available. Limited genotoxicity studies do not suggest carcinogenic potential.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for 1,3-dichlorobenzene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies Checked for Cancer Potency Values:

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,3-Dichlorobenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for 1,3-Dichlorobenzene (CAS Number 541-73-1)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for 1,3-dichlorobenzene is not available from the authoritative bodies listed in item number 5 (below). 1,3-Dichlorobenzene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for 1,3-dichlorobenzene is 3×10^{-3} mg/kg/day. Therefore, a reference concentration of 10 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,3-dichlorobenzene.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,3-Dichlorobenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 1,3-Dichlorobenzene (CAS Number 541-73-1)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for 1,3-dichlorobenzene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,4-Dichlorobenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for 1,4-Dichlorobenzene (CAS Number 106-46-7)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
RIVM (2001)	0.1	10 110	NOEL LOEL	100 1000	Equivalent values based on NOEL for multiple effects seen in dogs exposed to 1,4-dichlorobenzene for one year and LOEL for kidney and parathyroid toxicity in male rats exposed via gavage for 2 years.
NYS DEC (1997) Also used by: • US EPA ODW*	0.1	107 107	NOEL LOEL	1000 1000	Based on a subchronic NOEL for kidney toxicity in male rats exposed by gavage for 13 weeks and a chronic LOEL for kidney toxicity in male rats exposed by gavage for 2 years
ATSDR* Also used by: • US EPA RSL*	0.07	7	$BMDL_{1sd}$	100	Based on increased liver weight and increased serum alkaline phosphatase in male and female dogs orally exposed for one year (same dog study as was used by RIVM). Study LOEL was 36 mg/kg/day (time weighted).
WHO (2011)	0.107	107	LOEL	1000	Based on kidney and parathyroid toxicity in male rats exposed by corn oil gavage for 2 years.
CA EPA PHG*	0.013	13	NOEL	1000	Based on changes in liver and kidney weight in female rats orally exposed for 192 days.
HC PSAP	0.078	39	NOEL	500	Based on route to route extrapolation in rats exposed by inhalation for 76

					weeks.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. $BMDL_{1sd}$: 95% lower limit on benchmark dose at 1 standard deviation above the mean control response; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the WHO reference dose and one of the RIVM reference dose derivations for 1,4-dichlorobenzene is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (rat LOEL; 110 mg/kg/day when rounded to 2 significant digits). The RIVM reference dose is also supported by a chronic dog NOEL that is 10-fold lower than the rat LOEL, resulting in the same reference dose value. The basis for the NYS DEC and US EPA ODW reference dose includes the same chronic rat LOEL as used by RIVM and WHO, as well as a subchronic NOEL that is essentially equal to the chronic LOEL. The Health Canada value is based on an inhalation exposure study and is not chosen for derivation of an oral reference dose, given the availability of good quality oral data. The CA PHG value is based on a subchronic oral exposure study and is not preferred as data from good quality chronic studies are available. The ATSDR and US EPA RSL values are based on a chronic oral study in dogs (the same data used as support for the RIVM reference dose). ATSDR estimated a 95% lower limit on the benchmark dose associated with a one standard deviation increase above the control mean response and applied 10-fold uncertainty factors to account for animal-to-human and human variation. The dog study identified a lower LOEL than the rat studies used by other authoritative bodies, and the ATSDR derivation is more consistent with generally-accepted risk assessment practices. Therefore, the ATSDR reference dose (0.07 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,4-dichlorobenzene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/17/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/17/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/17/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,4-Dichlorobenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 1,4-Dichlorobenzene (CAS Number 106-46-7)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA HEAST (1997) Also used by: ♦ US EPA Region 3 (2003)	4.2×10^{-5}	0.024	linearized multistage model	body surface area[2]	Based on the combined incidence of liver adenomas and carcinomas in male mice exposed by gavage for two years
Health Canada (1987)	6.6×10^{-5} to 2.4×10^{-4}	--[3]	linearized multistage model	body surface area[2]	Range based on hepatocellular adenomas in male mice and adrenal gland phaeochromocytomas in male mice exposed by gavage for two years.
Cal EPA (1997)	1.9×10^{-4}	5.4×10^{-3}	linearized multistage model	BW ¾ [4]	Based on the same tumor data as the US EPA value
NYS DEC (1997)	9.1×10^{-5}	0.011	linearized multistage model (extra risk)	BW ¾ [4]	Based on the same tumor data as the US EPA value

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]No cancer potency factor was derived. The risk specific dose was obtained from the drinking water unit risk range of 1.2×10^{-7} to 4.3×10^{-7} per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day.
[4]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.

2. Recommendation and Rationale

The basis for the various cancer potency values for are essentially identical with respect to choice of study, species and tumor data, and all three values were derived using a linearized multistage approach to model the dose-response data. Health Canada also used an additional data set for adrenal gland tumors in male mice exposed by gavage to get a range of risk-specific water concentrations for their Water Quality and Health program. The NYS DEC and Cal EPA both used BW ¾ scaling for interspecies extrapolation, while the US EPA (HEAST and Region 3 RBC) and Health Canada used body surface area scaling. Cal EPA also used an adjustment for intercurrent mortality that reduced their cancer potency factor by about 2-fold compared to the NYS DEC value. Survival did not differ significantly between control and dosed animals in the critical study, and a clear technical rationale was not provided for the adjustment used by Cal EPA. Therefore, the NYS DEC cancer potency factor (0.011 per mg/kg/day) is the toxicity value recommended for use in the derivation of a cancer-based soil cleanup objective for 1,4-dichlorobenzene. The 1,4-dichlorobenzene risk specific dose calculated from this toxicity value is 9.1×10^{-5} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 1997. Public Health Goal for 1,4-Dichlorobenzene in Drinking Water. Office of Environmental Health Hazard Assessment. Last accessed (01/18/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

Health Canada. 1987. Water Quality and Health. Guidelines for Canadian Drinking Water Quality. Healthy Environments and Consumer Safety. Last accessed (01/18/2018) at https://www.canada.ca/en/health-canada/services/environmental-workplace-health/water-quality/drinking-water/canadian-drinking-water-guidelines.html

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for 1,4-Dichlorobenzene. Albany, NY: Division of Water.

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 997-1).

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,4-Dichlorobenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for 1,4-Dichlorobenzene (CAS Number 106-46-7)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: • US EPA RSL • US EPA HEAST (1997) • CA EPA REL	800	7.5×10^4	NOEL	100	Based on increased liver weights in male rats exposed by inhalation for 6 hours/day and 7 days/week in a multigenerational study. Study LOEL = 2.25×10^5 mcg/m^3.
ATSDR*	60**	1.6×10^3	$BMCL_{10}$	30	Based on nasal olfactory lesions in female rats exposed by inhalation for 6 hours/day, 5 days/week for 104 weeks. Study LOEL = 1.3×10^4 mcg/m^3. A time-weighted HEC was obtained by estimating the benchmark concentration at 10% above the background response.
HC PSAP	270 [2]	6.7×10^4	NOEL	500	Based on increased liver and kidney weights and urinary protein in rats exposed by inhalation 5 hours/day, 5 days/week for 76 weeks. Study LOEL = 4.5×10^5 mcg/m^3. A tolerable daily intake of 0.078 mg/kg/day was derived based on default assumptions for rat body weight and respiration rate.

RIVM (2001)	670	6.7×10^4	NOEL	100	Based on the same study used by Health Canada (1998).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

[2]Derived from a per-unit-body-weight tolerable daily intake based on default assumptions of 70 kg adult body weight and 20 m^3 per day respiration rate.

$BMCL_{10}$: 95% lower confidence limit on benchmark concentration at 10% response above background; HEC: human equivalent concentration; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

**The ATSDR value is reported as 0.01 parts per million (ppm). For 1,4-dichlorobenzene, 1 ppm = 6.01 mg/m^3.

2. Recommendation and Rationale

The available reference concentrations for 1,4-dichlorobenzene derived by authoritative bodies from the list in item 5 (below) are based on two different rat studies that reported similar effects and similar NOEL points of departure, and on a third rat study that reported effects on the respiratory tract following chronic exposure. The ATSDR value is based on nasal lesions in rats exposed to 1,4-dichlorobenzene by inhalation for 104-weeks. The point of departure was derived using the EPA's inhalation dosimetric adjustment methodology (US EPA, 1994) and calculation of the regional gas deposition ratio between rats and humans, treating 1,4-dichlorobenzene as a Category 1 gas. However, 1,4-dichlorobenzene does not have some of the characteristics of a Category 1 gas as defined by EPA's guidance (US EPA, 1994), which include water solubility and lack of significant accumulation in the blood. Also, no evidence is provided suggesting the nasal lesions are the result of local absorption and metabolism, which is another defining characteristic of a Category 1 gas. The ATSDR does not provide a justification for this categorization, and therefore the value is derived in a manner not entirely consistent with EPA's guidance. The US EPA IRIS value is based on increased liver weights in rats exposed via inhalation in a 2-generation study, while the Health Canada and RIVM values are based on increased liver and kidney weights and urinary protein levels in rats exposed via inhalation for 76 weeks, with an additional 36 weeks of observation. The US EPA derivation includes a total uncertainty factor of 100, including a factor of 10 accounting for human variability, a factor of 3 combined with a pharmacokinetic adjustment (equal to 1) to account for animal-to-human variability and a factor of 3 to account for the use of a subchronic study. The latter uncertainty factor was reduced from 10 based on other data suggesting that rodent liver lesions generally did not progress with longer duration of exposure to 1,4-dichlorobenzene. RIVM applied 100-fold uncertainty factors to account for animal-to-human and human variability, while Health Canada applied a total uncertainty factor of 500. Health Canada derivation included a 10-fold factors to account for human and animal-to-human variability, but also included a factor of 5 to account for uncertainties regarding carcinogenicity. They also included an indirect adjustment for inhalation intake in rats compared to inhalation intake in humans by deriving a dose per unit body weight tolerable daily intake from the inhalation point of departure, using default assumptions for rat respiration rate and body weight. The additional factor regarding carcinogenic uncertainty is inappropriate in the current context, since non-cancer and cancer effects are being assessed separately. The indirect pharmacokinetic adjustment based on default body weights and breathing rates is also not consistent with currently-accepted risk assessment practice. The US EPA IRIS derivation is most consistent with generally accepted risk assessment practice since it explicitly employs a pharmacokinetic adjustment for a gas that causes systemic effects, and adjusts the animal-to-human uncertainty factor accordingly. Therefore, the US EPA reference concentration (800 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,4-dichlorobenzene.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/19/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/19/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/19/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/19/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/19/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/19/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. **Authoritative Bodies**

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,4-Dichlorobenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 1,4-Dichlorobenzene (CAS Number 106-46-7)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA RSL	0.16	6.3×10^{-6} [2]	linear multistage	body surface area[3]	Estimated from route-to-route extrapolation of an oral cancer potency factor of 0.022 per mg/kg/day, which was based on the incidence of combined hepatocellular adenomas and carcinomas in male mice exposed by gavage for two years.
US EPA OPP*	0.25	4.0×10^{-6}	--	--	Based on liver tumors in male and female mice exposed by inhalation. Limited details provided.
CA EPA CPF	0.091	1.1×10^{-5}	linear multistage	body surface area[3]	Based on same study as US EPA RSL. Estimated from route-to-route extrapolation of an oral cancer potency factor of 0.04 per mg/kg/day.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]The value was originally reported as an inhalation cancer slope factor (per mg/kg/day) and was converted to a unit risk by assuming a 70 kg adult breathes 20 m^3 of air per day.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

Both the US EPA RSL and CA EPA unit risks are based on an increased incidence of liver tumors in mice exposed by gavage to 1,4-dichlorobenzene for two years. However, these values are derived via oral-to-inhalation route extrapolation from oral cancer potency factors that were not recommended as the oral cancer toxicity value for 1,4-dichlorobenzene. The US EPA OPP unit risk appears to be derived from liver tumor data from an inhalation study in mice. However, the OPP documentation provides little detail about the data set or the methods used to derive the unit risk, and cites as the basis for the unit risk a 2006 revised final draft toxicological review from the EPA IRIS program that is not available on the IRIS or NCEA web sites. The IRIS draft toxicological review available on the web site is an external review draft dated 2003 and concludes that data appropriate for conducting an inhalation cancer risk assessment are not available. Since no clearly documented toxicity values from the authoritative bodies listed in item 5 (below) are based on inhalation data, and at least one authoritative body derived a unit risk using exposure route extrapolation, a default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a unit risk from the recommended cancer potency factor. The recommended oral cancer potency factor for 1,4-dichlorobenzene is 0.011 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for 1,4-Dichlorobenzene). Therefore the unit risk of 3.1×10^{-6} per mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for 1,4-dichlorobenzene. The 1,4-dichlorobenzene risk specific air concentration calculated from this toxicity value is 0.32 mcg/m^3.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: December 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/14/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

US EPA OPP (United States Environmental Protection Agency, Office of Pesticide Programs). Pesticide Reregistration Status. Last accessed (01/14/2018) at http://www.epa.gov/opp00001/reregistration/status.htm.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/14/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health

United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,1-Dichloroethane
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for 1,1-Dichloroethane (CAS Number 75-34-3)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA PPRTV Also used by: • US EPA RSL	0.2	714	NOEL	3000	Based on moderate daily CNS depression and increased urinary enzyme markers for renal damage in rats exposed for 13 weeks by gavage.
CA EPA PHG	0.04	40	NOEL	1000	Based on route-to-route extrapolation from a 13-week study in cats exposed by inhalation where kidney damage was observed.
US EPA HEAST (1997)	0.1	115	NOEL	1000	Based on route to route extrapolation from a 13-week rat inhalation study where no effect was observed. The rats in this study and the cats in the study used by CA EPA PHG were exposed simultaneously, along with rabbits and guinea pigs.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The available reference dose values for 1,1-dichloroethane derived by authoritative bodies from the list in item 5 (below) all have significant uncertainties due to study quality issues and problems in data interpretation. The US EPA PPRTV reference dose is the only value derived from route-specific data and is based on evidence of transient central nervous system depression after dosing and changes in some urinary enzyme markers suggestive of kidney damage in rats exposed by gavage. US EPA noted that results were not presented for several urinary and serum biochemical markers that were assayed in

the study, raising uncertainties about whether or not those results showed any treatment-related effects. The urinary enzyme marker identified as the critical effect in the study showed erratic results, with transient increases above control levels at weeks 6 and 8, and then lower levels than controls at week 12. According to US EPA PPRTV, these changes included the lowest dose group, but this group was identified as a NOEL in the assessment without any explanation of this apparent inconsistency. The CA EPA PHG reference dose is based on route-to-route extrapolation from a limited 13-week inhalation study which observed kidney toxicity in cats. The study limitations include a small number of animals per exposure group (two per sex) and an unconventional exposure design where groups of four different species (rats, guinea pigs and rabbits, in addition to cats) were all simultaneously exposed in the same chamber. The exposure design also exposed the same animals consecutively to the two different exposure concentrations, rather than exposing separate groups of animals concurrently. Serum biochemical indicators of kidney effects were only observed in cats during the high exposure phase of the study and corresponded with observed kidney histopathology after study termination. However, no direct observations of the kidney were made in cats during the low exposure phase, and it is not clear that the low exposure level can be unambiguously identified as NOEL. The US EPA HEAST reference dose is based on route to route extrapolation from a subchronic inhalation NOEL in rats from the same study used as the basis of the CA EPA PHG reference dose. No adverse effects were observed in rats at either exposure level. The inhaled dose at the lower of the two exposure levels was calculated and used as the point of departure. However, the highest NOEL is more typically used as the point of departure, and as noted for the cat data, it is unclear how to unambiguously assign effect level qualifiers to the different exposure phases in this study. Since the database for 1,1-dichloroethane is very limited, and all three reference dose derivations have significant uncertainties, a reference dose for use in derivation of an oral non-cancer-based soil cleanup objective for 1,1-dichloroethane is not recommended. The development of the oral-based soil cleanup objective will use the recommended cancer toxicity value.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/20/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/20/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund . Last accessed (01/20/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/20/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: 1,1-Dichloroethane
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 1,1-Dichloroethane (CAS Number 75-34-3)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
Cal EPA (2002)	1.8×10^{-4}	5.7×10^{-3}	multistage time-to-tumor model	body surface area[2]	Based on mammary gland adenocarcinomas observed in female rats exposed by corn oil gavage in a chronic bioassay.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.

2. Recommendation and Rationale

The Cal EPA cancer potency factor is the only available factor from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. The Cal EPA cancer potency factor (0.0057 per mg/kg/day) is therefore the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for 1,1-dichloroethane. The 1,1-dichloroethane risk specific dose calculated from this toxicity value is 1.8×10^{-4} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2002. Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. Cancer Potency Values. Technical Support Document for Describing Available Cancer Potency Factors. Last accessed (01/18/2018) at http://www.oehha.ca.gov/air/hot_spots/pdf/TSDNov2002.pdf.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,1-Dichloroethane
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for 1,1-Dichloroethane (CAS Number 75-34-3)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA HEAST (1997) Also used by: • US EPA Region 3 (2004)	500	5×10^5	NOEL	1,000	Based on kidney damage in cats exposed by inhalation six hours per day, five days per week for 13 weeks. Study LOEL = 1×10^6 mcg/m^3.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The US EPA value is the only available reference concentration for 1,1-dichloroethane derived by an authoritative body from the list in item 5 (below). The US EPA HEAST reference concentration is based on kidney toxicity in a limited subchronic inhalation study in cats that used two exposure levels. The study is weakened by the small number of animals per exposure group (two), and the fact that the same animals were used for both exposure levels, meaning that the exposures to different levels of 1,1-dichloroethane did not happen concurrently, and in fact involved the same animals. Since the database for 1,1-dichloroethane is very limited, and the study used as the basis for the reference concentration has significant methodological limitations, a reference concentration for use in derivation of an inhalation non-cancer-based soil cleanup objective for 1,1-dichloroethane is not recommended. The development of the inhalation-based soil cleanup objective will use the recommended cancer toxicity value.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January,2018

4. References for Summary Table

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/16/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,1-Dichloroethane
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 1,1-Dichloroethane (CAS Number 75-34-3)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
Cal EPA (2002)	0.625	1.6×10^{-6}	multistage time-to-tumor model	body surface area [2]	Based on route-to-route extrapolation of an oral cancer potency factor of 5.7×10^{-3} per mg/kg/day, which is based on mammary gland adenocarcinomas observed in female rats in a 78-week corn oil gavage study.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.

2. Recommendation and Rationale

The Cal EPA unit risk is the only available value from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the Cal EPA unit risk (1.6×10^{-6} per mcg/m^3) is the toxicity value recommended for use in the derivation of a inhalation cancer-based soil cleanup objective for 1,1-dichloroethane. The 1,1-dichloroethane risk specific air concentration calculated from this toxicity value is 0.625 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2002. Technical Support Document for Describing Available Cancer Potency Factors, December. Sacramento, CA: Office of Environmental

Health Hazard Assessment, Air Toxicology and Epidemiology Section, California Environmental Protection Agency.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,1-Dichloroethene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for 1,1-Dichloroethene (CAS Number 75-35-4)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: • US EPA HEAST (1997) • US EPA Region 3 (2003) • US EPA ODW (2004)	0.05	4.6	$BMDL_{10}$	100	Based on 2 year drinking water study where liver toxicity (midzonal fatty changes) was observed in female rats. Study NOEL = 9 mg/kg/day. Study LOEL = 14 mg/kg/day
ATSDR (1994)	9×10^{-3}	9	LOEL	1000	Based on the same study a US EPA IRIS, but ATSDR considered the minimal hepatocellular swelling observed in female rats at the lowest dose a biologically significant effect
Health Canada (1994)	3×10^{-3}	9	LOEL	3000	Based on same study as US EPA IRIS, Health Canada considered the lowest dose a LOEL based on midzonal fatty changes in the livers of females.
WHO (2003)	0.05	4.6	$BMDL_{10}$	100	Based on same study as US EPA IRIS

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor; $BMDL_{10}$: lower bound on benchmark dose at 10% effect

2. Recommendation and Rationale

The basis for the four different reference doses for 1,1-dichloroethene is identical with respect to the choice of study and species. The critical effect for the ATSDR reference dose was minimal hepatic swelling at the lowest dose in female rats. In a recent update of the US EPA assessment (which is mirrored by the WHO assessment), the US EPA concluded that the minimal hepatic swelling was not a biologically significant effect because it was not accompanied by other biochemical, histopathological or functional changes. The US EPA, WHO and Health Canada reference dose values are based on midzonal fatty changes in liver. Health Canada considered the lowest dose (9 mg/kg/day) a LOEL, while the US EPA considered the statistically significant fatty changes in the liver at this dose a minimal adverse effect. The US EPA and WHO derived a lower point of departure than the ATSDR and Health Canada LOEL using a benchmark dose approach, but in doing so, reduced the uncertainty factor by 10 and 30-fold, respectively, in their derivation of the reference dose. Health Canada also used an addition uncertainty factor of 3 to account for limited evidence of carcinogenicity, which is not relevant in this context since cancer and non-cancer evaluations are being done separately. Based on the questionable biological significance of the minimal hepatic swelling, and the use of the more robust BMDL approach, the US EPA reference dose (0.05 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,1-dichloroethene.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1994. Toxicological Profile for 1,1-Dichloroethene. U.S. Department of Health and Human Services, Public Health Service. May. https://www.atsdr.cdc.gov/toxprofiledocs/index.html

Health Canada. 1994. Water Quality and Health. Guidelines for Canadian Drinking Water Quality. Healthy Environments and Consumer Safety. Last accessed (01/18/2018) at http://www.hc-sc.gc.ca/hecs-sesc/water/dwgsup.htm

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 997-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2004. Office of Drinking Water, Drinking Water Standards and Health Advisories. Washington, DC. EPA 822-R-04-005.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2003. Concise International Chemical Assessment Document. Last accessed (01/17/2018) at http://www.who.int/pcs/cicad/full_text/cicad51.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,1-Dichloroethene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 1,1-Dichloroethene (CAS Number 75-35-4)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
ATSDR US EPA IRIS	--	--	--	--	One limited epidemiology study provided no evidence of carcinogenicity. Animal studies do not suggest carcinogenicity by the oral route of exposure and are inadequate for deriving a cancer potency factor.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for 1,1-dichloroethene is not available from any of the authoritative bodies listed in item 5 (below). 1,1-Dichloroethene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure. The New York State Department of Health (NYSDOH) derived an inhalation unit risk (7.6×10^{-5} per mcg/m^3; see Inhalation Cancer Toxicity Value Documentation for 1,1-Dichloroethene) based on cancer effects distant from the site of contact, specifically, combined vascular and liver tumors in female mice exposed via inhalation 6 hours/day, 5 days/week for two years. The NYS DOH inhalation unit risk was derived using methods that are consistent with generally accepted risk assessment practices. A default route $_{Inhalation}$-to-route$_{Oral}$ extrapolation assuming a 70-kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a cancer potency factor from the inhalation unit risk. Therefore, the derived cancer potency factor of 0.27 per mg/kg/day is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for 1,1-dichloroethene. The 1,1-dichloroethen risk specific dose calculated from this toxicity value is 3.8×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological Profiles. Last accessed (01/16/2018) at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/16/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System
Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
    Health Effects Assessment Summary Tables
    Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: 1,1-Dichloroethene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for 1,1-Dichloroethene (CAS Number 75-35-4)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
NYSDOH (2017)	4.4	4.4×10^3	LOEL	1000	Based on increased incidence of degenerative lesions of the nasal cavity in mice exposed by inhalation 6 hours/day, 5 days/week, for two years.
US EPA IRIS Also used by: ◆ US EPA RSL	200	6.9×10^3	$BMCL_{10}$ [(2)]	30	Based on liver toxicity (midzonal fatty changes) in female rats exposed by inhalation 6 hours/day, 5 days/week, for 18 months. Study NOEL = 1.77×10^4 mcg/m^3; Study LOEL = 5.32×10^4 mcg/m^3.
CA EPA REL	70	2.0×10^4	NOEL	300	Based on increased mortality and liver toxicity in guinea pigs exposed continuously via inhalation for 90 days. Study LOEL (increased mortality) = 6.1×10^4 mcg/m^3; Study LOEL (liver effects) = 1.89×10^5 mcg/m^3.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
[2]$BMCL_{10}$ = the 95% lower bound on the modeled benchmark concentration associated with 10% incidence of the toxic effect.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The reference concentrations for 1,1-dichloroethene derived by authoritative bodies from the list in item 5 (below) are based on inhalation studies in rats, mice, and guinea pigs. The CA EPA based their derivation on a 90-day continuous exposure guinea pig study reporting increases in mortality and liver toxicity. The CA EPA assumed the default dosimetry of equal effects at equal air concentrations for a gas causing systemic toxicity, and applied a total uncertainty factor of 300 to the subchronic NOEL. The total uncertainty of 300 included 10-fold for intraspecies variability, 10-fold for a subchronic study and 3-fold for interspecies variability.

The US EPA based their reference concentration on liver toxicity in rats exposed by inhalation for 18 months. They made the same dosimetric adjustment used by the CA EPA (i.e., equal effects at equal air concentrations based on a gas causing systemic toxicity) and estimated a point of departure based on a $BMCL_{10}$. They applied a total uncertainty factor of 30, including 10-fold to account for intraspecies variability and 3-fold to account for interspecies variability. An additional uncertainty factor for a less than lifetime study was not considered necessary because the liver effects observed at interim sacrifices during the study were not progressing, and in fact were decreasing in incidence with increasing study duration.

In 2015, the National Toxicology Program (NTP 2015) published the results of a two-year inhalation study of 1,1-dichloroethene in rats and mice. The report was published after CA EPA and US EPA derived their reference concentrations. The study is unequivocally a substantially better toxicology study than the studies used by CA EPA and US EPA to derive their reference concentrations. Thus, the NYSDOH identified the most sensitive response in the study (the incidence of degenerative nasal cavity lesions in mice) and used it to derive their reference concentration. The NYSDOH also assumed equal effects at equal air concentrations for the animal-to-human dosimetric adjustment, and applied a total uncertainty factor of 1000 to the study LOEL. The total uncertainty of 1000 included 10-fold to account for use of a LOEL, 10-fold for intraspecies variability, 3-fold for interspecies variability, and 3-fold for database deficiencies. The NYSDOH did not use a modelled point of departure (i.e., a $BMCL_{10}$) because the effects occurred in nearly all study animals exposed to the lowest non-zero air concentration. Under these conditions, the benchmark modeling approach results in uncertain estimates of a theoretical NOEL (that is, a $BMCL_{10}$) that are not clearly superior to an estimated NOEL based on a conservative 10-fold uncertainty factor applied to a LOEL.

The CA EPA and US EPA derivations are based on studies in which the animals were exposed for less than their lifetimes. Chronic lifetime studies are preferred for the derivation of reference concentrations, and the NYSDOH derivation is based on a high quality, peer reviewed two-year (lifetime) inhalation study (NTP 2015) reporting a sensitive effect (increased degenerative nasal cavity lesions) in mice. Therefore, the NYSDOH reference concentration (4.4 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation noncancer based soil cleanup objective for 1,1-dichloroethene.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure

Levels. Last accessed (01/16/2018) at https://oehha.ca.gov/air/crnr/notice-adoption-air-toxics-hot-spots-program-technical-support-document-derivation

NTP (National Toxicology Program). 2015. National Toxicology Program, National Institutes of Health. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Vinylidene Chloride (CAS No. 75-35-4) in F344/N Rats and B6C3F1/N Mice (Inhalation Studies). Research Triangle Park, NC. Publication No. NTP TR 582.

NYSDOH (New York State Department of Health). 2017. 1,1-Dichloroethene Inhalation Reference Concentration. Albany NY: Bureau of Toxic Substance Assessment.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). Last accessed (01/16/2018) at https://www.epa.gov/iris.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). 2017. Last accessed (01/16/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,1-Dichloroethene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 1,1-Dichloroethene (CAS Number 75-35-4)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
NYSDOH (2017)	1.3×10^{-2}	7.6×10^{-5}	linearized multistage model	equal risk assumed at equal air concentrations	Based on combined vascular and liver tumors in female mice exposed via inhalation 6 hours/day, 5 days/week in a two-year study.
US EPA IRIS	--	--	--	--	Studies have been reviewed but weight of evidence is not sufficient to justify deriving an inhalation unit risk.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} air concentration), where 1×10^{-6} concentration = 1×10^{-6} / inhalation unit risk.

2. Recommendation and Rationale

The inhalation unit risk derived by the NYSDOH is based on an increased incidence of vascular and liver tumors observed in female mice exposed by inhalation to 1,1-dichloroethene for two years. The NYSDOH used the linearized multistage model to estimate the 95% lower confidence limit on the benchmark air concentration associated with a 10% tumor response (a $BMCL_{10}$). A default dosimetric adjustment factor of 1 was applied to obtain a human equivalent concentration, assuming equal risk for mice and humans at equal 1,1-dichloroethene air concentrations. The derivation is based on a high quality and peer reviewed two-year inhalation study, is consistent with generally accepted risk assessment practices, and is the only inhalation unit risk available for 1,1-dichloroethene from an authoritative body listed in item 5 (below). Therefore, the NYSDOH unit risk (7.6×10^{-5} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for 1,1-dichloroethene. The 1,1-dichloroethene risk specific air concentration calculated from this toxicity value is 1.3×10^{-2} mcg/m^3.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table

NYSDOH (New York State Department of Health). 2017. 1,1-Dichloroethene Inhalation Unit Risk. Albany NY: Bureau of Toxic Substance Assessment.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). Last accessed (8/17/2017) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,2-Dichloroethane
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for 1,2-Dichloroethane (CAS Number 107-06-2)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA OSRTI * Also used by: • US EPA RSL *	0.006	58	LOEL	10,000	Based on significant dose-related increases in kidney weight and kidney-to-body-weight ratio in male and female rats in a 13-week drinking water study.
CA EPA PHG	0.045	45.3	NOEL	1000	Based on renal lesions in female rats in the same 13-week drinking water study as used by US EPA OSRTI. Study LOEL = 90.6 mg/kg/day.
NYS DEC (1997)	5.8×10^{-3}	58	LOEL	10,000	Based on the same study as used by US EPA OSRTI.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis of the reference doses available from authoritative bodies listed below is identical with respect to study and species. All three values are derived from a 13-week drinking water study in rats where significant increases in absolute and relative kidney weights were observed at the lowest dose tested, although histopathological kidney lesions were only observed at higher doses. The NYS DEC and US EPA considered the lowest dose where kidney weight effects occurred to be a LOEL, while CA EPA did not consider those effects to be of toxicological significance, and identified this dose with only kidney weight changes unaccompanied by any histopathological changes as a NOEL. CA EPA estimated daily intake at the point of departure dose using a different method than US EPA and NYS DEC, resulting in a slightly lower dose from the same exposure group. Although the absolute and relative kidney weight changes observed at the lowest dose in this subchronic study could represent precursors for frank toxic effects at higher doses, the identification of this dose as a LOEL led NYS DEC and US EPA to apply default uncertainty factors totaling 10,000 to the LOEL. Exposure at the

level of the CA EPA reference dose is still over 1000 times lower than the dose level identified as a LOEL by the NYS DEC and US EPA, and the derivation of the CA EPA reference dose is more consistent with generally accepted risk assessment practice. In addition, a gavage study in rats run concurrently by the same investigators and spanning a larger range of doses observed a very similar LOEL (54 mg/kg/day time-weighted) and a slightly lower NOEL (26 mg/kg/day) for increased kidney weight in females. This suggests the lowest dose in the drinking water study is only a minimal LOEL and very close to a NOEL. Therefore, the CA EPA reference dose (0.045 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,2-dichloroethane.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/12/2018) at http://www.oehha.ca.gov/water/phg/allphgs.html.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for 1,2-Dichloroethane. Albany, NY: Division of Water.

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund . Last accessed (01/12/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/12/2018) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,2-Dichloroethane
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

6. Summary of Available Oral Cancer Potency Values for 1,2-Dichloroethane (CAS Number 107-06-2)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ♦ US EPA RSL	1.1×10^{-5}	0.091	linearized multistage model (with time-to-death analysis), extra risk	body surface area[2] with time weighting for gavage dosing, less-than-lifetime dosing and % metabolized	Based on the induction of several tumor types in rats and mice treated by corn oil gavage. The cancer potency factor is derived from the data set of hemangiosarcomas in male rats. Dose scaling not clearly specified in IRIS, but see NYS DEC (1997).
HC PSAP (see also TERA)	1.2×10^{-4}	-- [3]	linearized multistage model	body weight [4]	Based on the incidence of several tumor types in male and female rats and mice. HC PSAP derived a range of risk-specific doses and the lowest value is presented (limited methodology information available)
HC DWQ	1.8×10^{-5}	-- [5]	linearized multistage model	body surface area[2]	Based on circulatory system hemangiosarcomas in male rats exposed for 78 weeks by corn oil gavage.
RIVM (2001)	1.4×10^{-4}	-- [6]	linear extrapol-ation	body weight[3]	Based on the incidence of forestomach and mammary gland tumors in an oral study in rats. (limited methodology information available)

WHO (2011) *	8.6×10^{-5}	-- [5]	linearized multistage model	--	Based on the same study and data set as US EPA IRIS.
CA EPA PHG	2.1×10^{-5}	0.047	linear extrapol-ation from LED_{10} [7]	$BW^{¾}$ [8]	Based on the same study and data set as US EPA IRIS.
NYS DEC (1997)	1.7×10^{-5}	0.06	linearized multistage model	$BW^{¾}$ [8]	Based on the same study and review as US EPA IRIS.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]No cancer potency factor was derived. The risk specific dose was obtained by linear extrapolation from the modeled TD_{05} (6.2 mg/kg/day), the dose associated with a 5% increase in mean tumor incidence (not a lower-bound estimate; TERA)
[4]Factor for dose adjustment from animal to humans is 1.
[5]A cancer potency factor was not presented. The risk specific dose was obtained from the drinking water unit risk (in units of risk per microgram per liter in drinking water), assuming a 70 kg person drinks 2 liters of water per day.
[6]No cancer potency factor was derived. The risk specific dose was obtained by linear extrapolation from the lowest tumorigenic dose (not a lower-bound estimate).
[7]LED_{10} = lower bound on the dose associated with 10% tumor incidence above background.
[8]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

7. Recommendation and Rationale

The basis of the cancer potency factors appears to be identical with respect to the critical study. The basis of the US EPA, CA EPA, HC DWQ, WHO and NYS DEC cancer potency factors is increased liver hemangiosarcoma tumor incidence in male rats. The US EPA fit a quantal model with a time-to-death analysis and used body surface area scaling with time weighting for gavage dosing and less-than-lifetime exposure and adjustments for percent of administered dose metabolized. CA EPA estimated an LED_{10} based on $BW^{¾}$ scaling, making the same time-weighting adjustments as US EPA, but not adjusting for percent metabolized at the different doses. They then used a linear extrapolation from the LED_{10} to estimate the cancer potency factor. The NYS DEC adjusted the US EPA value to reflect $BW^{¾}$ scaling, rather than body surface area scaling, which was also used by HC DWQ. It is unclear which tumor data were used by RIVM and HC PSAP to derive their potency estimates, and both values represent linear extrapolations from a dose associated with an observed tumor incidence or a modeled mean tumor incidence (respectively) and therefore do not reflect lower-bound estimates on the 10^{-6} lifetime risk specific dose. WHO only provides its assessment as a range of risk-specific drinking water guideline concentrations and the methods used in the derivation are not fully documented. The CA EPA

derivation is most consistent with currently-accepted risk assessment practice in terms of method used for inter-species dose scaling and high-to-low dose extrapolation, and the effect of not adjusting for percent of administered dose metabolized is small compared to the effect of the different extrapolation procedures. Therefore, the CA EPA cancer potency factor (0.047 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for 1,2-dichloroethane. The 1,2-dichloroethane risk specific dose calculated from this toxicity value is 2.1×10^{-5} mg/kg/day.

8. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: November, 2004; no revision January, 2018

9. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/12/2018) at http://www.oehha.ca.gov/water/phg/allphgs.html.

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/12/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/12/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for 1,2-Dichloroethane. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/12/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/12/2018) at http://iter.ctcnet.net/publicurl/pub_search_list.cfm.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/12/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/12/2018) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/12/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html.

10. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,2-Dichloroethane
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

6. Summary of Available Inhalation Reference Concentrations for 1,2-Dichloroethane (CAS Number 107-06-2)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA OSRTI * Also used by: • US EPA RSL*	7	2.2×10^5	LOEL	3000	Based on neurobehavioral effects in exposed workers. Information on study details including exposure duration and potential confounding exposures not available.
ATSDR**	2.4×10^3	2.02×10^5	NOEL	90	Based on lack of any observed gross or histopathological effects in rats exposed by inhalation for two years. Only a single exposure level was tested in this study, therefore a LOEL was not established.
CA EPA REL	400	8.5×10^3	NOEL	30	Based on significant elevation of liver enzymes in rats exposed via inhalation for 12 months. Study LOEL = 4.2×10^4 mcg/m^3. A pharmcokinetic adjustment of 1.5-fold was applied to the animal NOEL to obtain a human equivalent concentration.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.
**The ATSDR value is reported as 0.6 parts per million (ppm). For 1,2-dichloroethane, 1 ppm = 4.05 mg/m^3.

7. Recommendation and Rationale

The reference concentrations for 1,2-dichloroethane derived by authoritative bodies from the list in item 5 (below) are based on lack of any observed effect in a single-dose rat study, effects on liver enzymes in another rat study and neurobehavioral effects in aircraft industry workers. The US EPA OSRTI value is based on an occupational study that lacks information on duration of employment or exposure, did not control for confounding exposures such as other solvents or alcohol consumption, had small numbers of study participants and failed to include medical evaluation of control (unexposed) workers or statistical analysis of observed health endpoints. US EPA noted that the neurobehavioral test methods were poorly described, but involved reaction times and error rates in the performance of several tasks compared to a control group. US EPA also considered the available chronic animal toxicity studies and chose to estimate a 95% lower-bound benchmark concentration (BMCL) point of departure from the same study used by CA EPA. The BMCL, expressed as the human-equivalent concentration was slightly higher than the human LOEL (2.7×10^5 versus 2.2×10^5 mcg/m^3). US EPA therefore chose the human study LOEL as their point of departure because it was lower than the BMCL. US EPA applied a total uncertainty factor of 3000 to the human LOEL, including factors of 10 to account for human variability, use of a LOEL and extrapolation from a sub-chronic point of departure. A factor of 3 was applied to account for database inadequacies, including the lack of clear effect levels in many of the available animal toxicity studies and lack of a comprehensive study of potential neurotoxicity in light of the human neurobehavioral effects from the occupational study. Given the deficiencies in the occupational study, adequate justification was not provided for selection of this study over available animal data as the basis of a reference concentration. The ATSDR point of departure was not adjusted for intermittent exposure (7 hours/day, 5 days per week). ATSDR applied a total uncertainty factor of 90, including 10-fold to account for intraspecies variability, 3-fold to account for interspecies variability after making a pharmacokinetic adjustment (equal to 1) based on a systemic effects caused by a category 3 gas, and 3-fold as a modifying factor for database deficiencies. The CA EPA based their derivation on liver enzyme changes in rats exposed for 12 months. They corrected for intermittent exposure and used a value of 1.5 to adjust for pharmcokinetic variability based on the relative absorption of 1,2-dichloroethane as a systemic gas in rats and humans. This adjustment is not consistent with currently-accepted guidance which recommends a default adjustment of 1 if partitioning coefficient data are unavailable or if the animal:human blood-air partitioning coefficient ratio is greater than 1. The CA EPA applied a total uncertainty factor of 30 to account for intra- and interspecies variability, with no additional factor to account for the subchronic study duration. Both the ATSDR and CA EPA derivations deviate somewhat from currently-accepted risk assessment practice. The two-year study used by ATSDR employed only one experimental air concentration, which was considered a NOEL. However, the air concentration at the LOEL identified in the 12-month study used by the CA EPA in their derivation is considerably lower than the two-year NOEL, suggesting the ATSDR NOEL point of departure may not be adequately health protective. Therefore the CA EPA reference concentration (400 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,2-dichlorethane.

8. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

9. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (1/12/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (1/12/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund . Last accessed (1/12/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (1/12/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

10. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,2-Dichloroethane
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 1,2-Dichloroethane (CAS Number 107-06-2)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2004)	0.04	2.6×10^{-5}	linearized multistage model, extra risk	not clearly specified	Estimated by route to route extrapolation of a oral cancer potency factor of 0.091 per mg/kg/day which was based on the incidence of hemangiosarcomas in male rats in a two-year gavage study.
Cal EPA (2002)	0.05	2.1×10^{-5}	multistage time-to-tumor model, extra risk	body surface area[2]	Based on route-to-route extrapolation from an oral cancer potency factor of 0.072 per mg/kg/day, which is based on the same data set reviewed in US EPA IRIS (2004).
RIVM (2001)	0.48	--[3]	linear extrapol.	--	Based on route-to-route extrapolation of an oral risk-specific dose of 0.014 mg/kg/day at a lifetime risk of 1 in 10,000, which was derived from tumor data in rats chronically exposed via gavage (possibly the same study as used by US EPA IRIS, but limited review information available).

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} concentration), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Cancer risk is only expressed as a risk-specific air concentration; a unit risk is not directly reported.

2. Recommendation and Rationale

The basis of the two well-documented inhalation unit risks derived by authoritative bodies is circulatory system hemangiosarcomas in male rats exposed via gavage. However, these values are derived via oral-to-inhalation route extrapolation from oral cancer potency factors that were not recommended as the oral cancer toxicity value for 1,2-dichloroethane. Since exposure route extrapolation is the basis of the unit risks from authoritative bodies, and in the absence of route-specific data, a default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a unit risk from the recommended oral cancer potency factor. The recommended oral cancer potency factor for 1,2-dichloroethane is 0.047 per mg/kg/day. Therefore the unit risk of 1.3×10^{-5} per mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,2-dichloroethane. The 1,2-dichloroethane risk specific air concentration calculated from this toxicity value is 0.074 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: November, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2002. Technical Support Document for Describing Available Cancer Potency Factors. Sacramento, CA. Last accessed (01/18/2018) at https://oehha.ca.gov/media/downloads/crnr/tsdcancerpotency.pdf

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water

Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *cis*-1,2-Dichloroethene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for *cis*-1,2-Dichloroethene (CAS Number 156-59-2)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL* ♦ US EPA ODW*	0.002	5.1	$BMDL_{10}$	3000	Based on increased relative kidney weight in male rats given gavage doses in corn oil for 90 days. A ten percent increase in relative kidney weight compared to controls was considered the benchmark response.
NYS DEC (1997)	0.03	32	NOEL	1000	Based on effects in blood (decreased hematocrit and hemoglobin) in the same study used by US EPA IRIS. Study LOEL = 97 mg/kg/day.
US EPA HEAST (1997)	0.01	32	NOEL	3000	Based on the same study and NOEL as NYS DEC.
RIVM (2009)*	0.03	32	NOEL	1000	Based on the same study and NOEL as NYS DEC.
CA EPA PHG*	0.01	32	LOEL	3000	Based on the same study as NYS DEC, but considered the lowest dose a LOEL.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.

$BMDL_{10}$: the 95% lower confidence limit on the benchmark dose corresponding to a 10% increase in relative kidney weight compared to controls; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor;

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the various reference doses for *cis*-1,2-dichloroethene is essentially identical with respect to choice of study and species. Four derivations (NYS DEC, US EPA HEAST, RIVM and CA EPA PHG) obtain a point of departure from lowest dose group (32 mg/kg/day), and all but CA EPA PHG consider that dose a NOEL for effects on blood parameters (hemaglobin and hematocrit). CA EPA PHG identified the same dose group as a minimal LOEL for increased relative kidney weight. US EPA IRIS fit a benchmark dose model for continuous endpoints to the relative kidney data and obtained a $BMDL_{10}$ as the point of departure based on that endpoint. NYS DEC and RIVM applied a 1000-fold uncertainty factor to the NOEL to account for animal-to-human and human variability, and the use of a subchronic NOEL. The US EPA HEAST included an additional factor of 3 for database uncertainties. CA EPA PHG considered sources of uncertainty to include animal-to-human and human variability, use of a subchronic LOEL and database limitations, suggesting default values for sources of uncertainty could result in a total uncertainty factor of 10,000 to 30,000. They cited US EPA guidelines to set the maximum total uncertainty factor to 3000. US EPA IRIS also applied a total uncertainty factor of 3000, including 10-fold factors each for animal-to-human and human variability, 10-fold for use of a subchronic study and an additional 3-fold uncertainty factor for database limitations. An additional uncertainty factor for database limitations appears justified in light of the limited available toxicological information for *cis*-1,2-dichloroethene. Increased relative kidney weight appears to be a more sensitive endpoint than changes in blood parameters and the US EPA IRIS benchmark dose modeling approach to obtaining a point of departure for that endpoint is more consistent with generally-accepted risk assessment practice than the CA EPA PHG LOEL approach. Therefore, the US EPA reference dose (0.002 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *cis*-1,2-dichloroethene.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

NYSDEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for 1,2-Dichloroethene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2009. Re-Evaluation of Some Human Toxicological Maximum Permissible Risk Levels Earlier Evaluated in the Period 1991-2001. RIVM Rapport 711701092. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701092html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/17/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/17/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *cis*-1,2-Dichloroethene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for *cis*-1,2-Dichloroethene (CAS Number 156-59-2)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1996) RIVM (2001) NYS DEC (1997)	--	--	--	--	No human or animal data available, generally nonpositive results in mutagenicity assays.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for *cis*-1,2-dichloroethene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1996. Toxicological profile for 1,2-Dichloroethene. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. https://www.atsdr.cdc.gov/toxprofiledocs/index.html

NYSDEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for *cis*-1,2-dichloroethene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 249-257. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *cis*-1,2-Dichloroethene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for *cis*-1,2-Dichloroethene (CAS Number 156-59-2)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
RIVM (2009)*	60	1.86×10^5	LOEL	3000	Based on lung and liver effects in female rats exposed via inhalation to *trans*-1,2-dichloroethene for 8 hours/day, 5 days/week for 16 weeks.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.

LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The RIVM value is the only available reference concentration for *cis*-1,2-dichloroethene derived by an authoritative body from the list in item 5 (below). The reference concentration is based on lung and liver effects in female rats exposed subchronically by inhalation to *trans*-1,2-dichloroethene. Based on new negative results in an *in vivo* genotoxicity test of the *cis*- isomer that was judged to be of better quality than previous genotoxicity studies, RIVM concluded that the two isomers no longer should be differentiated base on potential genotoxicity and, therefore, the same assessment could be applied to both isomers. This is the only available inhalation reference concentration from an authoritative body. Therefore, the reference concentration of 60 mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *cis*-1,2-dichloroethene.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: December, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2009. Re-Evaluation of Some Human Toxicological Maximum Permissible Risk Levels Earlier Evaluated in the Period 1991-2001. RIVM Rapport 711701092. Last accessed (01/19/2018) at http://www.rivm.nl/dsresource?objectid=rivmp:19214&type=org&disposition=inline&ns_nc=1 and http://www.tera.org/iter/rivm/12dichloroethene.pdf.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *cis*-1,2-Dichloroethene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for *cis*-1,2-Dichloroethene (CAS Number 156-59-2)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	No data in humans or animals and generally negative results in mutagenicity assays.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for *cis*-1,2-dichloroethene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *trans*-1,2-Dichloroethene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for *trans*-1,2-Dichloroethene (CAS Number 156-60-5)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL*	0.02	65	$BMDL_{1sd}$	3000	Based on decreased antibody forming cells in the spleens of male mice exposed via drinking water for 90 days. Study LOEL = 175 mg/kg/day.
NYS DEC (1997) Also used by: ♦ US EPA HEAST (1997) ♦ US EPA ODW	0.02	17	NOEL	1000	Based on increased serum alkaline phosphatase in male mice exposed via drinking water for 90 days. Study LOEL = 175 mg/kg/day.
WHO (2011)*	0.017	17	NOEL	1000	Based on the same study, effect and point of departure as NYS DEC.
RIVM (2009)*	0.03	30	NOEL	1000	Based on effects in blood (decreased hematocrit and hemoglobin) in male rats given *cis*-1,2-dichloroethene by gavage for 90 days. Study LOEL = 97 mg/kg/day. RIVM considers the RfD to apply to both isomers, based on lack of *in vivo* genotoxicity of the *cis*- isomer.
CA EPA PHG*	0.006	17	NOEL	3000	Based on the same study and effect as used by NYS DEC.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.

$BMDL_{1sd}$: 95% lower limit on benchmark dose associated with a 1-standard deviation change from the background level; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the various reference doses for *trans*-1,2-dichloroethene is identical with respect to choice of study and species, except for the RIVM value, which is based on data from a study where rats were exposed to the cis- isomer. Assessments based on compound-specific toxicity data are preferred, when available. All other assessments, with the exception of US EPA IRIS, identified the same point of departure (a NOEL of 17 mg/kg/day), based on observed changes in serum alkaline phosphatase levels in male mice. US EPA IRIS considered the observed reduction in antibody-forming cells in the spleens of male mice from the same study to be a more sensitive endpoint, based on a lower benchmark dose estimate. NYS DEC, CA EPA PHG and WHO applied 10-fold uncertainty factors to the NOEL to account for human variability, animal-to-human variability and the use of a subchronic study. CA EPA PHG included an additional uncertainty factor of 3 to account for the incompleteness of the toxicological database, including the lack of chronic studies. US EPA IRIS also applied a total uncertainty factor of 3000 to the $BMDL_{1sd}$, including a factor of 3 to account for database deficiencies, particularly the lack of reproductive toxicity studies. The US EPA IRIS identification of the point of departure based on benchmark-dose modeling, and their basis for an additional uncertainty factor of 3 for database deficiencies is more consistent with generally-accepted risk assessment practices. Therefore, the US EPA reference dose (0.02 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *trans*-1,2-dichloroethene.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/18/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for *trans*-1,2-Dichloroethene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2009. Re-Evaluation of Some Human Toxicological Maximum Permissible Risk Levels Earlier Evaluated in the Period 1991-2001. RIVM Rapport 711701092. Last accessed (01/18/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701092html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/18/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/18/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/18/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/18/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *trans*-1,2-Dichloroethene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for *trans*-1,2-Dichloroethene (CAS Number 156-60-5)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1996) RIVM (2001)	--	--	--	--	No human or animal data available.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for *trans*-1,2-dichloroethene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1996. Toxicological Profile for 1,2-Dichloroethene. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *trans*-1,2-Dichloroethene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. **Summary of Available Inhalation Reference Concentrations for *trans*-1,2-Dichloroethene (CAS Number 156-60-5)**

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA OSRTI * Also used by: • US EPA RSL*	60	1.9×10^5	LOEL	3000	Based on lung and liver effects in rats exposed via inhalation for 8 or 16 weeks.
• RIVM (2009)	60	1.85×10^5	LOEL	3000	Based on the same study data as US EPA PPRTV.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. **Recommendation and Rationale**

   The available reference concentrations for *trans*-1,2-dichloroethene from authoritative bodies listed in item 5 (below), are essentially identical in terms of critical study, effects, species and point of departure. RIVM reports their point of departure using a different level of precision than US EPA PPRTV, but both numbers are derived from the same LOEL. Otherwise, the RIVM and US EPA PPRTV assessments differ only in the cited bases for the components that contribute to their respective total uncertainty factor of 3000, but the resulting reference concentrations are the same. Therefore, the US EPA PPRTV reference concentration (60 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *trans*-1,2-dichloroethene.

3. **Review Dates**

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2009. Re-Evaluation of Some Human Toxicological Maximum Permissible Risk Levels Earlier Evaluated in the Period 1991-2001. RIVM Rapport 711701092. Last accessed (01/19/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701092html.

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund. Last accessed (01/19/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/19/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *trans*-1,2-Dichloroethene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for *trans*-1,2-Dichloroethene (CAS Number 156-60-5)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for *trans*-1,2-dichloroethene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Dieldrin
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Dieldrin (CAS Number 60-57-1)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: • US EPA HEAST (1997) • US EPA ODW (2004) • US EPA OPP (1997) • US EPA Region 3 (2004) • NYS DEC (1997) • ATSDR (2004)	5×10^{-5}	5×10^{-3}	NOEL	100	Based on liver lesions in rats exposed by diet for 2 years. Study LOEL = 0.05 mg/kg/day.
WHO (2003) Also used by: • Health Canada (1994)	1×10^{-4}	0.025	NOEL	250	Based on NOELs of 1 mg/kg in diet of dogs and 0.5 mg/kg in diet of rats, equivalent to 0.025 mg/kg/day in both species. Limited information is available on the precise studies and points of departure used to obtain the reference dose.
RIVM (2000)	1×10^{-4}	0.025	LOEL	250	Based on liver changes in both rats and dogs exposed by diet for a lifetime.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The basis for all reference doses for dieldrin, except the RIVM and WHO values, is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (5×10^{-3} mg/kg/day). The exact study forming the basis of the WHO value is not specified, and the documentation states that the uncertainty factor applied to the LOEL is 250 to take into account cancer effects observed in the mouse. The use of uncertainty factors to account for carcinogenic effects is not

relevant in this context since cancer and non-cancer evaluations are being done separately. The RIVM reference dose is based on a chronic feeding study that also reported liver effects in rats and dogs, but the point of departure was a LOEL and was 5-fold higher. The US EPA derivation included a total uncertainty factor of 100 to account for interspecies and intraspecies variability. The RIVM used an additional uncertainty factor of 2.5 to account for the use of a LOEL rather than the conventional factor of 10, which was suggested to be sufficient for the marginal effects observed at the LOEL. However, frank histopathological liver lesions were observed in rats in the study used by US EPA at a dose only 2-fold greater than the RIVM LOEL, suggesting that a deviation from accepted risk assessment practice is not supported in this case. Therefore, the US EPA reference dose (5×10^{-5} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for dieldrin.

3. Review Dates

Summary table completion: June, 2004; no revision January, 2018
Toxicity value recommendation: August, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological profile for Chlordane. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

Health Canada. 1994. Water Quality and Health. Guidelines for Canadian Drinking Water Quality. Healthy Environments and Consumer Safety. Last accessed (01/17/2018) at http://www.hc-sc.gc.ca/hecs-sesc/water/dwgsup.htm

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Endrin. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2004. EPA 822-R-04-005. Office of Drinking Water, Drinking Water Standards and Health Advisories. Washington, DC.

US EPA OPP (United States Environmental Protection Agency Office of Pesticide Programs). 1997. Reference Dose Tracking Report. Washington, DC: Office of Pesticide Programs, Health Effects Division. HED reviewed 08/08/86.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2003. Aldrin and Dieldrin in Drinking-Water, Background Document for the Development of WHO Guidelines for Drinking Water Quality. World Health Organization, Geneva. Last accessed (01/17/2018) at http://www.who.int/water_sanitation_health/dwq/chemicals/adrindieldrin.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Dieldrin
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Dieldrin (CAS Number 60-57-1)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2004) • US EPA OPP (1997) • US EPA HEAST (1997) • Cal EPA (1993)	6.25×10^{-8}	16	linearized multistage model, extra risk	body surface area [2]	Geometric mean of 13 potency factors based on increased incidence of liver carcinomas in several strains of mice exposed by diet.
NYS DEC (1997)	1.2×10^{-7}	8.32	linearized multistage model, extra risk	$BW^{¾}$ [3]	Based on the same liver tumor data as used by US EPA

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.

2. Recommendation and Rationale

The cancer potency factors derived by the US EPA and the NYS DEC are base on 13 male and female mouse data sets showing increased incidence of liver tumors in animals exposed to dieldrin in the diet. Both cancer potency estimates are based on the geometric mean of the potency estimates derived from the 13 individual data sets. The US EPA used body surface area scaling to extrapolate from rodent to human cancer potency, while the NYSDEC used $BW^{¾}$ scaling. The latter method is more consistent with currently accepted risk assessment practice. Therefore, the NYS DEC cancer potency factor (8.32 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for dieldrin. The dieldrin risk specific dose calculated from this toxicity value is 1.2×10^{-7} mg/kg/day.

3. Review Dates

Summary table completion: June, 2004; no revision January, 2018
Toxicity value recommendation: August, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency), 1993. Office of Environmental Health Hazard Assessment. Toxicity Criteria Database. Last accessed (01/17/2018) at https://oehha.ca.gov/chemicals

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Dieldrin. Albany, NY: Division of Water.

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA OPP (United States Environmental Protection Agency Office of Pesticide Programs). 1997. Reference Dose Tracking Report. Washington, DC: Office of Pesticide Programs, Health Effects Division. HED reviewed 08/08/86.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Dieldrin
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Dieldrin (CAS Number 60-57-1)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for dieldrin is not available from the authoritative bodies listed in item number 5 (below). Dieldrin is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for dieldrin is 5×10^{-5} mg/kg/day. Therefore, a reference concentration of 0.18 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for dieldrin.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Dieldrin
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for Dieldrin (CAS Number 60-57-1)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS* Also used by ♦ US EPA RSL*	2×10^{-4}	4.6×10^{-3}	linearized multistage model	body surface area[2]	The unit risk was estimated from an oral cancer potency factor using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. Dieldrin increased the incidence of liver carcinomas in several strains of mice exposed via the diet. The cancer potency factor is the geometric mean of 13 cancer potency factors.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million, where 1×10^{-6} air concentration = 1×10^{-6}/unit risk.
[2]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

Dieldrin is a toxicant that is expected to be absorbed into the body and cause systemic cancer effects following oral or inhalation exposure. A unit risk for dieldrin based on inhalation exposures is not available from the authoritative bodies listed in item number 5 (below). However, the US EPA IRIS derived a unit risk (4.6×10^{-3} per mcg/m^3) from their oral cancer potency factor (16 per mg/kg/day) using a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day. However, the recommended cancer potency factor for dieldrin is NYS DEC's value of 8.32 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for Dieldrin). Therefore, a unit risk of 2.4×10^{-3} per mcg/m^3 based on the same exposure route extrapolation used by US EPA is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for dieldrin. The risk specific air concentration calculated from this toxicity value is 4.2×10^{-4} mcg/m^3.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/19/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,4-Dioxane
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for 1,4-Dioxane (CAS Number 123-91-1)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW	0.03	9.6	NOEL	300	Based on increased incidences of renal tubular epithelial and hepatocellular degeneration and necrosis in male rats exposed via drinking water each day for 104 weeks. Study LOEL = 94 mg/kg/day.
WHO	0.096	9.6	NOEL	100	Based on same study and effects as used by US EPA IRIS
ATSDR*	0.1	9.6	NOEL	100	Based on same study and effects as used by US EPA IRIS
NYS DEC (2013)*	0.026	2.6 [(2)]	NOEL	100	Based on same study and effects as used by US EPA IRIS

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]The point of departure was adjusted by a dosimetric adjustment factor [(animal BW/human BW)$^{1/4}$] equal to (0.43kg/80kg)$^{1/4}$

NOEL: no-observed-effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the various reference doses for 1,4-dioxane is identical with respect to choice of study, species, sex, adverse effect and identification of the point of departure. The US EPA IRIS, WHO and ATSDR used uncertainty factors of 10 each for interspecies and intraspecies extrapolation, but the US EPA IRIS also used an additional uncertainty factor of 3 to compensate for concerns regarding developmental toxicity and deficiencies (lack of a multi-generation reproductive study) in the toxicity database for 1,4-dioxane. US EPA IRIS noted that although the toxicity database for 1,4-dioxane is large, a sole oral prenatal developmental toxicity study in rats indicated that developing fetus may be a target of toxicity. However, a review of the study showed that the NOEL and LOEL for maternal effects (10% reduction in body weight gain) and fetal effects (delayed ossification of the sternebrae and reduced fetal BW) were the same: 500 and 1000 mg/kg/day, respectively. These data do not indicate

that the fetus was more sensitive than the dams to 1,4-dioxane toxicity. Moreover, the reference dose based on kidney and liver toxicity is 52 times lower than the candidate reference dose (1.7 mg/kg/day) derived by US EPA IRIS for developmental toxicity, and would be protective of developmental effects. Nevertheless, the use of database uncertainty factor of 3 when either a developmental or multi-generation reproductive study is missing is consistent with generally accepted risk assessment practices.

The NYS DEC modified the point of departure using a dosimetric adjustment factor based on body weight scaling, according to US EPA recommendations (US EPA 2011). Consequently, they used an uncertainty factor of 3 (rather than 10) to account for interspecies extrapolation (i.e., for differences in pharmacodynamics between animals and humans). The NYS DEC also used the same database uncertainty factor of 3 as was used by US EPA IRIS, and applied a total uncertainty factor of 100 to the adjusted point of departure (2.6 mg/kg/day), rather than the 300-fold UF applied by the US EPA IRIS to the unadjusted point of departure (9.6 mg/kg/day). Although the US EPA IRIS and NYS DEC references doses are nearly equivalent, the NYS DEC derivation used the currently recommended method for interspecies extrapolation and is more consistent with generally accepted risk assessment practice. Therefore, the NYS DEC reference dose (0.026 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,4-dioxane.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: January, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/16/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

NYS DEC (New York State Department of Environmental Conservation). 2013. Draft New York State Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. 1,4-Dioxane. Albany, NY: Division of Water.

US EPA (U.S. Environmental Protection Agency). 2011. Recommended Use of Body Weight$^{3/4}$ as the Default Method in Derivation of the Oral Reference Dose. EPA/100/R11/0001. Last accessed (01/16/2018) at https://www.epa.gov/risk/recommended-use-body-weight-34-default-method-derivation-oral-reference-dose

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/16/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/16/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/16/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/16/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,4-Dioxane
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for 1,4-Dioxane (CAS Number 123-91-1)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW ♦ NYS DEC (2013)	1×10^{-5}	0.10	linear extrapolation from the $BMDL_{50HED}$[2] estimated using log-logistic model	$BW^{¾}$ [3]	Based on the combined incidence of hepatocellular adenomas and carcinomas in female mice exposed via drinking water each day for 2 years.
CA EPA CPF	3.7×10^{-5}	0.027	linearized multistage model	body surface area[4]	Based on the combined incidence of hepatocarcinomas and adenomas in female mice exposed via drinking water each day for 90 weeks.
CA EPA NL	7.1×10^{-5}	0.014	linearized multistage model	$BW^{¾}$ [3]	Based on same study and effects as used by CA EPA CPF.
WHO	1.8×10^{-4}	5.6×10^{-3} [5]	linearized multistage model	body weight[6]	Based on the incidence of hepatocellular tumors in rats exposed via drinking water each day for 2 years.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} cancer potency factor.
[2]$BMDL_{50HED}$:: the 95% lower confidence limit on the benchmark human equivalent dose (HED) associated with a 50% extra cancer risk.
[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$.
[4]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.
[5]A cancer potency factor was not derived, but was calculated from the water concentration (5.4 micrograms per liter) associated with an excess cancer risk of one-in-one million assuming a 60 kg person drinks 2 liters of water/day.
[6]Factor for dose adjustment from animals to humans is 1.

2. Recommendation and Rationale

The WHO and CA EPA CPF derivations of cancer potency factors for 1,4-dioxane are not consistent with generally accepted risk assessment practices as neither used the recommended animal-to-human

extrapolation based on $BW^{3/4}$. The US EPA IRIS cancer potency factor is based on a longer study in mice (2 years) than is the CA EPA NL cancer potency factors (90 weeks). Although 90 weeks is commonly identified as an adequate study length for a mouse carcinogenicity study, a longer study is preferred to a shorter study (other factors being similar) as the basis of a cancer potency factor. CA EPA NL corrected for less-than-lifetime exposures using an adjustment factor that increased the magnitude of the potency factor, but such mathematical adjustments are less preferred than actual data from a lifetime study. Moreover, whether such an adjustment is necessary for a 90 week study is questionable. Therefore, the US EPA IRIS cancer potency factor (0.10 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for 1,4-dioxane. The 1,4-dioxane risk specific dose calculated from this toxicity value is 1.0×10^{-5} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/16/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

CA EPA NL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Notification Levels for Chemicals in Drinking Water. Last accessed (01/16/2018) at https://oehha.ca.gov/water/notification-levels-chemicals-drinking-water

NYS DEC (New York State Department of Environmental Conservation). 2013. Draft New York State Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. 1,4-Dioxane. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/16/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/16/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/16/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/16/2018) at http://whqlibdoc.who.int/publications/2011/9789241548151_eng.pdf.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)

New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,4-Dioxane
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for 1,4-Dioxane (CAS Number 123-91-1)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
ATSDR	110*,**	3.2×10^4	LOEL	300	Based on nasal lesions (atrophy of the olfactory epithelium) in rats exposed by inhalation 6 hours/day, 5 days/week for 104 weeks.
CA EPA REL	3×10^3	8.3×10^4	NOEL	30	Based on no effects on liver, kidney or hematologic function in rats exposed by inhalation 7 hours/day, 5 days/week for 2 years.
US EPA IRIS	30**	3.2×10^4	LOEL	1000	Based on the same study and toxicity endpoints as ATSDR.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*The ATSDR value is reported as 0.03 parts per million (ppm). For 1,4-dioxane, 1 ppm = 3.60 mg/m^3.

**Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The reference concentrations for 1,4-dioxane derived by authoritative bodies from the list in item 5 (below) are based on two different chronic inhalation studies in rats. The study used by CA EPA used a single exposure level and reported no effects on liver, kidney or hematologic function, and identified this single exposure level as a NOEL. The study used by the ATSDR and US EPA IRIS is of higher quality than the study used by CA EPA. It used a control and three exposure levels and identified a sensitive toxicological endpoint (nasal lesions) at a LOEL (50 ppm) that is lower than the NOEL (111

ppm) from the study used by CA EPA. The ATSDR and US EPA IRIS derivations are similar in most respects. Both assumed a default pharmacokinetic adjustment (equal to 1) for a gas causing systemic effects when the ratio of the animal to human blood:air partitioning coefficients is greater than 1. Both also applied uncertainty factors to the time-weighted air concentration at the LOEL for interspecies extrapolation (3), intraspecies extrapolation (10) and the use of a LOEL (10). However, the US EPA IRIS added an additional uncertainty factor of 3 for toxicological database deficiencies due to the lack of a multigenerational reproductive study, resulting in a total uncertainty factor of 1000 compared to the total uncertainty factor of 300 used by ATSDR. The use of a database uncertainty factor of 3 when either a developmental or multigenerational reproductive study is unavailable is consistent with generally accepted risk assessment practices. Therefore, the US EPA IRIS reference concentration (30 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,4-dioxane.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: January, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/16/2018) at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/16/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/16/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,4-Dioxane
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for 1,4-Dioxane (CAS Number 123-91-1)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS* Also used by: US EPA RSL*	0.2	5.0×10^{-6}	linear extrapolation from $BMLC_{10}$ [(2)]	default DAF[3] (equal to 1)	Based on combined tumor incidence (nasal, liver, kidney, peritoneal, mammary gland, and Zymbal gland) in male rats exposed to 1,4-dioxane via inhalation 6 hours/day, 5 days/week for 2 years.
CA EPA CPF	0.13	7.7×10^{-6}	linearized multistage model	body surface area[4]	Calculated from the oral cancer potency factor (0.027 per mg/kg/day), which was derived from a single data set of combined incidence of hepatocarcinomas and adenomas in female mice exposed in drinking water for 90 weeks.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} concentration), where 1×10^{-6} air concentration = 1×10^{-6} /unit risk.

[2]$BMLC_{10}$: The 95% lower confidence limit on the benchmark air concentration associated with a 10% (relative to controls) increase in the incidence of cancer.

[3]A default dosimetric adjustment factor (DAF) equal to 1 was based on consideration of 1,4-dioxane as a gas causing systemic effects and for which the ratio of the blood:air partitioning coefficients between animals and humans is greater than 1.

[4]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The CA EPA PHG unit risk (7.7×10^{-6} per mcg/m^3) is based on extrapolation from the oral cancer potency factor, which is derived from a 90-week mouse drinking water study, while the US EPA IRIS unit risk (5×10^{-6} per mcg/m^3) is based on a chronic (2-year) study in which rats were exposed by inhalation. Chronic studies using the more relevant inhalation exposure route are preferred to oral studies for derivation of inhalation unit risk values. Therefore, the US EPA IRIS unit risk of 5.0×10^{-6} per mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for 1,4-dioxane. The 1,4-dioxane risk specific air concentration calculated from this toxicity value is 0.2 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: December, 2004: revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/19/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/19/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Endosulfan
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Endosulfan (technical grade) (CAS Number 115-29-7)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA OCSPP (2010) ♦ US EPA HEAST (1997)	6×10^{-3}	0.6	NOEL	100	Based on reduced body weight gain in male and female rats and increased incidence of marked progressive glomerulonephrosis and blood vessel aneurysms in male rats exposed via the diet in a 2-year study. Study LOEL = 2.9 mg/kg/day (male rats).
WHO (2011)	6×10^{-3}	0.6	NOEL	100	Based on same study, species, and effects used by US EPA IRIS.
ATSDR (2015)*	5×10^{-3}	0.45	NOEL	100	Based on reduced immune response to tetanus toxin in male rats exposed in the diet for 22 weeks. Study LOEL = 0.9 mg/kg/day.
NYS DEC (2013)*	1.6×10^{-3}	0.16 (2)	$BMDL_{10}$ (3)	100	Based on same study, species, and effects used by US EPA IRIS.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]The point of departure was adjusted by a dosimetric adjustment factor [(animal BW/human BW)$^{1/4}$] equal to $(0.515kg/80kg)^{1/4}$

[3]$BMDL_{10}$: The 95% lower confidence limit on the benchmark dose associated with a 10% (relative to controls) increase in the incidence of an adverse effect.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA IRIS, WHO and NYS DEC all based their endosulfan reference dose on reduced body weight gain and kidney and blood vessel toxicity reported in a chronic dietary study in rats. The ATSDR based its reference dose on immune system effects in a subchronic rat study. The ATSDR derivation uses a NOEL obtained from a study that exposed the animals for less than their lifetimes as the point of departure (POD). Use of a NOEL as the POD from a subchronic study is less preferred for the derivation of chronic reference doses when a chronic study providing data suitable for benchmark dose modeling is available. Therefore the ATSDR value is not considered further. The EPA and WHO applied a total uncertainty factor of 100 (10 each for inter- and intraspecies extrapolation) to a NOEL POD. The NYS DEC used a benchmark dose as the POD, and then accounted for pharmacokinetic differences using a dosimetric adjustment factor based on body weight scaling, according to US EPA recommendations (US EPA 2011). Consequently, they used an uncertainty factor of 3 (rather than 10) to account for interspecies extrapolation (i.e., for differences in pharmacodynamics between animals and humans). The NYS DEC also included an additional uncertainty factor of 3 to account for uncertainties regarding the possibility that young animals may be more sensitive than older animals to effects of endosulfan on the male reproductive tract and the nervous system (CA EPA, 2006; 2008; NYS DEC, 2013). The NYS DEC derivation used benchmark dose modeling and the currently recommended method for interspecies extrapolation, both of which are more consistent with generally accepted risk assessment practice. The NYS DEC derivation also accounts for the possibility that children may have increased vulnerability to endosulfan health effects. Therefore, the NYS DEC reference dose (1.6×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for endosulfan technical grade.

The information in this fact sheet is applicable to the sum of endosulfan I, endosulfan II and endosulfan sulfate. Technical grade endosulfan is a mixture of the isomers endosulfan I and endosulfan II, which make up 94% of the content (ATSDR, 2015). Endosulfan sulfate is a reaction product found in technical grade endosulfan and is also a persistent environmental degradate of endosulfan.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: August, 2004: revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). 2015. Toxicological Profile for Endosulfan. Last accessed (01/7/2018) at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA (California Environmental Protection Agency). 2006. Development of Health Criteria for School Site Risk Assessment Pursuant to Health and Safety Code Section 901(g): Proposed Child-Specific Reference Dose (chRD) for School Site Risk Assessment – Endosulfan. Draft Report. Last accessed (01/7/2018) at http://oehha.ca.gov/public_info/public/kids/chrd031706.html.

CA EPA (California Environmental Protection Agency). 2008. Office of Environmental Health Hazard Assessment's Findings on the Health Effects of Endosulfan. Last accessed (01/7/2018) at https://oehha.ca.gov/media/downloads/pesticides/report/endosulfantacfindingsoehha2007.pdf

NYS DEC (New York State Department of Environmental Conservation). 2013. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Endosulfan (technical grade). Albany, NY: Division of Water.

US EPA (U.S. Environmental Protection Agency). 2011. Recommended Use of Body Weight$^{3/4}$ as the Default Method in Derivation of the Oral Reference Dose. EPA/100/R11/0001. Last accessed (01/7/2018) at https://www.epa.gov/risk/recommended-use-body-weight-34-default-method-derivation-oral-reference-dose

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/7/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/7/2018) at http://www.epa.gov/iris/.

US EPA OCSPP (United States Environmental Protection Agency Office of Chemical Safety and Pollution Prevention). 2010. Endosulfan: The Health Effects Division's Human Health Risk Assessment. June 10 memo to M. Biscoe (Pesticide Re-Evaluation Division) from D. Wilbur, J. Facey, and S. Recore (Health Effects Division). Washington, DC: US EPA OCSPP.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/7/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/7/2018) at http://whqlibdoc.who.int/publications/2011/9789241548151_eng.pdf.

6. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Endosulfan
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Endosulfan (technical grade) (CAS Number 115-29-7)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
ATSDR (2000)	--	--	--	--	Studies evaluating the carcinogenicity of endosulfan in humans are not available. Several studies in rodents do not provide convincing evidence for carcinogenicity.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for endosulfan technical grade is not available.*

The information in this fact sheet is applicable to the sum of endosulfan I, endosulfan II and endosulfan sulfate. Technical grade endosulfan is a mixture of the isomers endosulfan I and endosulfan II, which make up 94% of the content (ATSDR, 2000). Endosulfan sulfate is a reaction product found in technical grade endosulfan.

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: June, 2004; no revision January, 2018
Toxicity value recommendation: August, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2000. Toxicological Profile for Endosulfan. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. http://www.atsdr.cdc.gov/toxprofiles/tp41.html

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Endosulfan
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Endosulfan (technical grade) (CAS Number 115-29-7)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for endosulfan is not available from the authoritative bodies listed in item number 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Endosulfan is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects after oral or inhalation exposure. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the recommended reference dose (1.6×10^{-3} mg/kg/day) based on systemic effects (see Oral Non-Cancer Toxicity Value Documentation for Endosulfan). Therefore, a reference concentration of 5.6 mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation noncancer-based soil cleanup objective for endosulfan.

The information in this fact sheet is applicable to the sum of endosulfan I, endosulfan II and endosulfan sulfate. Technical grade endosulfan is a mixture of the isomers endosulfan I and endosulfan II, which make up 94% of the content (ATSDR, 2013). Endosulfan sulfate is a reaction product found in technical grade endosulfan and a persistent environmental degradate of endosulfan.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). 2013. Toxicological Profile for Endosulfan. Draft for Public Comment. Last accessed (01/16/2018) at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

7. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Endosulfan
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Endosulfan (technical grade) (CAS Number 115-29-7)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for endosulfan is not available.*

The information in this fact sheet is applicable to the sum of endosulfan I, endosulfan II and endosulfan sulfate. Technical grade endosulfan is a mixture of the isomers endosulfan I and endosulfan II, which make up 94% of the content (ATSDR, 2000). Endosulfan sulfate is a reaction product found in technical grade endosulfan.

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2000. Toxicological Profile for Endosulfan. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Endrin
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Endrin (CAS Number 72-20-8)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL	3×10^{-4}	0.025	NOEL	100	Based on mild histological lesions in the liver, slightly increased relative liver weights and occasional convulsions in male and female dogs in a 2-year feeding study. Study LOEL = 0.05 mg/kg/day.
WHO (2003)	2×10^{-4}	0.025	NOEL	100	Based on same study and analysis as US EPA IRIS (2004).
ATSDR	3×10^{-4}	0.025	NOEL	100	Based on same study and analysis as US EPA IRIS (2004).
RIVM (2001)	2×10^{-4}	0.05	NOEL	250	Based on same 2-year dog study as US EPA IRIS, except study NOEL and LOEL were set at 0.05 mg/kg/day and 0.1 mg/kg/day, respectively.
		0.025	NOEL	125	Based on liver and kidney weight changes in male and female rats in a 2-year feeding study. Additional details not available.
CA EPA (2016)	2.2×10^{-5}	0.022	$BMDL_{05}$[2]	1000	Based on the same study as US EPA IRIS.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.
[2]$BMDL_{05}$: 95% lower confidence limit on the benchmark dose associated with a 5% increase (relative to controls) in the incidence of an adverse effect.

2. Recommendation and Rationale

The reference doses derived by the US EPA IRIS, WHO, ATSDR and RIVM are essentially identical, with the differences among them being primarily a consequence of small differences in interpretation of the principle study and/or methods used in the derivations. The original endrin reference dose was derived by the US EPA IRIS based on liver and neurological toxicity in a 2-year dog feeding study, using a default food factor (2.5% body weight) to approximate the dose at the NOEL. A total uncertainty factor of 100 (10 each for interspecies and intraspecies differences) was applied to the NOEL to obtain the reference dose.

CA EPA used food consumption data from the same dog study to obtain the endrin doses and then used benchmark dose modeling to obtain their point of departure (a $BMDL_{05}$). CA EPA then applied a total uncertainty factor of 1000 (10 for interspecies extrapolation and 100 for intraspecies extrapolation) to obtain the reference dose. CA EPA uses a higher default uncertainty (30) factor for intraspecies differences, and then applied an additional uncertainty factor of 3 to be protective of children, based on this subpopulation being more sensitive to neurotoxicants.

Although CA EPA's derivation uses methods more consistent with current risk assessment practice for estimating doses and obtaining the point of departure, the use of an intraspecies uncertainty factor of 100 appears unnecessary in the absence of specific data showing a greater sensitivity of children to endrin. In addition, the standard uncertainty factor of 10 is designed to protect sensitive subpopulations, including children. Therefore, the US EPA reference dose (3×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer soil cleanup objective for endrin.

3. Review Dates

Summary table completion: February, 2004; revised January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological Profile for Endrin. US Department of Health and Human Services. Last accessed (01/24/2018) at https://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2016. Public Health Goals: Carbofuran, Diquat, Endrin, Picloram, Thiobencarb in Drinking Water. Last accessed (01/24/2018) at http://oehha.ca.gov/media/downloads/water/chemicals/phg/pesticidebatch092316_0.pdf

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment. Last accessed (01/24/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). Last accessed (01/24/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

WHO (World Health Organization). 2003. Endrin in Drinking-Water, Background Document for the Development of WHO Guidelines for Drinking Water Quality. Last accessed (01/24/2018) at http://www.who.int/water_sanitation_health/dwq/chemicals/endrin.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Endrin
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Endrin (CAS Number 72-20-8)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1996)	--	--	--	--	Human data are not available. Long-term dietary exposure to endrin did not produce carcinogenic effects in either sex of two strains of rats and three strains of mice. All of the studies have design limitations, which make the results difficult to interpret. One study showing a positive carcinogenic response also is limited by design flaws.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for endrin is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: February, 2004; no revision January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1996. Toxicological Profile for Endrin. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Endrin
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Endrin (CAS Number 72-20-8)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for endrin is not available from the authoritative bodies listed in item number 5 (below). Endrin is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for endrin is 3×10^{-4} mg/kg/day. Therefore, a reference concentration of 1.0 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for endrin.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Endrin
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Endrin (CAS Number 72-20-8)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration = 1×10^{-6} / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for endrin is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Ethylbenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Ethylbenzene (CAS Number 100-41-4)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2003) • US EPA HEAST (1997) • US EPA EPA NCEA (2003) • US EPA ODW (2004)	0.1	97.1	NOEL	1000	Based on histopathologic and organ weight changes in the liver and kidneys of rats exposed for 182 days by olive oil gavage. Study LOEL = 291 mg/kg/day.
NYS DEC (1997)	0.097	97	NOEL	1000	Based on same study as US EPA IRIS.
RIVM (2000)	0.1	97	NOEL	1000	Based on same study as US EPA IRIS.
WHO (2003)	0.097	97	NOEL	1000	Based on same study as US EPA IRIS.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The basis for the various reference doses for ethylbenzene is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (97 mg/kg/day). The only differences among the values are due to variations in the precision used to report the value. The US EPA reference dose (0.1 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for ethylbenzene.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Ethyl Benzene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 997-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA NCEA (National Center for Environmental Assessment). 2002. Toxicological Review of Benzene (Noncancer effects). U.S. Environmental Protection Agency. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=51760.

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2004. Drinking Water Standards and Health Advisories. Washington, DC. EPA 822-R-04-005.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2003. Ethylbenzene in Drinking-Water, Background Document for the Development of WHO Guidelines for Drinking Water Quality. World Health Organization, Geneva. http://www.who.int/water_sanitation_health/dwq/chemicals/ethylbenzene.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Ethylbenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Ethylbenzene (CAS Number 100-41-4)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
ATSDR	--	--	--	--	Studies evaluating the carcinogenicity of ethylbenzene following oral exposure in humans are not available. One long-term oral study in rats using a single dose level showed an increase in total tumors (types unspecified).
US EPA IRIS	--	--	--	--	Ethylbenzene is not classifiable as to human carcinogenicity based on lack of animal bioassays and human studies.
CA EPA CPF* Also used by: ♦ US EPA RSL	9.1×10^{-5}	0.011[3]	linearized multistage model	$BW^{3/4}$ [2]	Based on the inhalation unit risk using $route_{Inhalation}$-to $route_{Oral}$ extrapolation and a ratio of oral to inhalation uptake factors (i.e., 1/0.77).

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.
[2]Factor for dose (mg/kg/day) adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$.
[3]Oral slope factor (cancer potency factor) = inhalation slope factor (8.7×10^{-3} per mg/kg/day) x 1/0.77.
*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

Ethyl benzene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure. Two of the authoritative bodies listed in section 5 (see below) have derived an inhalation unit risk based on cancer effects distant from the site of contact. The inhalation unit risks of CA EPA CPF (2.5×10^{-6} per mcg/m^3) and the NYS DOH (1×10^{-6} per mcg/m^3) for ethyl benzene are based on renal tubule adenomas or carcinomas in male rats exposed by inhalation 6 hours/day, 5 days/week for 104 weeks. The CA EPA obtained its cancer potency factor by application of an oral to inhalation uptake factor (i.e., 1/0.77) to its inhalation unit risk. The NYS DOH inhalation unit risk was

derived using methods that were more consistent with generally accepted risk assessment practices, and is the recommended inhalation unit risk for ethylbenzene (see Inhalation Cancer Toxicity Value Documentation for Ethylbenzene). Thus, a default route $_{Inhalation}$-to-route$_{Oral}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a cancer potency factor from the inhalation unit risk. Therefore, a cancer potency factor of 3.5×10^{-3} per mg/kg/day based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for ethylbenzene. The ethylbenzene risk specific dose calculated from this toxicity value is 2.9×10^{-4} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: March, 2005; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological Profiles. Last accessed (01/17/2018) at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/17/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Ethylbenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Ethylbenzene (CAS Number 100-41-4)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL	1000	430,000	NOEL	300	Based on skeletal variations in rats and evidence of slightly reduced litter size in rabbits in developmental toxicity studies in both species. The animals were exposed by inhalation 6 to 7 hours/day, 7 days/week on gestation days 1 to 19 (rats) and 1 to 24 (rabbits). Study LOEL = 4.3×10^6 mcg/m^3.
CA EPA REL	2000	57,000 (13 ppm)*	$NOEL_{ADJ}$	30	Based on kidney toxicity and body weight reduction in rats and hyperplasia of the pituitary gland and liver toxicity in mice exposed by inhalation 6 hours/day, 5 days/week for 104 weeks. Study $LOEL_{ADJ}$ = 195,000 mcg/m^3 (45 ppm).*
ATSDR**	260 (0.06 ppm)*	74,000 (17 ppm)*	$LOEL_{HEC}$	300	Based on kidney toxicity in female rats exposed by inhalation 6 hours/day, 5 days/week for 104 weeks. PBPK modeling was used to estimate the $LOEL_{HEC}$.
RIVM (2001)	770	77,000	$NOEL_{ADJ}$	100	Based on liver and kidney toxicity in rats and mice exposed by inhalation for 6 hours/day, 5 days/week for 13 weeks. Study $LOEL_{ADJ}$ = 195,000 mcg/m^3 (45 ppm).*

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; $NOEL_{ADJ}$ or $LOEL_{ADJ}$: experimental NOEL or LOEL adjusted for continuous exposure by time-weighting experimental exposures; HEC: human equivalent concentration; UF: uncertainty factor.

*1 ppm = 4.34 mcg/m^3

**Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The reference concentrations for ethylbenzene derived by authoritative bodies from the list in item 5 (below) are based on liver and kidney effects in rats and mice, effects on the pituitary gland in mice, and developmental toxicity in rats and rabbits. RIVM based their value on a subchronic NOEL for liver and kidney effects in rats and mice exposed via inhalation for 13 weeks. The human equivalent concentration was estimated by adjusting for non-continuous exposure, but no pharmacokinetic adjustment was made. They applied a total uncertainty factor of 100, including 10-fold each to account for intra- and interspecies variability. An additional uncertainty factor to account for the use of a subchronic NOEL was not considered necessary because RIVM concluded that the subchronic NOEL was lower than their interpretation of the NOEL observed in a related chronic inhalation study (see below).

The CA EPA based their derivation on a chronic (104-week) inhalation NOEL for liver, kidney and pituitary effects in rats and mice. They adjusted the rodent exposure level for non-continuous exposure and used the default pharmacokinetic adjustment (equal to 1) for effects of a systemic gas when data for animal and human partitioning coefficients are not available. The exposure level in the 104-week study that was considered a LOEL by the CA EPA (45 ppm time weighted average) was considered a NOEL by RIVM. This same exposure level was a LOEL in the 13-week study, which led RIVM to conclude that the chronic NOEL (based on their interpretation) was not sufficiently protective of the effects seen in the subchronic study. The two agencies differ in their interpretation of the biological significance of pituitary hyperplasia in mice at the 45-ppm time-weighted average concentration in the 104-week study, but the incidence of this effect was statistically increased, supporting CA EPA's conclusion of a LOEL at that exposure concentration. CA EPA applied a total uncertainty factor of 30, including 10-fold to account for intraspecies variability and 3-fold to account for interspecies variability.

The US EPA based their value on developmental toxicity observed in rats and slightly reduced litter size in rabbits exposed only during gestation. No maternal toxicity was observed in either species. The human equivalent concentration was estimated based on a default pharmacokinetic adjustment (equal to 1) based on lack of partitioning coefficient data. No adjustment was made for non-continuous exposure. The US EPA applied a total uncertainty factor of 300, including 10-fold to account for intraspecies variability, 3-fold to account for interspecies variability and 10-fold for database deficiencies including the absence of multigenerational and chronic toxicity studies.

ATSDR based its value on the same study used by the CA EPA in its derivation. ATSDR identified the lowest exposure level in the study as a LOEL based on significant increases in the severity of nephropathy (as evaluated by a severity index). ATSDR used a pharmacokinetic model to obtain an internal dose metric (based on time-averaged arterial blood concentration of ethylbenzene) and a human equivalent air concentration corresponding to the lowest exposure level. A total uncertainty factor of 300 was used, including 10-fold for intraspecies variability, 3-fold for interspecies variability, and 10-fold for use of a LOEL. The severity index for nephropathy provides evidence of kidney toxicity (the most sensitive noncancer endpoint for ethylbenzene) at the lowest exposure level, and increases with

increasing exposure. The ATSDR derivation is more consistent with generally accepted risk assessment practices than those of the other agencies because it uses pharmacokinetic modeling to obtain dose metrics and human equivalent concentrations. Therefore, the ATSDR reference concentration (260 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for ethylbenzene.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/19/2018) at http://www.atsdr.cdc.gov/toxpro2.html, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/19/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/19/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/19/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Ethylbenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for Ethylbenzene (CAS Number 100-41-4)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS	--	--	--	--	Ethylbenzene is not classifiable as to human carcinogenicity based on lack of animal bioassays and human studies.
CA EPA CPF* Also used by: ♦ US EPA RSL	0.4	2.5×10^{-6}	linearized multistage model	$BW^{3/4}$ [2]	Based on renal tubule adenomas or carcinomas in male rats exposed via inhalation 6 hours/day, 5 days/week for 104 weeks.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million , where 1×10^{-6} air concentration = 1×10^{-6}/unit risk.
[2]Factor for dose (mg/kg/day) adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$.
*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA IRIS lists ethylbenzene as not classifiable as to human carcinogenicity in a review that was last revised in 1991. Subsequent to the US EPA IRIS review, a two-year inhalation bioassay conducted by the National Toxicology Program (NTP) showed clear evidence of carcinogenicity based on renal tubule neoplasms in male and female rats. Other cancer effects observed in this study included alveolar/bronchiolar adenomas and carcinomas in male mice, and hepatocellular adenomas and carcinomas in female mice. The CA EPA CPF based its unit risk on the increased incidence of renal tubular adenomas and carcinomas in male rats in the NTP study. The CA EPA calculated inhaled doses from the time-weighted experimental air concentrations and then extrapolated the animal doses to human doses using $BW^{3/4}$ scaling. However, this method (inhaled doses followed by $BW^{3/4}$ scaling) is not recommended for gases such as ethylbenzene that have Category 3 gas properties.

The NYS DOH derived a unit risk of 1.0×10^{-6} per mcg/m^3 for ethylbenzene based on the same tumor data from the NTP study. The point of departure was the 95% lower confidence limit on the air concentration associated with a 10% excess risk of renal tumors, calculated using the linearized multistage model (extra risk) and the default pharmacokinetic adjustment (equal to 1) for effects of a

systemic gas when blood:air partitioning coefficients are unknown or when the animal:human partitioning coefficient ratio is greater than 1. Since it is derived using methods more consistent with generally accepted risk assessment practices, the NYS DOH unit risk (1.0×10^{-6} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for ethylbenzene. The ethyl benzene risk specific air concentration calculated from this toxicity value is 1 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: March, 2005; no revision January, 2018

4. References for Summary Table

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/17/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Fluoranthene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Fluoranthene (CAS Number 206-44-0)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA HEAST (1997)	0.04	125	NOEL	3000	Based on nephropathy, increased liver weights, hematological alterations, and clinical effects in male and female mice in 90-day gavage study. Study LOEL = 250 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The US EPA value is the only available reference dose for fluoranthene from by an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the US EPA reference dose (0.04 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for fluoranthene.

3. Review Dates

Summary table completion: February, 2004; no revision January, 2018
Toxicity value recommendation: March, 2004; no revision January, 2018

4. References for Summary Table

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 (97-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Fluoranthene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Fluoranthene (CAS Number 206-44-0)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1995)	--	--	--	--	Human data are not available. In several studies of mice exposed dermally, carcinogenic effects were not observed.
RIVM (2001)	5.0×10^{-4}	0.002	--	--	Based on a relative potency factor of 0.01 applied to RIVM's cancer potency estimate for benzo(a)pyrene.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

RIVM's conclusion that fluoranthene is carcinogenic is based on limited and inadequate information. The US EPA and the International Agency for Research on Cancer both reviewed the studies on fluoranthene and concluded it is not classifiable as to human carcinogenicity based on no human data and inadequate data from animal studies. No oral cancer potency factor for fluoranthene is recommended.

3. Review Dates

Summary table completion: February, 2004; no revision January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. Toxicological Profile for Polycyclic Aromatic Hydrocarbons. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Fluoranthene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Fluoranthene (CAS Number 206-44-0)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for fluoranthene is not available from the authoritative bodies listed in item number 5 (below). Fluoranthene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for fluoranthene is 0.04 mg/kg/day. Therefore, a reference concentration of 140 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for fluoranthene.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Fluoranthene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Fluoranthene (CAS Number 206-44-0)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for fluoranthene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Fluorene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Fluorene (CAS Number 86-73-7)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2003) • US EPA ODW (2002)	0.04	125	NOEL	3000	Based on hematological effects in male and female rats in a 13-week gavage study. Study LOEL = 250 mg/kg/day.
RIVM (2001)	0.04	NA	NA	NA	Based on RIVM's evaluation of total petroleum hydrocarbons and its designation of fluorene as a non-carcinogenic aromatic with 9 to 16 carbons.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor. NA = not applicable.

2. Recommendation and Rationale

The US EPA reference dose is based on chemical-specific toxicity information for fluorene. The RIVM value is based on a generic approach for petroleum related chemicals and is not the result of a chemical specific evaluation. Therefore the US EPA reference dose (0.04 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for fluorene.

3. Review Dates

Summary table completion: February, 2004; no revision January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2002. Office of Drinking Water, Drinking Water Standards and Health Advisories. Washington, DC. EPA 822-R-02-038.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Fluorene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Fluorene (CAS Number 86-73-7)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1995)	--	--	--	--	Human data are not available. No convincing evidence of carcinogenic effects was observed in several limited or inadequate studies in animals.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for fluorene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: February, 2004; no revision January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. Toxicological Profile for Polycyclic Aromatic Hydrocarbons. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Fluorene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Fluorene (CAS Number 86-73-7)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for fluorene is not available from the authoritative bodies listed in item number 5 (below). Fluorene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for fluorene is 0.04 mg/kg/day. Therefore, a reference concentration of 140 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for fluorene.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

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Health Effects Assessment Summary Tables
New York State Department of Health
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Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Fluorene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Fluorene (CAS Number 86-73-7)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for fluorene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Heptachlor
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Heptachlor (CAS Number 76-44-8)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
General Population					
US EPA IRIS Also used by: • US EPA RSL • US EPA ODW* • US EPA HEAST (1997)	5×10^{-4}	0.15	NOEL	300	Based on increases in liver to body weight ratios in male rats in a 2-year feeding study with heptachlor. Study LOEL = 0.25 mg/kg/day.
NYS DEC (1997)	1.5×10^{-3}	0.15	NOEL	100	Based on the same study and effects used by US EPA IRIS.
CA EPA PHG*	1×10^{-4}	0.1	LOEL	1000	Based on the alteration of sex steroid-mediated behaviors in male rats after prenatal and early-in-life exposure to technical chlordane, which only contains 10% heptachlor. A study NOEL was not identified.
	1.5×10^{-3}	0.15	NOEL	100	Based on the same study and effects used by US EPA IRIS.
WHO (2011)	1×10^{-4}	0.025	NOEL	200	Based on histopathological changes in the liver in a 2-year dog feeding study using heptachlor epoxide. Study LOEL = 0.075 mg/kg/day.
Child-Specific Reference Dose (chRD)					
CA EPA chRD*	3×10^{-5}	0.03	LOEL	1000	Based on decreased performance on measures of cognitive function in male rats following pre- and postnatal exposure, through postnatal day 21, and suppression of the primary IgM and secondary IgG antibody responses in male rats following exposure during the last half of gestation through puberty. Neither study identified a NOEL.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor; IgM: immunoglobulin M; IgG: immunoglobulin G.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA, NYS DEC, and one of the CA EPA PHG reference doses for heptachlor are based on the same rat study. The US EPA used an extra uncertainty factor of 3 for the lack of a chronic toxicity study in a second species. However, there are chronic studies in mice assessing the cancer effects of heptachlor, and studies on reproductive toxicity. The database does not appear sufficiently inadequate to justify an additional uncertainty factor of 3. Thus, the use of this additional uncertainty factor was not considered necessary by either NYS DEC or CA EPA PHG. The WHO reference dose is based on a study with heptachlor epoxide, a breakdown product of heptachlor, and not on the parent chemical. The lower of the two CA EPA PHG reference doses is based on a study with technical chlordane, which only contains 10% heptachlor. Therefore, the NYS DEC (and the higher of the two CA EPA PHG) reference dose (1.5×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer soil cleanup objective for heptachlor. However, it should only be used to derive soil cleanup objectives based on adult exposures.

CA EPA has formally developed a program to derive reference doses for evaluating childhood exposures to contaminants in and around schools. This program stems from the possibility that children may be more sensitive than adults to contaminant exposures. CA EPA bases child-specific reference doses (chRD), when possible, on studies in young animals or children rather than on studies based on adult animal or humans and the use of an uncertainty factor to compensate for typically unknown adult-child differences in pharmacokinetics and pharmacodynamics. CA EPA identified such studies for heptachlor. CA EPA based their child-specific reference dose for heptachlor on developmental immunological and neurological effects in young male rats exposed prenatally and postnatally (up to 42 days total). The studies were published in a high-quality peer-reviewed journal, and both were used by ATSDR to derive an intermediate reference dose (i.e., minimal risk level) for heptachlor. Moreover, the LOEL for developmental effects is lower than the adult NOEL used by NYS DEC, US EPA, and CA EPA PHG (higher of two reference doses). This supports the use of a separate reference dose for childhood exposures. Thus, the CA EPA child-specific reference dose (3×10^{-5} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer soil cleanup objective for heptachlor. However, it should only be used to derive soil cleanup objectives based on child exposures.

3. Review Dates

Summary table completion: February, 2004; revised January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/13/2018) at http://www.atsdr.cdc.gov/toxpro2.html, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA chRD (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Child-Specific Reference Doses. Last accessed (01/13/2018) at http://www.oehha.ca.gov/public_info/public/kids/chrds.html.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/13/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Heptachlor. Albany, NY: Division of Water.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/13/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/13/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/13/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/13/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/13/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html, with

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Heptachlor
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Heptachlor (CAS Number 76-44-8)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA OPP (1997) ♦ US EPA HEAST (1997)	2.2×10^{-7}	4.5	linearized multistage model, extra risk	body surface area[2]	Two chronic dietary studies (Davis et al. 1965 and Reuber 1977; NCI 1977) showed heptachlor causes liver tumors in both sexes of two strains of mice. The cancer potency factor is the geometric mean of four separate cancer potency factors, each derived from a different dose response dataset
NYS DEC (1997)	1.3×10^{-6}	0.79	linearized multistage model, extra risk	BW ¾ [3]	Based on increased incidence in liver tumors in an 80-week dietary study in male and female mice (NCI 1977; also used by US EPA 2004). The cancer potency factor is the geometric mean of two separate cancer potency factors, one from each data set (male and female).

Cal EPA (1999)	2.4 x 10^{-7}	4.1	linearized multistage model, extra risk	BW ¾ [3]	Based on a geometric mean of three of the four datasets (Davis et al. 1965; NCI 1977) used by US EPA IRIS (2004). Calculation of slope factors also included correction for less than lifetime exposure for mice.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10^{-6} dose), where 1 x 10^{-6} dose = 1 x 10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.

2. Recommendation and Rationale

All the cancer potency factors derived by authoritative bodies use male and female mouse data sets showing an increased incidence of liver tumors from a National Cancer Institute study published in 1977 (NCI, 1977). However, the US EPA and Cal EPA values (4.5 per mg/kg/day and 4.1 per mg/kg/day, respectively) also use additional data from a study by Davis et al. (1965) that has significant study quality issues, including poor documentation, use of a single dose, use of heptachlor of unspecified purity, excessive early mortality and lack of data on tumor onset and cause of death. The Davis et al. (1965) study was not used in the calculation of the NYS DEC cancer potency factor (0.79 per mg/kg/day) for heptachlor because of these study quality issues. The NYS DEC value is also based on the more currently accepted BW ¾ scaling while the US EPA value is based on body surface area scaling. The NYS DEC cancer potency factor (0.79 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for heptachlor. The heptachlor risk specific dose calculated from this toxicity value is 1.3 x 10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: February, 2004; no revision January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1993. Toxicological Profile for Heptachlor and Heptachlor Epoxide. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service.

Davis, K. 1965. Pathology Report on Mice Fed Aldrin, Dieldrin, Heptachlor and Heptachlor Epoxide for Two Years. Internal FDA memorandum to Dr. A.J. Lehman, July 19 (as cited in US EPA IRIS (2004)).

Cal EPA (California Environmental Protection Agency). 2003. Public Health Goal for Heptachlor and Heptachlor Epoxide in Drinking Water. Division of Drinking Water and Environmental Management. Sacramento, CA. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

NCI (National Cancer Institute). 1977. Bioassay of Heptachlor for Possible Carcinogenicity. NCI Carcinogenesis Tech. Rep. Ser. No. 9. (Also published as DHEW Publication No. [NIH] 77-809).

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Heptachlor. Albany, NY: Division of Water.

Reuber, M.D. 1977. Histopathology of Carcinomas of the Liver in Mice Ingesting Heptachlor or Heptachlor Epoxide. Exp. Cell Biol. 45: 147-157.

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 (97-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA OPP (United States Environmental Protection Agency Office of Pesticide Programs). 1997. Reference Dose Tracking Report. Washington, DC: Office of Pesticide Programs, Health Effects Division. HED reviewed 08/08/86.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Heptachlor
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Heptachlor (CAS Number 76-44-8)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for heptachlor is not available from the authoritative bodies listed in item number 5 (below). Heptachlor is a systemic toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure.

A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the adult reference dose. The recommended hepatachlor oral reference dose for adult exposures is 1.5×10^{-3} mg/kg/day. Therefore, a reference concentration of 5.2 mcg/m^3 for adults based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for heptachlor.

3. Review Dates

Summary table completion: February, 2005, no revision January, 2018
Toxicity value recommendation: February, 2005, no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health

United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Heptachlor
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Heptachlor (CAS Number 76-44-8)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: ◆ US EPA Region 3 (2004) ◆ US EPA OPP (1997) ◆ US EPA HEAST (1997)	7.7×10^{-4}	1.3×10^{-3}	linearized multistage model, extra risk	body surface area[2]	Estimated from a route-to-route-extrapolation of oral cancer data based on liver tumors in both sexes of two strains of mice in two chronic dietary studies.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration = 1×10^{-6} / unit risk.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.

2. Recommendation and Rationale

The US EPA IRIS unit risk (1.3×10^{-3} per mcg/m^3) is the only available value derived by an authoritative body from the list in item 5 (below). However, this value is derived via oral-to-inhalation route extrapolation from an oral cancer potency factor that was not recommended as the oral cancer toxicity value for heptachlor. Since no toxicity values from the authoritative bodies listed in item 5 (below) are based on inhalation, and at least one authoritative body derived a unit risk using exposure route extrapolation, a default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a unit risk from the recommended cancer potency factor. The recommended oral cancer potency factor for heptachlor is 0.79 per mg/kg/day. Therefore the unit risk of 2.3×10^{-4} per mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for heptachlor. The heptachlor risk specific air concentration calculated from this toxicity value is 4.4×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA OPP (United States Environmental Protection Agency Office of Pesticide Programs). 1997. Reference Dose Tracking Report. Washington, DC: Office of Pesticide Programs, Health Effects Division. HED reviewed 08/08/86.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Hexachlorobenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Hexachlorobenzene (CAS Number 118-74-1)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW	8×10^{-4}	0.08	NOEL	100	Based on liver toxicity in male and female rats exposed *in utero*, during lactation and via diets for the remainder of their lifetime (130 weeks). Study LOEL = 0.29 mg/kg/day.
US EPA OSRTI*	1×10^{-5} [2]	0.01	LOEL	1000	Based on degenerative changes in primary ovarian follicles of monkeys exposed each day via gelatin capsules for 13 weeks. A study NOEL was not identified.
NYS DEC (1997)	8×10^{-4}	0.08	NOEL	100	Based on same study and effects used by US EPA IRIS
ATSDR	7×10^{-5}	0.022	LOEL	300	Based on the same study used by US EPA IRIS, but a different study LOEL, which was based on minimal hepatic effects (peribiliary lymphocytosis and fibrosis of the liver) in male rats. A study NOEL was not identified.
CA EPA	3×10^{-5}	0.01	LOEL	300	Based on the same study used by US EPA IRIS, but a different study LOEL, which was based on minimal hepatic effects (centrilobular basophilic chromogenesis) in female rats. A study NOEL was not identified.
HC PSAP	5×10^{-5}	0.05	NOEL	1000	Based on the same study used by US EPA IRIS and on liver effects in additional studies in rats and pigs exposed via the diet.
RIVM (2001)	5×10^{-4}	0.05	NOEL	100	Based on the same studies used by HC PSAP.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]US EPA OSRTI derived a subchronic reference dose from the study, but adopted the subchronic reference dose as the chronic reference dose because it is based on newer data and is lower than the US EPA IRIS chronic reference dose.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the all but one of the reference doses (i.e., US EPA OSRTI) for hexachlorobenzene is liver toxicity, generally in rats chronically exposed via the diet. The same study is used in all the derivations as one of or as the sole basis for the point of departure, but the interpretation of the effects at the lowest two doses differs among the various authoritative bodies. Agencies differed as to whether the lowest dose is a LOEL (CA EPA and ATSDR) or the second lowest dose is a NOEL (US EPA IRIS and NYS DEC). At the two lowest non-zero doses, two histopathological changes (peribiliary cytosis and hepatic fibrosis) in the liver were observed at a significantly increased incidence above the controls. However, these lesions were common in the controls (up to about 30%) and a clear dose-response relationship was not observed (all non-zero dose groups had similar frequencies). Another liver change (centrilobular basophilic chromogenesis) showed a positive dose-related trend in exposed animals, but the incidence at the lowest two dose groups did not differ significantly from the controls. The US EPA IRIS concluded that the peribiliary cytosis and fibrosis effects were not exposure related due to the lack of dose-response. That conclusion, and the lack of a statistically significant increase of centrilobular basophilic chromogenesis frequency at the two lowest doses, led US EPA IRIS to identify the second-lowest dose (0.08 mg/kg/day) as the NOEL. The ATSDR concluded that the increased frequency of histopathologic changes at the lowest dose indicated minimal liver toxicity at this dose, while the CA EPA concluded that the dose-related trend in centrilobular basophilic chromogenesis may have been biologically significant, although increased frequencies at the lowest two doses were not statistically significant. The ATSDR and CA EPA identified the lowest non-zero dose (0.01 or 0.022 mg/kg/day) as a minimal LOEL. HC and RIVM both identified a NOEL similar to the US EPA IRIS point of departure, although their calculations of the effective dose rate in the feeding study differ from the US EPA IRIS's and clear documentation of the source of the differences is not available.

The US EPA IRIS and RIVM applied an uncertainty factor of 100 to account for animal-to-human extrapolation and human variation. The ATSDR applied an additional uncertainty factor of 3 to account for the use of a minimal LOEL. The CA EPA also applied an additional uncertainty factor of 3 to account for the use of a LOEL of probable biological, but not statistical, significance. HC applied a total uncertainty factor of 1000, including an additional factor of 10 to account for the carcinogenicity of hexachlorobenzene. This additional factor of 10 is not applicable in the current context because cancer and non-cancer effects are assessed separately in the Brownfield Cleanup Programs. The high background rate and lack of a clear dose-related trend in the liver effects seen at the lowest doses suggests those effects were not clearly exposure related. Therefore, the US EPA reference dose (8×10^{-4} mg/kg/day) is the recommended liver-based reference dose.

The US EPA OSRTI derivation of subchronic reference dose was done much more recently than all the other derivations. It was based on new and substantial data that shows hexachlorobenzene is toxic to the mammalian ovary and may interfere with mechanisms regulating ovarian steroidogenesis. The LOEL for the subchronic database is 0.01 mg/kg-day for degenerative changes in primary ovarian follicles of female monkeys exposed to hexachlorobenzene for 13 weeks. It represents the most sensitive effect in the subchronic database. The US EPA OSRTI chose it as the principal study for the determination of the subchronic reference dose. The US EPA OSRTI applied a total uncertainty factor of 1000 to the LOEL to compensate for animal-to-human extrapolation (10), the use of a LOEL (10), and human variation (10). The US EPA OSRTI recognized that the new data and the application of uncertainty factor consistent with generally accepted risk assessment practices led to a subchronic reference dose that is lower than the US EPA IRIS chronic reference dose. Thus, the US EPA OSRTI adopted the subchronic reference dose as its chronic reference dose.

The US EPA OSRTI reference dose is lower than that of the US EPA IRIS reference dose, and in the absence of data on whether monkeys or mice are better surrogates for humans, the US EPA OSRTI reference dose (1×10^{-5} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for hexchlorobenzene**.**

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: August, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/16/2018) at http://www.atsdr.cdc.gov/mrls/index.asp , with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/16/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/16/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/16/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/16/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/16/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund . Last accessed (01/16/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/16/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment

Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Hexachlorobenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Hexachlorobenzene (CAS Number 118-74-1)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2003) • US EPA OPP (1997) • US EPA HEAST (1997) • ATSDR (2002)	6.2×10^{-7}	1.6	linearized multistage model, extra risk	body surface area[2]	Based on increased liver tumors in female rats exposed via diet for their lifetime.
Cal EPA (2002)	5.6×10^{-7}	1.8	linearized multistage model, extra risk	body surface area[2]	Based on pooled data for adrenal pheochromocytomas in female rats exposed via diet for two years and in female pups exposed during gestation, lactation and via diet for their lifetime.
Cal EPA (2003)	7.7×10^{-7}	1.294	linearized multistage model, extra risk	$BW^{¾}$ [3]	Based on female rat lifetime dietary exposure study used in Cal EPA (2002)
Cal EPA (2003)	9.2×10^{-7}	1.09	linear extrap. from LED_{10} [4]	$BW^{¾}$ [3]	Based on the two-generation dietary exposure study study used in Cal EPA (2002)
Health Canada (1993) (see also TERA, 2004)	1.2×10^{-6}	-- [5]	linear extrap. from TD_{05} [5]	body surface area[2]	Based on increased incidence of neoplastic nodules in female rat pups exposed during gestation, lactation and via diet for their lifetime.

RIVM (2001)	1.6×10^{-6}	-- [6]	linear extrapola-tion	body weight [7]	Based on increased incidence of neoplastic nodules in female rat pups exposed during gestation, lactation and via diet.
NYS DEC (1997)	1.0×10^{-6}	1.0	linearized multistage model, extra risk	$BW^{¾}$ [3]	Based on increased incidence of liver tumors in male hamsters exposed via diet for their lifetimes

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[4]LED_{10} = lower bound on the dose associated with 10% tumor incidence above background.
[5]No cancer potency factor was derived. The risk specific dose was obtained by linear extrapolation from the modeled TD_{05} (=0.06 mg/kg/d), the dose associated with a 5% increase in mean tumor incidence (not a lower-bound estimate; TERA, 2004)
[6]No cancer potency factor was derived. The risk specific dose was obtained by linear extrapolation from the lowest tumorigenic dose (not a lower-bound estimate)
[7]Factor for dose adjustment from animal to humans is 1.

2. Recommendation and Rationale

All of the cancer potency factors (or risk-specific doses in those cases without a cancer potency factor) derived by authoritative bodies except for Cal EPA are based on increased in incidence of liver tumors or neoplastic nodules in rats or hamsters. The Cal EPA values are based on an increased incidence of adrenal tumors in rats exposed *in utero* and during their lifetimes. The risk-specific dose estimates are all within a factor of about 3 of each other. The Cal EPA (2002) apparently derived their value by pooling adrenal tumor data from a study with a significant dose-response for that tumor with other data for the same tumor type that did not demonstrate a significant dose response. This derivation also pooled data from two different study designs – a conventional 2-year dietary study and a 2-generation dietary study. Cal EPA (2003) used data from these two studies, but derived separate cancer potency factors for the 2-year study and the 2-generation study using different extrapolation methods from each other and from the Cal EPA (2002) derivation. Of the 3 Cal EPA derivations, the cancer potency factor based on the 2-generation dietary study that used linear extrapolation from a LED_{10} estimated based on $BW^{¾}$ scaling (Cal EPA 2003) is most consistent with currently-accepted risk assessment practices. RIVM and Health Canada (as presented by TERA) both derived risk-specific doses based on linear extrapolations of observed tumor incidence data or a maximum likelihood estimate of modeled tumor dose response from a single study in rats. Neither derivation represents a lower-bound estimate on the risk-specific dose. The US EPA and NYS DEC both obtained cancer potency estimates from tumor incidence data in the liver, which the US EPA concluded was the primary target organ for hexachlorobenzene carcinogenicity. The US EPA used body surface area scaling in their derivation, while the NYSDEC used $BW^{¾}$ scaling. Of those two, the NYS DEC methodology is more consistent with currently accepted risk assessment practice. Although the NYSDEC cancer potency estimate and the Cal EPA (2003) cancer potency estimate based on the 2-generation dietary study are nearly the same, the Cal EPA derivation is somewhat more consistent with currently accepted risk assessment

practice than the NYSDEC derivation because the former uses a linear high-to-low dose extrapolation from a benchmark dose rather than extrapolating to low doses via a statistical model. Therefore, the Cal EPA cancer potency factor (1.09 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for hexachlorobenzene. The hexachlorobenzene risk-specific dose calculated from this toxicity value is 9.2×10^{-7} mg/kg/day.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: August, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological Profile for hexachlorobenzene. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

Cal EPA (California Environmental Protection Agency). 2002. Air Toxics Hot Spots Program Risk Assessment Guidelines: Part II Technical Support Document for Describing Available Cancer Potency Factors. Office of Environmental Health Hazard Assessment). Sacramento, CA.

Cal EPA (California Environmental Protection Agency). 2003. Public health goal for chemicals in drinking water: hexachlorobenzene. Office of Environmental Health Hazard Assessment. https://oehha.ca.gov/water/public-health-goals-phgs

Health Canada, Environment Canada. 1993. Priority Substances List Assessment Report: Hexachlorobenzene. Ottawa, Ministry of Public Works and Government Services. https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/canadian-environmental-protection-act-1999-priority-substances-list-assessment-report-hexachlorobenzene.html

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for hexachlorobenzene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/index-en.html

Toxicology Excellence for Risk Assessment (TERA). 2004. International toxicity estimates for risk database. Last accessed (01/17/2018) at http://www.tera.org/iter/

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 (97-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA OPP (United States Environmental Protection Agency Office of Pesticide Programs). 1997. Reference Dose Tracking Report. Washington, DC: Office of Pesticide Programs, Health Effects Division.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Hexachlorobenzene
Exposure Route: Inhalation
Toxicity: Non-cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Hexachlorobenzene (CAS Number 118-74-1)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	An inhalation reference concentration for hexachlorobenzene is not available from the authoritative bodies listed in item number 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Hexachlorobenzene is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the recommended reference dose based on systemic effects (1×10^{-5} mg/kg/day; see Oral Non-Cancer Toxicity Value Documentation). Therefore, a reference concentration of 0.035 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for hexachlorobenzene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
  Integrated Risk Information System
  Office of Drinking Water

Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
Health Effects Assessment Summary Tables
Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Hexachlorobenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for Hexachlorobenzene (CAS Number 118-74-1)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS*	2.0×10^{-3}	4.6×10^{-4}	linearized multistage model, extra risk	body surface area[2]	The unit risk was estimated from an oral cancer potency factor using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. Hexachlorobenzene caused increased liver tumors in female rats exposed via diet for their lifetime.
CA EPA CPF*	2.0×10^{-3}	5.1×10^{-4} [2]	linearized multistage model	body surface area[3]	Based on pooled data for adrenal pheochromocytomas in female rats exposed via the diet in a 2-year study and in female pups exposed during gestation, lactation and via the diet for their lifetime.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million, where 1×10^{-6} air concentration = 1×10^{-6}/unit risk.

[2]US EPA calculated a inhalation unit risk from an oral cancer potency factor (1.6 per mg/kg/day) using a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air/day.

[3]CA EPA calculated a inhalation unit risk from an oral cancer potency factor (1.8 per mg/kg/day) using a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air/day.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

Hexachlorobenzene is a toxicant that is expected to be absorbed into the body and cause systemic cancer effects following oral or inhalation exposure. A unit risk for hexachlorobenzene based on inhalation exposures is not available from the authoritative bodies listed in item number 5 (below). The US EPA and CA EPA inhalation unit risks for hexachlorobenzene are based on oral cancer potency factors (1.8 per mg/kg/day and 1.6 per mg/kg/day, respectively) that were considered, but not selected, as the recommended oral cancer potency factor. The recommended cancer potency factor for hexachlorobenzene is 1.09 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for hexachlorobenzene). A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive an inhalation unit risk from

the recommended oral cancer potency factor. Therefore, a unit risk of 3.1×10^{-4} per mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for hexachlorobenzene. The risk specific air concentration calculated from this toxicity value is 3.2×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/19/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *alpha*-Hexachlorocyclohexane (*alpha*-HCH)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for a*lpha*-Hexachlorocyclohexane (*alpha*-HCH) (CAS Number 319-84-6)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
ATSDR (2003)	8×10^{-3}	0.8	NOEL	100	Based on very slight histological changes and increased liver weight male and female rats in a 2-year feeding study. Study LOEL = 3.5 mg/kg/day.
RIVM (2001)	1×10^{-3}	0.1	NOEL	100	Based on liver toxicity in male and female rats in a 90-day feeding study. Study LOEL = 0.5 mg/kg/day.
NYS DEC (1997)	5×10^{-4}	0.5	NOEL	1000	Based on the same study reviewed in ATSDR (2003). Doses were calculated differently because of reduced survival, including in control group. Study LOEL = 2.5 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The basis for the ATSDR and NYS DEC reference doses for *alpha*-HCH is essentially identical with respect to choice of study, species and adverse effect. The RIVM reference dose is also based on rat liver toxicity observed in a different study, but RIVM only applied a total uncertainty factor of 100 (rather than 1000) to a subchronic rat NOEL. The point-of-departure estimates reported by ATSDR and NYS DEC differ slightly due to different assumptions used to convert exposure concentration in feed to a daily dose. The NYS DEC added an extra 10-fold uncertainty factor in calculating their reference dose to account for use of a less-than-lifetime study. Although a few animals survived and were exposed in the study for up to 107 weeks, mean survival ranged from 54 - 58 weeks in the control and three lowest dose groups and was 36 weeks in the high-dose group. Because of the added uncertainty introduced into the point-of-departure estimate due to high mortality, the NYS DEC reference dose (5×10^{-4} mg/kg/day)

is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *alpha*-HCH.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological profile for hexachlorocyclohexanes (HCH). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

NYSDEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Alpha-Hexachlorocyclohexane. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. p 258-262. http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *alpha*-Hexachlorocyclohexane (*alpha*-HCH)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for *alpha*-Hexachlorocyclohexane (*alpha*-HCH) (CAS Number 319-84-6)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2003) • US EPA HEAST (1997) • ATSDR (2003)	1.6×10^{-7}	6.3	linearized multistage model, extra risk	body surface area[2]	Dietary alpha-HCH has been shown to cause increased incidence of liver tumors in males and females of five mouse strains and in a strain of rats. The cancer slope factor is based on tumor incidence data from a strain of male mice in an individual study, which gave the highest estimate of potency.
NYS DEC (1997)	2.9×10^{-7}	3.4	linearized multistage model, extra risk	$BW^{¾}$ [3]	Based on the same study and review as US EPA IRIS (2004).
Cal EPA (2004)	3.7×10^{-7}	--[4]	--	--	Based on a Proposition 65 no significant risk level. Details of derivation unavailable.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[4]A cancer potency factor is not reported. The value is reported as a daily intake in micrograms associated with a excess lifetime cancer risk of one-in-one hundred thousand. The risk-specific dose was obtained assuming 70kg adult body weight.

2. Recommendation and Rationale

The basis for the two well-documented cancer potency factors derived by authoritative bodies is identical with respect to study, species and tumor incidence data. The Cal EPA cancer potency factor is the basis for the Proposition 65 program no significant risk level, but details of its derivation are unavailable. The US EPA used body surface area interspecies scaling, while the NYS DEC used $BW^{3/4}$ scaling. The two agencies used different adjustment methods to account for the short exposure duration used in the study, but the effect of these adjustments appears to be essentially equal, so that almost the entire difference between the two values is attributable to the difference in scaling methods. The NYS DEC value is based on the more current and generally accepted scaling method. Therefore, the NYS DEC cancer potency factor (3.4 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for *alpha*-HCH. The *alpha*-HCH risk specific dose calculated from this toxicity value is 2.9×10^{-7} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2004. Toxicity Criteria Database. Office of Exposure and Health Hazard Assessment. Last accessed (01/18/2018) at https://oehha.ca.gov/chemicals

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological profile for hexachlorocyclohexanes (HCH). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Alpha-Hexachlorocyclohexane. Albany, NY: Division of Water.

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 (97-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System

- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *alpha*-Hexachlorocyclohexane (*alpha*-HCH)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for a*lpha*-Hexachlorocyclohexane (*alpha*-HCH) (CAS Number 319-84-6)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for *alpha*-HCH is not available from the authoritative bodies listed in item number 5 (below). *alpha*-HCH is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for *alpha*-HCH is 5×10^{-4} mg/kg/day. Therefore, a reference concentration of 1.8 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *alpha*-HCH.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *alpha*-Hexachlorocyclohexane (*alpha*-HCH)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for *alpha*-Hexachlorocyclohexane (*alpha*-HCH) (CAS Number 319-84-6)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for *alpha*-HCH is not available from the authoritative bodies listed in item number 5 (below). *alpha*-HCH is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral cancer potency factor based on cancer effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a unit risk from the cancer potency factor. The recommended oral cancer potency factor for *alpha*-HCH is 3.4 per mg/kg/day. Therefore, a unit risk of 9.7×10^{-4} per mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for *alpha*-HCH. The risk specific air concentration calculated from this toxicity value is 1.0×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *beta*-Hexachlorocyclohexane (*beta*-HCH)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for *beta*-Hexachlorocyclohexane (*beta*-HCH) (CAS Number 319-85-7)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
RIVM (2001)	2×10^{-5}	0.02	NOEL	1000	Based on observed infertility in a subchronic rat reproductive toxicity study. Limited information available.
NYS DEC (1997)	1×10^{-5}	0.1	LOEL	10000	Based on increased liver and kidney weights in a 13-week rat feeding study.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The basis for the NYS DEC reference dose for *beta*-HCH is a subchronic oral study in rats in which a dose-related increase in liver and kidney weights was observed. A significant increase in kidney weights was observed in the female rats at the lowest dose tested. The RIVM reference dose is based on infertility in a rat subchronic reproductive study, but documentation is too limited for adequate evaluation of its derivation. Therefore, the NYS DEC reference dose (1×10^{-5} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *beta*-HCH.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

NYSDEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Beta-Hexachlorocyclohexane. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

5. Authoritative Bodies Checked for Reference Doses

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *beta*-Hexachlorocyclohexane (*beta*-HCH)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for *beta*-Hexachlorocyclohexane (*beta*-HCH) (CAS Number 319-85-7)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2003) • US EPA HEAST (1997) • ATSDR (2003)	5.6×10^{-7}	1.8	linearized multistage model, extra risk	body surface area[2]	Based on the incidence of benign hepatomas or hepatocellular carcinomas in male mice in a chronic feeding study with only one non-zero dose group.
NYS DEC (1997)	1.0×10^{-6}	0.96	linearized multistage model, extra risk	$BW^{3/4}$ [3]	Based on the same study and toxicological endpoints as US EPA IRIS (2004).
Cal EPA (2004)	6.7×10^{-7}	--[4]	--	--	Based on a Proposition 65 no significant risk level. Details of derivation unavailable.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[4]A cancer potency factor is not reported. The value is reported as a daily intake in micrograms associated with a excess lifetime cancer risk of one-in-one hundred thousand. The risk-specific dose was obtained assuming 70kg adult body weight.

2. Recommendation and Rationale

The basis of both well-documented cancer potency factors derived by authoritative bodies is identical with respect to study, species, critical effect and tumor dose-response data. The Cal EPA cancer potency factor is the basis for the Proposition 65 program no significant risk level, but details of its derivation are unavailable. The US EPA derived their cancer potency estimate using a multistage model and a body surface area interspecies dose extrapolation, while the NYS DEC used the same model, but applied an interspecies dose extrapolation based on $BW^{3/4}$ scaling. The NYS DEC interspecies scaling factor is more consistent with currently accepted risk assessment practice. Therefore, the NYS DEC cancer

potency factor (0.96 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for *beta*-HCH. The *beta*-HCH risk specific dose calculated from this toxicity value is 1.0×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2004. Toxicity Criteria Database. Office of Exposure and Health Hazard Assessment. Last accessed (01/17/2018) at https://oehha.ca.gov/chemicals

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological profile for hexachlorocyclohexanes (HCH). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

NYSDEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Beta-Hexachlorocyclohexane. Albany, NY: Division of Water.

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 (97-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *beta*-Hexachlorocyclohexane
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for *beta*-Hexachlorocyclohexane (*beta*-HCH) (CAS Number 319-85-7)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for *beta*-HCH is not available from the authoritative bodies listed in item number 5 (below). *beta*-HCH is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for *beta*-HCH is 1.0×10^{-5} mg/kg/day. Therefore, a reference concentration of 0.035 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *beta*-HCH.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *beta*-Hexachlorocyclohexane
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for *beta*-Hexachlorocyclohexane (*beta*-HCH) (CAS Number 319-85-7)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for *beta*-HCH is not available from the authoritative bodies listed in item number 5 (below). *beta*-HCH is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral cancer potency factor based on cancer effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a unit risk from the cancer potency factor. The recommended oral cancer potency factor for *beta*-HCH is 0.96 per mg/kg/day. Therefore, a unit risk of 2.7×10^{-4} per mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for *beta*-HCH. The risk specific air concentration calculated from this toxicity value is 3.7×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *delta*-Hexachlorocyclohexane (*delta*-HCH)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for *delta*-Hexachlorocyclohexane (*delta*-HCH) (CAS Number 319-86-8)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
ATSDR (2003) RIVM (2001)	--	--	--	--	Toxicity studies reviewed, but a chronic reference value was not derived because adequate studies are lacking.
NYS DEC (1997)	0.025	25	NOEL	1000	Based on an inconclusive finding of liver cell hypertrophy in male rats in a 48-week feeding study. Study LOEL = 50 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The NYS DEC value is the only available reference dose for *delta*-HCH from an authoritative body listed in item 5 (below) and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the NYS DEC reference dose (0.025 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *delta*-HCH.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological profile for hexachlorocyclohexanes (HCH). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Delta-Hexachlorocyclohexane. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *delta*-Hexachlorocyclohexane (*delta*-HCH)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for *delta*-Hexachlorocyclohexane (*delta*-HCH) (CAS Number 319-86-8)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Human data are not available. Cancer effects were not observed in a few limited or inadequate oral studies in mice and rats.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for *delta*-HCH is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *delta*-Hexachlorocyclohexane (*delta*-HCH)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. **Summary of Available Inhalation Reference Concentrations for *delta*-Hexachlorocyclohexane (*delta*-HCH) (CAS Number 319-86-8)**

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. **Recommendation and Rationale**

An inhalation reference concentration for *delta*-HCH is not available from the authoritative bodies listed in item number 5 (below). *delta*-HCH is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for *delta*-HCH is 0.025 mg/kg/day. Therefore, a reference concentration of 88 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *delta*-HCH.

3. **Review Dates**

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. **References for Summary Table**

5. **Authoritative Bodies**

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *delta*-Hexachlorocyclohexane (*delta*-HCH)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for *delta*-Hexachlorocyclohexane (*delta*-HCH) (CAS Number 319-86-8)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for *delta*-HCH is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *gamma*-hexachlorocyclohexane (*gamma*-HCH)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for *gamma*-Hexachlorocyclohexane (*gamma*-HCH) (CAS Number 58-89-9)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA HEAST (1997) ♦	3×10^{-4}	0.33	NOEL	1000	Based on liver and kidney toxicity in male and female rats exposed via the diet in an 18-week feeding study. Study LOEL = 1.55 mg/kg/day.
NYS DEC (1997)	3×10^{-4}	0.33	NOEL	1000	Based on the same study, species, and effects used by US EPA IRIS.
US EPA OPP (2002)*	1.6×10^{-3}	0.47	NOEL	300	Based on increased incidence of periacinar hepatocyte hypertrophy, increased liver/spleen weight, and decreased platelets in rats exposed via the diet in a 2-year study.
US EPA ODW*	5×10^{-3}	0.47	NOEL	100	Based on same study, species, and effects as used by US EPA OPP.
WHO (2011)*	5×10^{-3}	0.47	NOEL	100	Based on same study and species as US EPA OPP, but slightly different set of effects (increased incidence of periacinar hepatocellular hypertrophy, increased liver and spleen weights and increased mortality).
CA EPA PHG*	1.2×10^{-5}	0.012	LOEL	1000	Based on changes in the cell mediated and humoral components of immunological responses in mice exposed via the diet in a 24-week study. A NOEL was not identified.
RIVM (2001)	4×10^{-5}	0.012	LOEL	300	Based on same study, species, and effects used by CA EPA PHG.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The study used as the basis for the CA EPA and RIVM reference dose showed immunological effects of *gamma*-HCH at much lower doses than did the studies used by the other agencies. The study LOEL (0.012 mg/kg/day) for immunological effects is 28 and 40 times lower than the NOELs used by US EPA IRIS/NYS DEC and US EPA OPP/US EPA ORD/WHO, respectively. The study used by CA EPA and RIVM was published in a peer-reviewed journal. It was used by ATSDR to derive an intermediate reference dose (i.e., minimal risk level) for *gamma*-HCH. Thus, three public health agencies considered the results robust enough to support a reference dose. Therefore, the US EPA (all five), NYS DEC, and WHO reference doses are not selected as toxicity values for use in the derivation of an oral non-cancer-based soil cleanup objective for *gamma*-HCH.

CA EPA applied a total uncertainty factor of 1000 to the study LOEL to compensate for animal to human extrapolation (10), the use of a LOEL (10), and human variation (10). RIVM applied a total uncertainty factor of 300 to the study LOEL to compensate for animal to human extrapolation (10), the use of a LOEL (3), and human variation (10). RIVM considered the use of an uncertainty factor of 3 for the use to be justified given "rather marginal response" at the LOEL. Neither agency provided a rationale to support the absence of an uncertainty factor to compensate for the use of a subchronic study.

CA EPA noted there were significant reductions in the five immunological responses at the LOEL, which suggested "that lower doses and/or longer exposures would also give lower values compared to controls". In addition, CA EPA noted that the average reduction in the five immunological tests compared to control values was over 40%, whereas only a 10% reduction appeared necessary to show statistical significance. Given the strength of the immunological response, the potential for longer exposures to produce effects at doses lower than 0.012 mg/kg/day, the lack of an uncertainty factor for the use of a subchronic study by either agency, and the larger total uncertainty factor of CA EPA, the CA EPA reference dose (1.2×10^{-5} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *gamma*-HCH.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. **References for Summary Table and Recommendation and Rationale**

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/20/2018) at http://www.atsdr.cdc.gov/toxpro2.html, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. *gamma*-Hexachlorocyclohexane. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/20/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/20/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/20/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA OPP (United States Environmental Protection Agency, Office of Pesticide Programs). 2002. Reregistration Eligibility Decision For Lindane. Case 315. Last accessed (01/20/2018) at http://www.epa.gov/oppsrrd1/reregistration/lindane/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/20/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *gamma*-Hexachlorocyclohexane (*gamma*-HCH)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for *gamma*-Hexachlorocyclohexane (*gamma*-HCH) (CAS Number 58-89-9)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA CPF Also used by ♦ CA EPA PHG*	9.1×10^{-7}	1.1	linearized multistage model	body surface area[2]	Based on incidence data for liver tumors in a single strain of male mice exposed via the diet in a 110-week study.
US EPA RSL*	9.1×10^{-7}	1.1	linearized multistage model	body surface area[2]	US EPA RSL adopted the CA EPA cancer potency factor.
NYS DEC (1997)	1.4×10^{-6}	0.71	linearized multistage model	$BW^{3/4}$ [3]	Based on the same tumor data used by CA EPA.
US EPA HEAST (1997	7.7×10^{-7}	1.3	linearized multistage model	body surface area[2]	Based on liver tumors in a mouse feeding study. (Derivation poorly documented, value is listed as "Under Review".)

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.
[2]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.
[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

All the *gamma*-HCH cancer potency factors derived by authoritative bodies are based on dose-response data for liver tumors in mice. The CA EPA (and US EPA RSL) and NYS DEC values are derived from the same lifetime mouse feeding study and differ only in the scaling factor used to relate the rodent dose to an equivalent human dose. The US EPA HEAST value is poorly documented, and its precise basis is unclear. The NYS DEC derivation includes using the interspecies scaling factor that is more consistent with generally accepted risk assessment practice. Therefore, the NYS DEC cancer potency

factor (0.71 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for *gamma*-HCH. The *gamma*-HCH risk specific dose calculated from this toxicity value is 1.4×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/20/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/20/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. *gamma*-Hexachlorocyclohexane. Albany, NY: Division of Water.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/20/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (1/20/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *gamma*-Hexachlorocyclohexane (*gamma*-HCH)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for *gamma*-Hexachlorocyclohexane (*gamma*-HCH) (CAS Number 58-89-9)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for *gamma*-HCH is not available from the authoritative bodies listed in item number 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

gamma-HCH is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the recommended reference dose based on systemic effects (1.2×10^{-5} mg/kg/day; see Oral Non-Cancer Toxicity Value Documentation for *gamma*-HCH). Therefore, a reference concentration of 0.042 mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *gamma*-HCH.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health

United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *gamma*-Hexachlorocyclohexane (*gamma*-HCH)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for *gamma*-Hexachlorocyclohexane (*gamma*-HCH) (CAS Number 58-89-9)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA CPF*	3.2×10^{-3}	3.1×10^{-4}	linearized multistage model	body surface area[2]	The unit risk was estimated from an oral cancer potency factor using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. The cancer potency factor was based on incidence of liver tumors in a single strain of male mice exposed via the diet in a 110-week study
US EPA RSL*	3.2×10^{-3}	3.1×10^{-4}	linearized multistage model	body surface area[2]	US EPA RSL adopted the CA EPA CPF unit risk.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million, where 1×10^{-6} air concentration = 1×10^{-6}/unit risk.
[2]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

gamma-HCH is a toxicant that is expected to be absorbed into the body and cause systemic cancer effects following oral or inhalation exposure. A unit risk for *gamma*-HCH based on inhalation exposures is not available from the authoritative bodies listed in item number 5 (below). However, the CA EPA derived a unit risk 3.1×10^{-4} per mcg/m^3) from their oral cancer potency factor (1.1 per mg/kg/day) using a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day. This value was adopted by US EPA RSL. However, the recommended cancer potency factor for *gamma*-HCH is NYS DEC's value of 0.71 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for *gamma*-HCH). Therefore, a unit risk of 2×10^{-4} per mcg/m^3 based on the same exposure route extrapolation used by CA EPA is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for *gamma*-HCH. The risk specific air concentration calculated from this toxicity value is 5×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/20/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/20/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Indeno[1,2,3-cd]pyrene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Indeno[1,2,3-cd]pyrene (CAS Number 193-39-5)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
--	--	--	--	--	A reference dose for indeno[1,2,3-cd]pyrene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

2. Recommendation and Rationale

Indeno[1,2,3-cd]pyrene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). Reference doses derived from chemical-specific toxicity data are available for six polycyclic aromatic hydrocarbons identified as priority contaminants in the Brownfield Cleanup Program (acenaphthene, anthracene, benzo[a]pyrene, fluoranthene, fluorene, and pyrene, see NYS, 2006). Indeno[1,2,3-cd]pyrene is chemically similar to each of these six listed polycyclic aromatic hydrocarbons. Each of these six priority contaminants could be used to represent the noncancer toxicity of indeno[1,2,3-cd]pyrene. Similarity of chemical structure cannot be used as a basis of choosing a chemical surrogate for indeno[1,2,3-cd]pyrene because toxicity data are insufficient to accurately describe the relationship between the chemical structure and non-cancer toxicity of polycyclic aromatic hydrocarbons. The recommended reference dose for benzo[a]pyrene is lower than that of the other five polycyclic aromatic hydrocarbons. Without data on which of these six polycyclic aromatic hydrocarbons would be the best surrogate for indeno[1,2,3-cd]pyrene, the recommended reference dose for benzo[a]pyrene (3×10^{-4} mg/kg/day, see Oral Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for indeno[1,2,3-cd]pyrene.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Indeno[1,2,3-cd]pyrene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Indeno[1,2,3-cd]pyrene (CAS Number 193-39-5)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ◆ NYS DEC (2017)	1×10^{-5}	0.1	--	--	Based on a relative potency factor of 0.1 applied to the US EPA IRIS benzo[a]pyrene cancer potency factor of 1 $(mg/kg/day)^{-1}$.
CA EPA CPF	8.3×10^{-7}	1.2	--	--	Based on a potency equivalency factor of 0.1 applied to the CA EPA CPF benzo[a]pyrene cancer potency factor of 12 $(mg/kg/day)^{-1}$.
RIVM (2001)	5.0×10^{-5}	0.02 (2)	--	--	Based on a relative potency factor of 0.1 applied to the RIVM benzo[a]pyrene cancer potency factor[2] of 0.2 $(mg/kg/day)^{-1}$.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2]A cancer potency factor was not reported. The derivation directly extrapolates from an experimental dose with significant increased tumor incidence above background to the environmental dose associated with a one-in-one million risk level; the risk-specific dose is not a lower-bound estimate.

2. Recommendation and Rationale

Indeno[1,2,3-cd]pyrene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). The cancer potency factors for indeno[1,2,3-cd]pyrene available from the authoritative bodies listed in item 5 (below) are based on a cancer potency factor for benzo[a]pyrene (also a polycyclic aromatic hydrocarbon) and the application of a relative potency factor for indeno[1,2,3-cd]pyrene (see Chapter 5.1.5 of NYS (2006) for discussion of relative potency factors). The recommended cancer potency factor for benzo[a]pyrene is 1 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for Benzo[a]pyrene). The benzo[a]pyrene cancer potency factor is multiplied by the recommended relative potency factor of 0.1 for indeno[1,2,3-cd]pyrene (NYS 2006) to obtain a cancer potency factor of 0.1 per mg/kg/day. This is the toxicity value

recommended for use in the derivation of an oral cancer-based soil cleanup objective for indeno[1,2,3-cd]pyrene. The indeno[1,2,3-cd]pyrene risk specific dose calculated from this toxicity value is 1×10^{-5} mg/kg/day.

3. Review Dates

Summary table completion: February, 2004; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/13/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

NYS DEC (New York State Department of Environmental Conservation). 2017. Draft Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Indeno[1,2,3-cd]pyrene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/13/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/13/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Indeno[1,2,3-cd]pyrene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Indeno[1,2,3-cd]pyrene (CAS Number 193-39-5)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for indeno[1,2,3-cd]pyrene is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Indeno[1,2,3-cd]pyrene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). A reference concentration based on chemical-specific inhalation toxicity data for indeno[1,2,3-cd]pyrene is not available from the authoritative bodies listed in item 5 (below).

Benzo[a]pyrene is the only polycyclic aromatic hydrocarbon identified as a priority contaminant in the Brownfield Cleanup Program for which a reference concentration is available. Benzo[a]pyrene is chemically similar to indeno[1,2,3-cd]pyrene and can be used to represent its noncancer inhalation toxicity (see Inhalation Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene). Therefore, based on using benzo[a]pyrene as a chemical surrogate, a reference concentration of 2×10^{-3} mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for indeno[1,2,3-cd]pyrene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Indeno[1,2,3-cd]pyrene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Indeno[1,2,3-cd]pyrene (CAS Number 193-39-5)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2009)	9.1×10^{-3}	1.1×10^{-4}	--	--	Based on the unit risk for benzo[a]pyrene (which is derived from the increased incidence of respiratory tract tumors in hamsters exposed by inhalation) and application of a potency equivalency factor of 0.1.
Health Canada (1994)	1.33×10^4 reported as TC_{05} [(2)]; linear equivalent specific concentration = 0.27	-- [3]	--	--	Based on reported TC_{05} for benzo[a]pyrene (derived from the increased incidence of respiratory tract tumors in hamsters exposed by inhalation) and application of a relative potency factor of 0.12. The relative potency factor for indeno[1,2,3-cd]pyrene is based on its ability (relative to benzo[a]pyrene) to induce lung tumors in rats exposed by lung implantation.
US EPA IRIS	1.6×10^{-2}	6×10^{-5}	--	--	Based on application of a relative potency factor of 0.1 to the US EPA IRIS unit risk for benzo[a]pyrene, which is derived from the same study used by CA EPA and Health

					Canada.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10^{-6} air concentration), where 1 x 10^{-6} concentration = 1 x 10^{-6} / inhalation unit risk.

[2]TC_{05} = The concentration in air (expressed in mcg/m^3) associated with a 5% increase in incidence or mortality due to tumors.

[3]No cancer potency factor was derived. The risk specific air concentration was obtained by linear extrapolation from the modeled TC_{05}.

2. Recommendation and Rationale

The unit risk values for indeno[1,2,3-cd]pyrene are based on benzo[a]pyrene and the application of relative potency factors. The recommended unit risk value for benzo[a]pyrene is 6 x 10^{-4} per mcg/m^3 (see Inhalation Cancer Toxicity Value Documentation for benzo[a]pyrene). Application of the recommended relative potency factor (0.1) for indeno[1,2,3-cd]pyrene to the unit risk for benzo[a]pyrene yields a unit risk of 6 x 10^{-5} per mcg/m^3, which is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for indeno[1,2,3-cd]pyrene (see Chapter 5.1.5 of technical support document [NYS 2006] for discussion of recommended relative potency factors). The indeno[1,2,3-cd]pyrene risk specific air concentration calculated from this toxicity value is 1.6 x 10^{-2} mcg/m^3.

3. Review Dates

Summary table completion: November, 2004; revised January, 2018
Toxicity value recommendation: December, 2004; revised January, 2018

4. References for Summary Table

CA EPA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2009. Technical Support Document for Cancer Potency Factors 2009. Appendix B: Chemical-Specific Summaries of the Information Used to Derive Unit Risk and Cancer Potency Values. Last accessed (01/19/2018) at http://oehha.ca.gov/air/crnr/technical-support-document-cancer-potency-factors-2009.

Health Canada. 1994. Priority Substances List Assessment Report Polycyclic Aromatic Hydrocarbons:. Ottawa: Environment Canada, Ministry of Public Works and Government Services. Last accessed (01/17/2018) at https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/canadian-environmental-protection-act-priority-substances-list-assessment-report-polycyclic-aromatic-hydrocarbons.html

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/19/2018) at http://www.dec.ny.gov/chemical/34189.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry

California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System
Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
    Health Effects Assessment Summary Tables
    Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Manganese
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Inorganic Manganese

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
General Population					
US EPA IRIS Also used by: • US EPA RSL • US EPA ODW • US EPA HEAST (1997)	0.14 (food)	0.14	NOEL	1	Based on the estimated daily intake of Mn from three studies and the US EPA conclusion that an appropriate reference dose without risk of central nervous system effects is 10 mg/day (0.14 mg/kg/day). Depending on individual diets a normal intake may be well over 10 mg Mn/day, especially from a vegetarian diet (although bioavailability is lower for a vegetarian diet).
	0.05 (non-food)	0.14	NOEL	3	
WHO (2011)*	0.06 (water)	0.18	NOEL	3	Based on the upper limit for adult manganese intake from dietary surveys (11 mg/day) and divided by the average adult body weight of 60 kg.
Child-Specific Reference Dose (chRfD)					
CA EPA chRD*	0.03 (non-food)	0.09	non-dietary NOEL	3	The non-dietary NOEL is based on a mid-range dietary intake (5 mg/day) from Freeland-Graves et al. (1994) subtracted from the Food and Nutrition Board (2002) upper limit for adult manganese intake from food, water, and supplements (11 mg/day) and divided by the average body adult body weight of 70kg.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.
NOEL: no observed effect level; UF: uncertainty factor.
*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The reference doses for manganese derived by authoritative bodies from the list in item 5 (below) are all based on estimated human daily intake of manganese from food, water, and supplements. All are derived using methods that reflect general consistency with current risk assessment practice. The US EPA (non-food) and WHO (water) derivations both use a 3-fold uncertainty factor while the US EPA (food) derivation uses a 1-fold uncertainty factor. In the US EPA (non-food) and WHO derivations, the 3-fold uncertainty factor was used to account for increased uptake of manganese from drinking water. The US EPA also cited the potential for health effects from lifetime consumption of drinking water containing 2 mg/L manganese, infants consuming formula typically containing higher concentrations of manganese than human milk, and increased absorption of manganese through the blood-brain barrier in neonates as reasons for using the uncertainty factor. Though US EPA and WHO used similar NOELs and uncertainty factors, more detailed background documentation on the basis for the uncertainty factor was available for the US EPA (non-food) derivation. Therefore, the US EPA reference dose (0.05 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for manganese. However, it should only be used to derive soil cleanup objectives based on adult exposures.

CA EPA has formally developed a program to derive reference doses for evaluating childhood exposures to contaminants in and around schools. This program stems from the possibility that children may be more sensitive than adults to contaminant exposures. CA EPA bases child-specific reference doses (chRD), when possible, on studies in young animals or children rather than on studies based on adult animal or humans and the use of an uncertainty factor to compensate for typically unknown adult-child differences in pharmacokinetics and pharmacodynamics. CA EPA derived four separate child-specific reference doses for manganese, one based on human data and three based on animal data. The human-based child reference dose (0.03 mg/kg/day) is based on a non-dietary NOEL obtained by subtracting a mid-range dietary manganese intake from an adult upper limit magnesium intake for food, water and supplements, divided by an adult body weight of 70 kg. An uncertainty factor of 3 was used to account for differences between children and adults in gastrointestinal absorption, biliary excretion, blood-brain barrier, and transferrin receptors. The animal-based child reference doses (0.01, 0.08, and 0.02 mg/kg/day) were all based on neurobehavioral effects in studies of neonatal rats exposed to manganese. CA EPA noted that the animal-based child reference doses based on studies in very young rats fell into a narrow range, and that the average of these reference doses (0.035 mg/kg/day) is comparable to the child reference dose based on human data (0.03 mg/kg/day). Based on these considerations, CA EPA adopted the child reference dose based on human data. Therefore, the CA EPA child-specific reference dose (0.03 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer soil cleanup objective for manganese. However, it should only be used to derive soil cleanup objectives base on child exposures.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: August, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA chRD (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Child-Specific Reference Doses. Last accessed (01/12/2018) at http://www.oehha.ca.gov/public_info/public/kids/chrds.html.

Food and Nutrition Board. 2002. Dietary Reference Intakes: Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. pp. 10-1 - 10-22. Washington, DC: National Academy Press.

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US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/12/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/12/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2012 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/12/2018) at http://water.epa.gov/drink/standards/hascience.cfm.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/12/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/12/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Manganese
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Manganese

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Human data are not available, but there is suggestive evidence of carcinogenicity in several studies in rats and mice given Mn by subcutaneous, interperitoneal, and intramuscular injection, and by gavage.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for manganese is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: August, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Manganese
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Inorganic Manganese

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: • US EPA RSL	0.05	50	$LOEL_{HEC}$ [2]	1000	Based on impairment of neurobehavioral function from occupational exposure to manganese dioxide (MnO_2). The LOEL is derived from an occupational-lifetime integrated respirable dust concentration of MnO_2 (based on 8-hour TWA occupational exposure multiplied by individual work histories in years).
ATSDR	0.3*	34	$BMCL_{10}$ (3)	100	Based on the same study as US EPA IRIS (2011).
CA EPA REL	0.09	26	$BMCL_5$ (4)	300	Based on the same study as US EPA IRIS (2011).
WHO (2000)	0.15	7.2	$BMCL_5$ (5)	50	Based on the same study as US EPA IRIS (2011).
NYS DOH (1989)	0.3	150	NOEL	500	Based on pulmonary effects (inflammation) in subchronic studies in animals. The NOEL is the air concentration corresponding to the average time-weighted inhaled dose at which no pulmonary effects were observed in studies of several species, including rats, hamsters, rhesus monkeys

					and squirrel monkeys.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.
[2]$LOEL_{HEC}$: The human equivalent air concentration at the LOEL. The $LOEL_{HEC}$ was adjusted for continuous exposure (i.e., $10m^3$/day/20 m^3/day x 5 days/7 days).
[3]$BMCL_{10}$: The 95% lower confidence limit on benchmark concentration associated with a 10% response in the incidence of an adverse effect above background. The $BMCL_{10}$ was adjusted for continuous exposure (i.e., 8 hours/24 hours x 5 days/7 days).
[4]$BMCL_5$: The 95% lower confidence limit on benchmark concentration associated with a 5% response in the incidence of an adverse effect above background. The $BMCL_5$ was adjusted for continuous exposure (i.e., $10m^3$/day/20 m^3/day x 5 days/7 days).
[5]The $BMCL_5$ was adjusted for continuous exposure (i.e., 8 hours/24 hours x 5 days/7 days).

NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor; TWA: time weighted average

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The reference concentrations for manganese derived by authoritative bodies from the list in item 5 (below) are all based on an occupational study that showed nervous system effects in workers exposed to manganese in air, except for the NYS DOH value, which is based on pulmonary inflammation in animals. When available, adequate human data are chosen over animal data for the derivation of reference concentrations. The ATSDR, CA EPA and WHO reference concentrations use benchmark air concentrations as the point of departure, while the US EPA reference concentration uses the study LOEL. Deriving reference concentrations using modeled benchmark air concentrations as the point of departure is more consistent with generally accepted risk assessment practice. The differences among the reference concentrations derived by ATSDR, CA EPA and WHO stem primarily from the value of the benchmark air concentrations, and the uncertainty factors chosen to account for the greater exposure or sensitivity of children and for database limitations. All of the derivations use an uncertainty factor of 10 for intraspecies sensitivity. ATSDR also applies an uncertainty factor of 10 for database limitations (total uncertainty factor of 100), WHO applies an additional uncertainty factor of 5 to account for developmental effects of manganese in young children (total uncertainty factor of 50). The CA EPA applies additional uncertainty factors of 3 to account for use of a subchronic study and 10 to address the expectation that the still-developing brains of newborn and infant children are more sensitive to the effects of manganese, and that those effects may be long-lasting (total uncertainty factor of 300). All of the derivations appear scientifically defensible, and there is no compelling information to unequivocally choose one derivation over another. The CA EPA derivation offers the most protection for children and is also the only derivation that accounts for the less than chronic exposure (average of 5.3 years out of a 70-year lifetime) in the epidemiology study on which the reference concentration is based. Therefore, the CA EPA reference concentration (0.09 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for manganese.

3. Review Dates

Summary table completion: November, 2004; revised January, 2018
Toxicity value recommendation: December, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/15/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/15/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

NYS DOH (New York State Department of Health). 1989. Ambient Air Criteria Document for Manganese. Bureau of Toxic Substance Assessment. Albany, NY: New York State Department of Health.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at http://www.epa.gov/reg3hwmd/risk/human/index.htm

WHO (World Health Organization). 2000. Air Quality Guidelines for Europe. Last accessed (01/15/2018) at http://www.euro.who.int/en/health-topics/environment-and-health/air-quality/publications/pre2009/who-air-quality-guidelines-for-europe,-2nd-edition,-2000-cd-rom-version.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Manganese
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Manganese

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA (2004)	--	--	--	--	No data on humans and chronic inhalation studies in animals are not available.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An inhalation unit risk for manganese is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: November, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Mercury (Elemental)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Elemental Mercury (CAS Number 7439-97-6)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: • US EPA RSL • US EPA HEAST (1997)	0.3	9	LOEL	30	Based on several studies of workers exposed by inhalation reporting neurobehavioral impairments (i.e., hand tremors, effects on memory, and autonomic dysfunction).
ATSDR Also used by: • RIVM (2001)	0.2	6.2	LOEL	30	Based on one of the studies used by US EPA IRIS (2004).
CA EPA REL*	0.03	9	LOEL	300	Based on the same occupational studies used by US EPA IRIS (2004).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The reference concentrations for elemental mercury derived by authoritative bodies from the list in item 5 (below) are all based on central nervous system effects observed in workers exposed via inhalation to mercury vapor in several industries. The US EPA IRIS and CA EPA derived essentially identical points of departure by choosing a value approximately representing a median LOEL from the several occupational studies reviewed. The ATSDR used the exposure data from one of those studies to obtain

their LOEL estimate. The unadjusted LOEL estimates from the three derivations are nearly identical, but the US EPA IRIS and CA EPA used an occupational inhalation rate (10 m^3/day vs. 20 m^3/day) to adjust for discontinuous daily exposure while ATSDR used daily exposure duration (8 hr/day vs. 24 hr/day) as the adjustment factor. The adjustment based on occupational inhalation rate is more consistent with generally accepted risk assessment practice. The US EPA IRIS applied a total uncertainty factor of 30 including 10-fold to account for the combination of human variability and use of a LOEL and 3-fold to account for database deficiencies including the lack of developmental and reproductive toxicity studies. The CA EPA applied a total uncertainty factor of 300, including a 10-fold factor to account for the use of a LOEL and a total factor of 30 to account for human variability. The 30-fold factor includes 3-fold to account for human toxicokinetic variability and 10-fold to account for the greater susceptibility of children and the developing nervous system. Both the US EPA IRIS and CA EPA choices of uncertainty factors deviate somewhat from default values. No clear justification is provided by the US EPA IRIS for decreasing the default uncertainty factors for human variability and use of a LOEL by, in effect, 3-fold each. The CA EPA effectively increased the uncertainty factor accounting for human variability from 10 to 30 based on greater susceptibility of children and their developing nervous system. CA EPA presents data from animal studies on elemental and inorganic mercury demonstrating effects on the developing nervous system and also mentions similar human data for methyl mercury exposure. The CA EPA application of uncertainty factors that deviate from default values is better supported. Therefore, the CA EPA reference concentration (0.03 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for elemental mercury.

3. Review Dates

Summary table completion: September, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/17/2018) https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/17/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/17/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Mercury (Elemental)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Elemental Mercury (CAS Number 7439-97-6)

Agency	Risk Specific Concentration[1] (mcg/m^3)	Cancer Potency Factor $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Epidemiological studies of inhalation exposure to mercury were inadequate to derive a cancer potency value.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} concentration = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An inhalation unit risk for mercury is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Division of Drinking Water and Environmental Management
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Mercury (Inorganic)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Inorganic Mercury Salts

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS [2] Also used by: ♦ US EPA RSL (mercuric chloride) ♦ US EPA ODW (mercuric chloride) ♦ US EPA HEAST (1997)	3×10^{-4}	0.266 0.317 0.633 (these values represent lowest effect levels in the most sensitive animal model for human effects but were not used directly to derive the RfD)	LOEL	1000	Based on a review and workshop discussions of the entire inorganic mercury data base and the conclusion that autoimmune kidney effects (mercuric-mercury-induced autoimmune glomerulo-nephritis) observed in Brown Norway Rats represent the most sensitive effect in a sensitive species that is a good surrogate for effects in humans. A DWEL[3] of 0.010 mg/L was recommended as a consensus value based on the weight of evidence from the studies using Brown Norway rats and limited human tissue data. The reference dose is back-calculated from the DWEL.
CA EPA PHG	1.6×10^{-4} [4]	0.16	NOEL	1000	Based on decreases in body weight gain and increases in absolute and relative kidney weights observed in a 6-month Fisher 344 rat gavage study with mercuric chloride. The study LOEL was 0.33 mg/kg/day and all doses were converted from 5 to 7 day exposures.
RIVM (2001) Also used by: • WHO (2011)	2×10^{-3}	0.23	NOEL	100	Based on the same study as CA EPA PHG except doses were not time-weighted (limited review information available).

HC DWQ *	4.3×10^{-4}	0.0043	LOEL	10	A tolerable daily intake of 0.03 milligrams per day was obtained based on a blood level of methyl mercury thought be associated with the onset of neurological symptoms and the corresponding adult daily intake. Details are limited. The value applies to all forms of mercury in water.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.
[2]Reference dose value is for mercuric chloride (CAS No. 7487-94-7).
[3]Drinking Water Equivalent Level: A lifetime exposure concentration protective of adverse noncancer effects that assumes all of the exposure to a contaminant comes from drinking water.
[4]The reference dose value is inferred from the derivation of CA EPA's public health goal for drinking water, by dividing by 20% relative source contribution and 70 kg body weight and multiplying by 2 L/day drinking water consumption.

NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.
*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the various reference doses for inorganic mercury salts is kidney effects in rats exposed orally or subcutaneously to mercuric chloride, except for the drinking water guideline value derived by HC DWQ, which is based on a blood level associated with neurological effects of methyl mercury in humans, and is then applied to all forms of mercury in water. The HC DWQ value is based on a form of mercury not relevant to inorganic forms in soil, and therefore is not considered further. The US EPA convened a Peer Review Workshop on mercury issues from which a consensus recommendation for a DWEL of 0.01 mg/L was made, based on the weight of evidence from the entire inorganic mercury database, but especially based on studies using Brown Norway rats and limited human tissue data. The detailed basis of the DWEL derivation as a consensus value is not clear from the US EPA IRIS documentation. The US EPA reference dose was back-calculated from this consensus DWEL and includes a total uncertainty factor of 1000 which accounts for use of a LOEL (10-fold), use of subchronic studies (10-fold) and interspecies and intraspecies variability (a combined 10-fold factor). The CA EPA and RIVM both based their derivations on the same NOEL dose in a single subchronic gavage study in rats. The CA EPA time weighted the 5 days/week dosing regimen and applied a total uncertainty factor of 1000 to account for interspecies and intraspecies variability and the use of a subchronic study. RIVM did not time weight the gavage doses and did not include an additional 10-fold uncertainty factor to account for the use of a subchronic study. The studies with Brown Norway rats used as the principal studies in the US EPA derivation have design deficiencies including small sample sizes, few dose groups and durations of only two to three months. However, the US EPA Peer Review panel concluded that Brown Norway rat was the preferred animal model for mercury-induced autoimmune glomerulonephritis and that it was a sensitive surrogate for mercury-induced kidney effects in humans. The study used by CA EPA was six months in duration and included more dose groups and more animals per dose than the three principal US EPA studies, but may have been less sensitive for the critical kidney effect because it did not use the preferred animal model (i.e., Brown Norway rats). If the US EPA IRIS derivation had been based on the Brown Norway rat studies in a conventional non-cancer assessment, an additional uncertainty factor of 3 would likely have been used to account for the use of a sub-chronic LOEL. This would result in a reference dose closer to the CA EPA value. Since the CA

EPA derivation is somewhat more transparent than the US EPA IRIS derivation, the CA EPA reference dose (1.6×10^{-4} mg/kg/day as Hg^{2+}) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for inorganic mercury salts.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/19/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/19/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/19/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/19/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/19/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/19/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/19/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health

United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Mercury (Inorganic)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Mercury Salts

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Human data are inadequate; several limited epidemiological studies were confounded by possible or known concurrent exposures to other chemicals, including human carcinogens.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for inorganic mercury salts is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: August, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Mercury (Organic/Methyl)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Methyl Mercury (CAS Number 22967-92-6)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: • US EPA RSL	1×10^{-4}	1.47×10^{-3}	$BMDL_{05}$	10	Based on neurological endpoints in children in a study of 900 infant-mother pairs in an island population exposed to mercury in pilot whale. Umbilical cord blood mercury concentrations were used in the dose-response assessment. A one compartment model was used to estimate maternal daily ingested mercury dose ($BMDL_{05} = 1.47 \times 10^{-3}$ mg/kg/day) from maternal blood mercury concentration, which were estimated from umbilical cord blood mercury concentrations. Children were given neurobehavioral tests at 7 years of age.
ATSDR	3×10^{-4}	1.3×10^{-3}	NOEL	4.5	Based on neurological endpoints in a study of over 700 infant-mother pairs in an island population exposed to mercury in fish. Maternal blood mercury concentrations, which were estimated from maternal hair mercury concentrations using an empirically derived factor for the hair:blood ratio, were used in the dose-response assessment. A one compartment model was used to estimate maternal daily ingested dose (NOEL = 1.3×10^{-3} mg/kg/day) from a maternal blood mercury concentration. Children were

					given neurobehavioral tests at predetermined ages through 5.5 years of age.
HC DWQ	4.3×10^{-4}	4.3×10^{-3}	LOEL	10	Based on a blood level of methyl mercury associated with the onset of neurological symptoms. Details are limited. The value applies to all forms of mercury in water.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.
$BMDL_{05}$: 95% lower confidence limit for a 5% effect level above the background response.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The various reference doses for methyl mercury are based on epidemiological studies using total mercury concentrations in blood or hair as the dose metric and surrogate for methyl mercury exposure. The drinking water quality guideline value derived by HC DWQ is based on a blood concentration associated with neurological effects of methyl mercury in humans, and is then applied to all forms of mercury in water. Details on the derivation are limited and preclude an adequate evaluation of this value. Therefore, it is not considered further.

The US EPA and the ATSDR both based their reference doses on studies of that evaluated the neurobehavioral effects in children prenatally exposed to methyl mercury[2] from maternal consumption of pilot whales and fish, respectively. Both reference doses were sufficiently strong to be considered as the toxicity value recommended for use in the derivation of an oral non-cancer soil cleanup objective for methyl mercury.

The US EPA based their reference dose primarily on the results of an epidemiological study conducted in the Faroe Islands, which evaluated several neurological endpoints in children of mothers exposed to methyl mercury primarily through the consumption of pilot whales. Nine hundred infant-mother pairs were included in the study and at 7 years of age, children were tested on a variety of tasks designed to assess performance in specific behavioral domains. Mercury concentrations measured in umbilical cord blood were used as the dose metric for prenatal exposure in the dose-response assessment. The authors of the study state that almost all mercury in the blood was methylmercury. Benchmark dose analyses were performed on several endpoints from all three studies, and the reference dose was based on the scores of the Faroe Island children on several neurobehavioral tests, with supporting analyses from the New Zealand study and the integrative analysis of all three studies. The selected $BMDL_{05}$ (expressed as a concentration of mercury in cord blood) was converted to a $BMDL_{05}$ assuming maternal and cord blood concentrations were equal. In turn, maternal blood concentrations were converted to a daily ingested dose using a one compartment model to provide an estimate of maternal mercury intake during pregnancy (i.e., a BMDL expressed as mg mercury/kg/day). The US EPA applied an intraspecies uncertainty factor of 10 to the $BMDL_{05}$ for reduced performance on neurobehavioral tests to obtain the reference dose.

The ATSDR based their reference dose on the results of an epidemiological study conducted in the Seychelles Islands, which reported no evidence of adverse neurobehavioral or other effects in children of mothers consuming fish containing methyl mercury. The study followed over 700 infant-mother pairs, and children were evaluated with a variety of neurobehavioral tests at specific ages up to 5.5 years

[2] The investigators in the primary studies assumed most of the mercury in pilot whales and fish is methyl mercury [Grandjean et al., 1997; Davidson et al., 1998].

old. Maternal hair mercury concentration at birth was used in the dose-response assessment as the index of prenatal exposure. The study did not provide any evidence of adverse effects, thus, the ATSDR identified the mean maternal mercury hair concentration as the study NOEL. The agency converted the mean maternal mercury hair concentration to a mean maternal mercury blood concentration using a hair:blood concentration ratio of 250 for total mercury, selected from a range of values in the scientific literature. Then, the ATSDR converted the maternal mercury blood NOEL to a daily ingested dose NOEL (mg/kg/day)) using a one compartment model to provide an estimate of maternal intake during pregnancy. The agency applied a total uncertainty factor of 4.5 to the NOEL to account for human pharmacokinetic and pharmacodynamic variability (3) and a modifying factor (1.5) for domain-specific mercury-related effects seen in the Faroe study, but not yet fully assessed in the Seychelles children (i.e., the results of the full range of domain-specific neurobehavioral tests from the Seychelles were not available to ATSDR).

The US EPA derived its reference dose using methods more consistent with generally accepted risk assessment practice. The US EPA used a benchmark dose as its point of departure from a study that showed a dose response relationship between methyl mercury in cord blood and indicators of neurotoxicity. In contrast, the ATSDR derived its reference dose based on a free-standing NOEL from a study that showed no discernable effects at any exposure level, and therefore provided no dose--response information. In addition, the US EPA used a more direct measurement of prenatal methyl mercury exposure (mercury concentrations in cord blood) than did ATSDR, which used maternal mercury hair concentrations. The ATSDR derivation required using a hair:blood concentration ratio of 250. ATSDR states that precise basis of this factor is “unclear,” and that the ratio (ranging from 140 to 370 in the literature) can vary based on the location of the hair sampled and the distance of the sampled hair from the skin. Thus, in addition to using a less direct measure of prenatal exposure, use of the hair:blood ratio introduces additional uncertainty in estimating the maternal blood level and dose at the NOEL. In summary, the US EPA derivation is based on a larger study, a preferred point of departure metric (benchmark dose rather than a NOEL), and a more certain estimate of prenatal exposure. Therefore, the US EPA reference dose (1×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer soil cleanup objective for methyl mercury.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/18/2018) at https://www.atsdr.cdc.gov/mrls/index.asp.

ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological Profile for Mercury. Last accessed (11/8/2017) at https://www.atsdr.cdc.gov/toxprofiles/TP.asp?id=115&tid=24.

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality: Guideline Technical Documents. Last accessed (01/18/2018) at https://www.canada.ca/en/health-canada/services/publications/healthy-living/guidelines-canadian-drinking-water-quality-guideline-technical-document-mercury.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/18/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Mercury (Organic/Methyl)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Methyl Mercury (CAS Number 22967-92-6)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS	--	--	--	--	US EPA characterizes methyl mercury as a possible human carcinogen based on inadequate data in humans and limited evidence of carcinogenicity in animals.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for methyl mercury is not available* from any of the authoritative bodies listed in item 5 (below). The US EPA classifies methyl mercury as a possible human carcinogen based on inadequate evidence of carcinogenicity in epidemiological studies and limited evidence of carcinogenicity in animals. The US EPA states that interpretation of the available human studies is limited by poor study design and incomplete descriptions of methodology and/or results, and that interpretation of studies showing cancer effects in animals is complicated by deficiencies in study design, failure to achieve the maximum tolerated dose, or the observation of positive results only at doses exceeding the maximum tolerated dose.

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (11/8/2017) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Mercury (Organic/Methyl)
Exposure Route: Inhalation
Toxicity: Non-cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Methyl Mercury (CAS Number 22967-92-6)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	An inhalation reference concentration for methyl mercury is not available from the authoritative bodies listed in item number 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Methyl mercury is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the recommended reference dose based on systemic effects (1×10^{-4} mg/kg/day; see Oral Non-cancer Toxicity Value Documentation). Therefore, a reference concentration of 0.35 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for methyl mercury.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs

Office of Superfund Remediation and Technology Innovation
Health Effects Assessment Summary Tables
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World Health Organization

Chemical Name: Mercury (Organic/Methyl)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Methyl Mercury (CAS Number 22967-92-6)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	An inhalation unit risk for methyl mercury is not available from the authoritative bodies listed in item number 5 (below).

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An inhalation unit risk for methyl mercury is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table

5. Authoritative Bodies)

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
  Integrated Risk Information System
  Office of Drinking Water

Office of Pesticide Programs
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Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Methylene Chloride
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Methylene Chloride (CAS Number 75-09-2)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL	6×10^{-3}	0.19	$BMDL_{10}$ internal dose metric	30	Based on liver effects (histological changes) in rats exposed by drinking water for two years. An internal HED was estimated based on internal dose metrics obtained with a rat PBPK model combined with $(\text{body weight})^{0.75}$ scaling.[2]
NYS DEC (1997) Also used by: ♦ US EPA HEAST (1997) ♦ RIVM (2001) ♦ CA EPA PHG* ♦ ATSDR	0.06	6	NOEL	100	Based on the same study and liver effects as used by US EPA IRIS. Study LOEL = 53 mg/kg/day (males), 58 mg/kg/day (females).
HCPSAP	0.05	5	NOEL	100	Based on the same data as NYS DEC.
WHO (2003)	6×10^{-3}	6	NOEL	1000	Based on the same data as NYS DEC.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.
[2]Factor for dose adjustment from animal to humans is $(\text{animal body weight/human body weight})^{0.25}$.
$BMDL_{10}$: 95% lower limit on benchmark dose at 10% response level above background; HED: human equivalent dose; PBPK: physiologically-based pharmacokinetic; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the various reference doses for methylene chloride are essentially identical with respect to choice of study, species and adverse effect. US EPA IRIS obtained a point of departure by estimating an internal dose metric in rats using a PBPK model and fitting a benchmark dose model to the rat dose-response data expressed on the internal-dose scale. The rat internal-dose $BMDL_{10}$ was adjusted to account for possible differences in metabolite elimination rates between rats and humans by using $(\text{body-weight})^{0.75}$ scaling to estimate an internal-dose HED. A human PBPK model was used with Monte Carlo simulation modeling to estimate the 1st percentile human external dose associated with the internal-dose HED. The other assessments all identified a NOEL point of departure (6 or 5 mg/kg/day) from the same data, and all but WHO applied 10-fold uncertainty factors to the NOEL to account for animal-to-human and human variability. Health Canada reported the nominal dose rate of 5 mg/kg/day as the study NOEL, rather than the observed dose rate of 5.85 mg/kg/day (rounded to 6). The WHO included an extra 10-fold uncertainty factor in the derivation of a reference dose as the basis of a drinking water guideline to account for carcinogenic potential. Since cancer and non-cancer health effects are being evaluated separately in the current context, this additional uncertainty factor is considered unnecessary for deriving a reference dose. US EPA IRIS applied a total uncertainty factor of 30 to the point of departure, including factors of 3 (combined with detailed pharmacokinetic adjustments) to account for both animal-to-human and human variability. Another factor of 3 was included to account for database deficiencies, including the lack of an oral 2-generation reproductive study, limitations of the available inhalation 2-generation reproductive study and inadequate information on possible neurodevelopmental toxicity. The US EPA IRIS assessment is more consistent with generally-accepted risk assessment practices. Therefore, the US EPA IRIS reference dose (6×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for methylene chloride.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/12/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/12/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/12/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Methylene Chloride. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/12/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/12/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/12/2018) at http://www.epa.gov/iris/.

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/12/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Methylene Chloride
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Methylene Chloride (CAS Number 75-09-2)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS* Also used by: ♦ US EPA RSL	5×10^{-4}	2×10^{-3}	linear extrapolation from the $BMDL_{10}$ (internal dose)	PBPK and $BW^{¾}$ [2]	Based on increased incidence of hepatocellular adenomas and carcinomas in male mice exposed via drinking water for 2 years.
US EPA HEAST (1997) [3]	1.3×10^{-4}	7.5×10^{-3}	linearized multistage model, extra risk	body surface area[4]	Based on hepatocellular tumors and neoplastic nodules in mice in separate studies of lifetime (2 year) drinking water and inhalation exposure. The cancer potency factor was calculated as the arithmetic mean of the cancer potencies from each study.
NYS DEC (1997)	1.6×10^{-4}	6.2×10^{-3}	linearized multistage model, extra risk	$BW^{¾}$ [2]	Based on the same liver tumor data in male mice exposed by drinking water for 2 years as the US EPA IRIS derivation.
CA EPA PHG CA EPA TCDB	7.1×10^{-5} to 2.5×10^{-4}	4.0×10^{-3} to 1.4×10^{-2}	varies	varies	A range of cancer potency factors was derived based on several methods for calculating dose metrics and applied to the same liver tumor data in male mice exposed by drinking water for 2 years as the US EPA IRIS derivation.

HC DWQ*	4.8×10^{-3}	2×10^{-4} [5]	--	--	Based on increased liver tumor incidence in mice exposed by inhalation for 2 years and a PBPK-based exposure-route extrapolation to derive a drinking water unit risk. Full details of the derivation are not provided.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[3]The details for this assessment were presented in a previous version of US EPA IRIS for dichloromethane; that assessment was superseded by the current IRIS update (11/18/2011), but the details of the outdated IRIS derivation were used to provide the basis of the EPA HEAST and RSL assessments.
[4]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[5]A cancer slope factor was not reported; the value is derived from the reported risk-specific drinking water concentration of 0.169 mg/L, assuming a 70 kg adult ingests 2 L of water per day.
$BMDL_{10}$: 95% lower limit on the dose at a benchmark response of 10% above background; PBPK: physiologically-based pharmacokinetic model.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2.Recommendation and Rationale

Most of the cancer potency factors derived by authoritative bodies use the same data set showing an increased incidence of liver tumors in male mice exposed for two years via drinking water. US EPA HEAST also used data on increased incidence of liver tumors in female mice exposed via inhalation in its derivation of a cancer potency factor. The HC DWQ value is based solely on the female mouse inhalation data using a exposure-route extrapolation.

US EPA IRIS obtained an internal dose $BMDL_{10}$ in mice using a PBPK model and fitting a benchmark dose model to the mouse dose-response data expressed on the internal dose scale. The mouse internal dose $BMDL_{10}$ was adjusted to account for possible differences in metabolite elimination rates between mice and humans by using (body weight)$^{0.75}$ scaling to estimate an internal-dose human-equivalent $BMDL_{10}$. An internal-dose cancer slope factor was obtained by linear extrapolation of this human-equivalent internal-dose $BMDL_{10}$ to zero risk at zero dose. A human PBPK model was used with Monte Carlo simulation modeling to estimate the mean human internal dose associated with a unit oral external exposure (1 mg/kg/d). By dividing the internal-dose cancer slope factor by the mean internal dose per unit oral exposure, US EPA IRIS obtained a cancer potency factor expressed in external dose units (risk per (mg/kg/d)).

US EPA HEAST used the arithmetic average of the potency estimates based on drinking water and inhalation data sets to derive their value. The NYS DEC value is essentially equivalent to the US EPA HEAST value based on the drinking water study, except that the NYS DEC applied $BW^{¾}$ scaling for animal-to-human extrapolation, rather than body surface area scaling as used by US EPA HEAST. US EPA HEAST justified combining oral and inhalation tumor incidence data by noting that methylene chloride is rapidly absorbed by either route. NYS DEC chose to use data from the most relevant route of administration to derive an oral potency estimate.

CA EPA PHG derived a range of possible cancer potency values based on the male mouse drinking water data by applying dosimetry estimates based on administered dose, physiologically-based pharmacokinetic (PBPK) modeling of internal metabolites, and regression relationships between administered dose and PBPK-modeled internal metabolite dose with varying assumptions for absorbed dose. The CA EPA PHG documentation for methylene chloride in drinking water states that the derivation based on continuous PBPK modeling of internal metabolite dose is preferred as "the best measure of carcinogenic action in the mouse." The highest potency values derived by CA EPA were based on PBPK-modeled internal metabolites (0.014 – 0.016 per mg/kg/d), while the oral potency value used to derive the public health goal was the lowest value presented (0.004 per mg/kg/d). Furthermore, there is conflicting documentation on the CA EPA web site (Cal EPA TCDB) regarding their accepted oral cancer potency factor for methylene chloride.

The US EPA IRIS assessment is most consistent with generally-accepted risk assessment practices. Therefore, the US EPA IRIS cancer potency factor (2×10^{-3} per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for methylene chloride. The methylene chloride risk specific dose calculated from this toxicity value is 5×10^{-4} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/15/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

CA EPA TCDB (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Toxicity Criteria Database. Last accessed (01/15/2018) at https://oehha.ca.gov/chemicals

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/15/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Methylene Chloride. Albany, NY: Division of Water.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/15/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Methylene Chloride
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Methylene Chloride (CAS Number 75-09-2)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL	600	1.7×10^4	$BMDL_{10}$ internal dose metric	30	Based on liver effects (histological changes) in rats exposed by inhalation for two years. An internal HED was estimated based on internal dose metrics obtained with a rat PBPK model combined with $(body\ weight)^{0.75}$ scaling.[2]
US EPA HEAST (1997)	3×10^3	6.95×10^5	NOEL	100	Based on the same study and liver effects used by US EPA IRIS. Complete documentation of derivation unavailable.
ATSDR	1×10^3 **	3.1×10^4	NOEL	30	Based on the same study and liver effects used by US EPA IRIS.
CA EPA REL	400	4.9×10^4	LOEL	100	Based on formation of COHb[3] above 2% in human workers in an occupational study. Workers were exposed to average measured concentrations of 40 ppm during the workday, adjusted to 14 ppm for continuous exposure.
NYS DOH (1988)	60	5.0×10^4 to 9.5×10^4	NOEL	1000	Air guideline based on evaluation of cancer and non-cancer effects. Value is

					primarily based on liver toxicity (increased incidences of fatty changes and multinucleated hepatocytes) in rats exposed 6 hours/day, 5 days/week for up to 104 weeks. The inhaled dose at the NOEL was adjusted for children assuming a 70 to 80% relative source contribution from air.
RIVM (2001) TERA	3×10^3	2.8×10^4	LOEL	10	Based on direct adoption of a WHO (2000) ambient air guideline value as a tolerable daily concentration in air. The WHO guideline is based on a modeled estimate of 24-hour exposure associated with a 0.1% increase above background in blood COHb[2] levels allocated to methylene chloride exposure.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[3]COHb: carboxyhemoglobin

$BMDL_{10}$: 95% lower limit on benchmark dose at 10% response level above background; HED: human equivalent dose; PBPK: physiologically-based pharmacokinetic; NOEL: no observed effect level; LOEL: lowest observed effect level; ppm: parts per million; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.
**The ATSDR value is reported as 0.3 parts per million (ppm). For methylene chloride, 1 ppm = 3.47 mg/m^3.

2. Recommendation and Rationale

The reference concentrations for methylene chloride derived by authoritative bodies from the list in item 5 (below) are based either on liver toxicity in rats exposed via inhalation or blood carboxyhemoglobin (COHb) levels in workers exposed to methylene chloride in workplace air. US EPA IRIS obtained a point of departure for liver toxicity by estimating an internal dose metric in rats using a PBPK model and fitting a benchmark dose model to the rat dose-response data expressed on the internal dose scale. The rat internal dose $BMDL_{10}$ was adjusted to account for possible differences in metabolite elimination rates between rats and humans by using (body-weight)$^{0.75}$ scaling to estimate an internal-dose HED. A human PBPK model was used with Monte Carlo simulation modeling to estimate the 1st percentile human external exposure concentration associated with the internal-dose HED. US EPA HEAST, ATSDR and NYS DOH all base their values on the same chronic rat inhalation study, but appear to have identified different NOEL points of departure. The details of the

US EPA HEAST derivation are not available. ATSDR notes that liver effects including cytoplasmic vacuolization consistent with fatty changes and multinucleated hepatocytes were significantly increased in females at the exposure level the US EPA HEAST considered a NOEL (200 ppm, in Nitschke et al., 1988). The NYS DOH considered the same level a NOEL, but also noted in its documentation that it is possible the level may represent a LOEL. ATSDR adjusted their NOEL exposure level (50 ppm, in Nitschke et al., 1988) for non-continuous exposure and used a default pharmacokinetic adjustment (equal to 1) based on a ratio of rat to human blood:air partitioning coefficients greater than 1. The NYS DOH also adjusted their NOEL concentration for non-continuous exposure, and used the inhaled dose (based on default inhalation rates and body weights) at the NOEL to calculate an air concentration for children. The NYS DOH also included an adjustment assuming a 70 to 80% relative source contribution from air. In contrast, US EPA HEAST did not adjust its NOEL exposure level for intermittent exposure or pharmacokinetic differences. US EPA IRIS applied a total uncertainty factor of 30 to the point of departure, including factors of 3 (combined with detailed pharmacokinetic adjustments) to account for both animal-to-human and human variability. Another factor of 3 was included to account for database deficiencies, including limitations of the available inhalation 2-generation reproductive study and lack of information on possible neurodevelopmental and immune-system toxicity. ATSDR applied a total uncertainty factor of 30, including 10-fold to account for human variability and 3-fold (combined with a pharmacokinetic adjustment) to account for animal-to-human variability. The NYS DOH used a total uncertainty factor of 1000 because of uncertainties surrounding continuous and intermittent exposure, the possibility that 200 ppm is a LOEL, and the potential carcinogenicity of methylene chloride. Values derived with additional uncertainty factors based on carcinogenicity are not chosen in the current context, as non-cancer and cancer risks are being evaluated separately.

The CA EPA REL derivation is based on an occupational study where blood COHb was elevated above 2% in workers exposed daily to an average air level of 40 ppm (equal to 14 ppm adjusted for continuous exposure). COHb above 2% was identified as an effect level for aggravating angina in some individuals, based on previous studies. CA EPA applied a total uncertainty factor of 100, including factors of 10 each accounting for human variability and the use of a LOEL. Length of employment was not reported in the study, but the use of an uncertainty factor to account for subchronic exposure was not considered necessary, based on experimental data showing that COHb levels did not increase after 5 consecutive days of exposure.

The RIVM (2001) value was obtained by direct adoption of a WHO (2000) ambient air guideline value, which is in turn based on a minimal detectable increase in COHb with continuous methylene chloride exposure. Details of that derivation are not available from the WHO ambient air guideline documentation, but TERA reports that the value represents a human LOEL with a 10-fold total uncertainty factor, which is not consistent with currently-accepted risk assessment practice.

The US EPA IRIS and CA EPA derivations are most consistent with generally-accepted risk assessment practices. The CA EPA value is based on data from a well-conducted human study and is preferred over the value derived from an animal study. Therefore, the CA EPA REL reference concentration (400 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for methylene chloride.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/12/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/12/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

Nitschke KD, Burek JD, Bell TJ, et al. 1988. Methylene Chloride: A 2-year inhalation toxicity and oncogenicity study in rats. Fundam Appl Toxicol 11:60-67.

NYS DOH (New York State Department of Health). 1988. Letter from N. Kim, Director, Division of Environmental Health Assessment to T. Allen, Director, New York State Department of Environmental Conservation Division of Air. November 28, 1988.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/12/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/12/2018) at https://www.tera.org/iter/

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/12/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/12/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/12/2018) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

WHO (World Health Organization). 2000. Air Quality Guidelines for Europe. Last accessed (01/12/2018) at http://www.euro.who.int/en/what-we-publish/abstracts/air-quality-guidelines-for-europe.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment

Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Methylene Chloride
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Methylene Chloride (CAS Number 75-09-2)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS* Also used by: ♦ US EPA RSL	100	1×10^{-8}	linear extrapolation from the $BMDL_{10}$ (internal dose)	PBPK and $BW^{¾}$ [2]	Based on combined lung and liver tumors in male mice from a 2-year inhalation study.
CA EPA CPF	1.0	1.0×10^{-6}	Linearized multistage model	A partial pharmaco-kinetic adjustment was used to account for saturation of mixed function oxidase metabolic pathways	Based on the female mouse lung tumor data from the same study as used by US EPA IRIS.
NYS DOH (1988)	0.25	4.0×10^{-6}	Linearized multistage model	Delivered dose of carcinogenic agent was assumed to be linearly proportional to administered dose across all doses. Body surface area[3] was used to account for species differences in sensitivity	Based on combined incidence of lung and liver tumors in female mice in same study as used by US EPA IRIS.
NYS DOH (1988)	27	3.7×10^{-8}	Linearized multistage model	A PBPK model was used to compensate for	Based on combined incidence of lung and liver tumors in

				interspecies differences in metabolism by the glutathione pathway; Equal sensitivity of mice and humans assumed.	female mice in same study as used by US EPA IRIS.
HC PSAP	2.2×10^{6} reported as a TC_{05} [4]; linear equivalent risk specific concentration = 44	-- [5]	Linearized multistage model	PBPK modeling was used to account for species differences in metabolism	Based on the same female mouse lung tumor data as used by CA EPA CPF.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[4]TC_{05} = The concentration in air (expressed in mcg/m^3) associated with a 5% increase in incidence or mortality due to tumors. The TC_{05} represents a maximum likelihood estimate rather than a lower-bound estimate.
[5]The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported, but would be equal to 1×10^{-6} divided by the 10^{-6} risk-specific concentration.
$BMDL_{10}$: 95% lower limit on the dose at a benchmark response of 10% above background; PBPK: physiologically-based pharmacokinetic model.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The inhalation unit risks derived by authoritative bodies are all based on the same study, which reported an increased incidence of lung and liver tumors in male and female mice exposed to methylene chloride via inhalation for two years. US EPA IRIS derived their unit risk based on combined liver and lung tumors in male mice, while the other assessments are all based on tumor incidence (either combined or lung tumors alone) in female mice. US EPA IRIS obtained similar unit risk estimates with the female combined tumor data. The largest potency estimates are obtained using only the female lung tumor data. The HC PSAP value is reported as a TC_{05} and is a maximum likelihood estimate rather than a lower bound risk-specific air concentration. The CA EPA derivation used a modified pharmacokinetic adjustment that only accounts for species differences in saturation of oxidative metabolism. However, the weight of scientific evidence indicates that species variability in methylene chloride carcinogenicity is primarily attributable to variation in the glutathione metabolic pathway (rather than the oxidative pathway), which is not accounted for in the CA EPA analysis. The US EPA IRIS derivation and one of the NYS DOH (1988) derivations accounted for species differences in glutathione metabolism via PBPK modeling, while a second NYS DOH (1988) derivation assumed linearity between administered dose and delivered dose across all doses. When available, the use of

PBPK modeling to estimate internal doses and to account for species variability in pharmacokinetics is preferred. US EPA IRIS obtained an internal-dose $BMDL_{10}$ in mice using a PBPK model and fitting a benchmark dose model to the mouse dose-response data expressed on the internal-dose scale. The mouse internal-dose $BMDL_{10}$ was adjusted to account for possible differences in metabolite elimination rates between mice and humans by using $(body\text{-}weight)^{0.75}$ scaling to estimate an internal-dose human-equivalent $BMDL_{10}$. An internal-dose cancer slope factor was obtained by linear extrapolation of this human-equivalent internal-dose $BMDL_{10}$ to zero risk at zero dose. A human PBPK model was used with Monte Carlo simulation modeling to estimate the mean human internal dose associated with a unit exposure concentration (1 mcg/m^3). By dividing the internal-dose cancer slope factor by the mean internal dose per unit exposure concentration, US EPA IRIS obtained a cancer potency factor expressed in external exposure concentration units (risk per (mcg/m^3)). The NYS DOH (1988) PBPK-based derivation assumed that humans and mice are equally sensitive to the same delivered dose, but does not account for differences in metabolite elimination. The US EPA IRIS derivation is more consistent with generally-accepted risk assessment practices. Therefore, the US EPA IRIS unit risk (1×10^{-8} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for methylene chloride. The methylene chloride risk specific air concentration calculated from this toxicity value is 100 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: September, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Cancer Potency Factors. Last accessed (01/15/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/15/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

NYS DOH (New York State Department of Health). 1988. Letter from N. Kim, Director, Division of Environmental Health Assessment to T. Allen, Director, New York State Department of Environmental Conservation Division of Air. November 28, 1988.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment

Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Methyl Ethyl Ketone
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Methyl Ethyl Ketone (CAS Number 78-93-3)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA HEAST (1997) ♦ US EPA ODW (2004)	0.6	639	LED_{05}	1000	Based on decreased pup weight in offspring of male and female rats exposed to 2-butanol (a metabolic precursor and surrogate for methyl ethyl ketone) in a multigenerational reproductive/developmental drinking water study. Study NOEL = 594 mg/kg/day. Study LOEL = 1771 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; LED_{05}: lower limit on effective $dose_{05}$; UF: uncertainty factor.

2. Recommendation and Rationale

The US EPA reference dose is the only available reference dose for methyl ethyl ketone from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the US EPA reference dose (0.6 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for methyl ethyl ketone.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: March, 2004; no revision January, 2018

4. References for Summary Table

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response. 9200.6-303 997-1).

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2004. Office of Drinking Water, Drinking Water Standards and Health Advisories. Washington, DC. EPA 822-R-04-005.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Methyl Ethyl Ketone
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Methyl Ethyl Ketone (CAS Number 78-93-3)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1992)	--	--	--	--	Human data consist of limited and inconclusive epidemiology studies of workers. Chronic animal studies to evaluate the carcinogenicity of methyl ethyl ketone are not available

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for methyl ethyl ketone is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1992. Toxicological Profile for 2-Butanone. Update. U.S. Department of Health and Human Services, Public Health Service. Last accessed (01/18/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Methyl Ethyl Ketone
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Methyl Ethyl Ketone (CAS Number 78-93-3)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2004)	5×10^3	1.5×10^6	BMCL[2]	300	Based on developmental toxicity (skeletal variations) in mice exposed via inhalation for 7 hours/day during days 6 to 15 of gestation.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
[2]BMCL: 95% lower bound on the benchmark concentration associated with a 10% incremental increase in the observed response.
UF: uncertainty factor.

2. Recommendation and Rationale

The US EPA value is the only available reference concentration for methyl ethyl ketone from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore the US EPA reference concentration (5×10^3 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for methyl ethyl ketone.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Methyl Ethyl Ketone
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Methyl Ethyl Ketone (CAS Number 78-93-3)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Studies of humans chronically exposed to MEK are inconclusive, and MEK has not been tested for carcinogenicity in animals by the oral or inhalation routes.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for methyl ethyl ketone is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System

National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 2-Methylphenol
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for 2-Methylphenol (CAS Number 95-48-7)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA HEAST (1997)	0.05	50	NOEL	1000	Based on decreased body weight and neurotoxicity in rats exposed via gavage to 4-methylphenol in a 90-day subchronic study and 2-methylphenol a 90-day neurotoxicity study. Study LOELs = 150 mg/kg/day.
RIVM (1991; 2001); TERA	0.05 (2)	50	LOEL	1000	Based on marginal nervous system effects in rats exposed daily via to 4-methylphenol in a 90-day subchronic study and 2-methylphenol a 90-day neurotoxicity study (same studies as used by US EPA IRIS). The lowest dose was considered a LOEL.
WHO (1996)	0.17	50	NOEL	300	Based on the results of subchronic studies that establish a NOEL of 50 mg/kg/day for all methylphenol isomers.
ATSDR*	0.1 (3)	100 (4)	LOEL	1000	Based on increased incidences of bronchiole hyperplasia of the lung and follicular degeneration of the thyroid gland in female mice exposed via the diet to a mixture containing 60% 3-methylphenol and 40% 4-methylphenol in a 2-year study. A study NOEL was not identified.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.
[2]According to TERA, applies to 2-methylphenol, but RIVM identifies it as the reference dose for "methylphenols".
[3]Applies to a 60:40 mixture of 3-methylphenol and 4-methylphenol and to 2-methylphenol alone.

[4]Based on a 60:40 mixture of 3-methylphenol and 4-methylphenol

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA IRIS reference dose for 2-methylphenol is the only value from an authoritative body listed in item 5 (below) that was adequately documented and derived from studies of animals exposed only to 2-methylphenol. It was derived using methods that are consistent with generally accepted risk assessment practices, including the use of a total uncertainty factor of 1000 to compensate for animal to human extrapolation (10), use of a subchronic study (10), and human variation (10). However, a factor of 10 for the use of a subchronic study may be larger than necessary given that results of 4-week and 13-week studies of methylphenol isomers provided little evidence to suggest a significant increase in toxicity with longer exposures (NTP, 1992). The RIVM reference dose is the same as the US EPA value. According to TERA, it is based on the same studies used by US EPA in their derivation of a reference dose for 2-methylphenol. However, RIVM identified 50 mg/kg/day as a marginal effect level, and applied a total uncertainty factor of 1000. According to TERA, a 1000-fold uncertainty factor compensates for animal to human extrapolation (10), use of a marginal effect level (10), and human variation (10). The WHO derived a reference dose by applying an uncertainty factor of 300 (for human variation (10), use of a subchronic study (10) and animal to human extrapolation (3)) to a NOEL of 50 mg/kg/day for all methyl phenol isomers based on the results of several subchronic studies. The use of an interspecies uncertainty factor of 3 rather than 10 based on “rapid and complete metabolism” is not adequately justified in their documentation. The ATSDR reference dose for a methylphenol mixture is based on a LOEL derived from a 2-year study in mice fed a 60:40 mixture of 3-methylphenol and 4-methylphenol. The ATSDR reference dose was derived using methods that are consistent with generally accepted risk assessment practices, including the use of a total uncertainty factor of 1000 to compensate for animal to human extrapolation (10), use of a LOEL (10), and human variation (10). The use of an uncertainty factor of 10 for the use of a LOEL appears appropriate given that the incidence of bronchiole hyperplasia of the lung at the LOEL was 42/50 compared to a control rate of 0/50.

The study used by ATSDR was peer-reviewed, conducted following good laboratory practices by the National Toxicology Program, and represents state-of-the-art science. It was published after US EPA/RIVM derived their reference doses for 2-methylphenol. The original reports of the studies used by US EPA/RIVM could not be located on the internet or in local libraries, but based on the limited description of the study in the US EPA derivation, it is very unlikely that the 1987 studies used by US EPA/RIVM were better than the NTP (2008) study in design, methodology, and reporting. A study based on 2 years of exposure would typically be preferred over a 90-day study as the basis of a chronic reference dose, other factors being similar. The US EPA/RIVM derivations are based on a gavage study in rats, and it is possible that the pharmacokinetics and pharmacodynamics of methylphenols differ between dietary and gavage doses (ATSDR, 2008). This raises concerns given that dietary doses are more likely to mimic human chronic oral exposures at Brownfield sites than gavage doses, and other study quality factors being similar, would be preferable to gavage doses for use in deriving soil cleanup objectives for 2-methylphenol.

Although the three isomers only differ in the location of a methyl group on the parent phenol molecule, concerns could be raised about the use of a reference dose for a methylphenol mixture as the basis for a reference dose for 3-methylphenol. However, experimental evidence of animal studies on the relative toxicity of the three methylphenol isomers (2-, 3-, and 4-methylphenol) show a similar spectrum of

toxicities and occasional differences in potencies for specific types of toxicity (ATSDR, 2008; NTP, 1992; WHO, 1996). Based on a series of 4-week and 13-week dietary studies, for example, the NTP (1992) concluded that 2-methylphenol may be somewhat less toxic than 3-methylphenol and 4-methylphenol, and that 4-methylphenol or a 3-/4-methylphenol mixture appears to be more irritating, resulting in proliferative lesions at contact areas, than 2-methylphenol or 3-methylphenol. According to TERA, the reference doses for 2-, 3-, and 4-methylphenol are all the same, which would indicate a similar degree of potency. ATSDR (2008) concluded that the intermediate and chronic reference doses (i.e., minimal risk levels) based on the 60:40 mixture of 3- and 4-methylphenol also can be adopted for 2-, 3-, and 4-methylphenol individually. Therefore, the ATSDR reference dose (0.1 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 2-methylphenol.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological Profiles. Last accessed (01/17/2018) at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

NTP (National Toxicology Program). 1992. NTP Report on the Toxicity Studies of Cresols (CAS NOS. 95-48-7, 108-39-4, 106-44-5) in F344/N Rat and B6C3F1 Mice (Feed Studies). NTP TOX 9. Last accessed (01/17/2018) at https://ntp.niehs.nih.gov/ntp/htdocs/st_rpts/tox009.pdf?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=tox009

NTP (National Toxicology Program). 2008. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Cresols (CAS NO. 1319-77-3) in Male F344/N Rats and Female B6C3F1 Mice (Feed Studies). NTP TR 550. NIH Publication No. 08-5891. Last accessed (01/17/2018) at http://ntp.niehs.nih.gov/?objectid=9B58ADF7-F1F6-975E-78A23152B1596409.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 1991. Voorstel voor de humaan-toxicologische onderbouwing van C-(toetsings)warden. [Proposal for the Toxicological Basis for the Determination of C-values]. RIVM Rapport 725201005. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/725201005.html

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/17/2018) at https://www.tera.org/iter/

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/17/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 1996. IPCS International Programme on Chemical Safety. Health and Safety Guide No. 100. Cresols Health and Safety Guide. Last accessed (01/17/2018) at http://www.inchem.org/documents/hsg/hsg/hsg100.htm.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 2-Methylphenol
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 2-Methylphenol (CAS Number 95-48-7)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Based on limited human data and dermal studies in animals, the data were considered inadequate derive a cancer potency value.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for 2-methylphenol is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 2-Methylphenol
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for 2-Methylphenol (CAS Number 95-48-7)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
CA EPA REL*	600 [(2)] (0.17 mg/kg/day)	1.75×10^5 (50 mg/kg/day)	NOEL	300	The reference concentration was estimated from a reference dose [based on decreased body weights and neurotoxicity (tremors, salivation, lacrimation) in rats exposed daily via gavage to 2-methylphenol in a 90-day study] using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. Study LOEL = 150 mg/kg/day.
RIVM (1991; 2001)*; TERA	170 [(3)] (0.05 mg/kg/day)	1.75×10^5 (50 mg/kg/day)	LOEL	1000	The reference concentration was estimated from a reference dose [based on decreased nervous system effects in rats exposed daily via gavage to 3-methylphenol in 90-day studies] using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. Study LOELs = 150 mg/kg/day.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.
[2]Applies to any mixture of 2-, 3-, and 4-methyphenol.
[3]According to TERA, applies to 3-methylphenol, but RIVM identifies it as the reference concentration for "methylphenols".
*****Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.
NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

2. Recommendation and Rationale

2-Methyphenol is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. A reference concentration for 2-methyphenol based on inhalation exposures is not available from the authoritative bodies listed in item number 5 (below). The CA EPA derived a reference concentration (600 mcg/m^3) for methylphenol mixtures from a reference dose for 2-methylphenol (0.17 mg/kg/day) using a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day. The

RIVM derived a reference concentration (170 mcg/m^3) for 2-methylphenol from a reference dose for methylphenols (0.05 mg/kg/day) using the same default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation as CA EPA. However, the recommended oral reference dose for 2-methylphenol is 0.1 mg/kg/day (see Oral Non-Cancer Toxicity Value Documentation for 2-methylphenol). Given that at least two authoritative bodies derived a reference concentration using exposure route extrapolation, a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the recommended reference dose. Therefore, a reference concentration of 350 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 2-methylphenol.

3. **Review Dates**
4.

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

5. References for Summary Table and Recommendation and Rationale

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/12/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 1991. Voorstel voor de humaan-toxicologische onderbouwing van C-(toetsings)warden. [Proposal for the Toxicological Basis for the Determination of C-values]. RIVM Rapport 725201005. Last accessed (01/12/2018) at http://www.rivm.nl/bibliotheek/rapporten/725201005.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/12/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/12/2018) at www.tera.org/iter/

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 2-Methylphenol
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 2-Methylphenol (CAS Number 95-48-7)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for 2-methylphenol is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 3-Methylphenol
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for 3-Methylphenol (CAS Number 108-39-4)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA HEAST (1997)	0.05	50	NOEL	1000	Based on decreased body weight and neurotoxicity in rats exposed via gavage to 3-methylphenol in a 90-day subchronic study and a 90-day neurotoxicity study. Study LOELs = 150 mg/kg/day.
RIVM (1991; 2001); TERA	0.05 (2)	50	LOEL	1000	Based on marginal nervous system effects in rats exposed via gavage to 3-methylphenol in a 90-day subchronic study and a 90-day neurotoxicity study (same studies as used by US EPA IRIS. A study NOEL was not identified.
WHO (1996)	0.17	50	NOEL	300	Based on the results of subchronic studies that establish a NOEL of 50 mg/kg/day for all methylphenol isomers.
ATSDR*	0.1 (3)	100 (4)	LOEL	1000	Based on increased incidences of bronchiole hyperplasia of the lung and follicular degeneration of the thyroid gland in female mice exposed via the diet to a mixture containing 60% 3-methylphenol and 40% 4-methylphenol in a 2-year study. A study NOEL was not identified.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.
[2]According to TERA, applies to 3-methylphenol, but RIVM identifies it as the reference dose for "methylphenols".
[3]Applies to a 60:40 mixture of 3-methylphenol and 4-methylphenol and to 3-methylphenol alone.
[4]Based on a 60:40 mixture of 3-methylphenol and 4-methylphenol

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA IRIS reference dose for 3-methylphenol is the only value from an authoritative body listed in item 5 (below) that was adequately documented and derived from studies of animals exposed only to 3-methylphenol. It was derived using methods that are consistent with generally accepted risk assessment practices, including the use of a total uncertainty factor of 1000 to compensate for animal to human extrapolation (10), use of a subchronic study (10), and human variation (10). However, a factor of 10 for the use of a subchronic study may be larger than necessary given that results of 4-week and 13-week studies of methylphenol isomers provided little evidence to suggest a significant increase in toxicity with longer exposures (NTP, 1992). The RIVM reference dose is the same as the US EPA value. According to TERA, it is based on the same studies used by US EPA in their derivation of a reference dose for 3-methylphenol. However, RIVM identified 50 mg/kg/day as a marginal effect level, and applied a total uncertainty factor of 1000. According to TERA, a 1000-fold uncertainty factor compensates for animal to human extrapolation (10), use of a marginal effect level (10), and human variation (10). The WHO derived a reference dose by applying an uncertainty factor of 300 (for human variation (10), use of a subchronic study (10) and animal to human extrapolation (3)) to a NOEL of 50 mg/kg/day for all methyl phenol isomers based on the results of several subchronic studies. The use of an interspecies uncertainty factor of 3 rather than 10 based on "rapid and complete metabolism" is not adequately justified in their documentation. The ATSDR reference dose for a methylphenol mixture is based on a LOEL derived from a 2-year study in mice fed a 60:40 mixture of 3-methylphenol and 4-methylphenol. The ATSDR reference dose was derived using methods that are consistent with generally accepted risk assessment practices, including the use of a total uncertainty factor of 1000 to compensate for animal to human extrapolation (10), use of a LOEL (10), and human variation (10). The use of an uncertainty factor of 10 for the use of a LOEL appears appropriate given that the incidence of bronchiole hyperplasia of the lung at the LOEL was 42/50 compared to a control rate of 0/50.

The study used by ATSDR was peer-reviewed, conducted following good laboratory practices by the National Toxicology Program, and represents state-of-the-art science. It was published after US EPA/RIVM derived their reference doses for 3-methylphenol. The original reports of the studies used by US EPA/RIVM could not be located on the internet or in local libraries, but based on the limited description of the study in the US EPA derivation, it is very unlikely that the 1987 studies used by US EPA/RIVM were better than the NTP (2008) study in design, methodology, and reporting. A study based on 2 years of exposure would typically be preferred over a 90-day study as the basis of a chronic reference dose, other factors being similar. The US EPA/RIVM derivations are based on a gavage study in rats, and it is possible that the pharmacokinetics and pharmacodynamics of methylphenols differ between dietary and gavage doses (ATSDR, 2008). This raises concerns given that dietary doses are more likely to mimic human chronic oral exposures at Brownfield sites than gavage doses, and other study quality factors being similar, would be preferable to gavage doses for use in deriving soil cleanup objectives for 3-methylphenol.

Although the three isomers only differ in the location of a methyl group on the parent phenol molecule, concerns could be raised about the use of a reference dose for a methylphenol mixture as the basis for a reference dose for 3-methylphenol. However, experimental evidence of animal studies on the relative toxicity of the three methylphenol isomers (2-, 3-, and 4-methylphenol) show a similar spectrum of toxicities and occasional differences in potencies for specific types of toxicity (ATSDR, 2008; NTP,

1992; WHO, 1996). Based on a series of 4-week and 13-week dietary studies, for example, the NTP (1992) concluded that 2-methylphenol may be somewhat less toxic than 3-methylphenol and 4-methylphenol, and that 4-methylphenol or a 3-/4-methylphenol mixture appears to be more irritating, resulting in proliferative lesions at contact areas, than 2-methylphenol or 3-methylphenol. According to TERA, the reference doses for 2-, 3-, and 4-methylphenol are all the same, which would indicate a similar degree of potency. ATSDR (2008) concluded that the intermediate and chronic reference doses (i.e., minimal risk levels) based on the 60:40 mixture of 3- and 4-methylphenol also can be adopted for 2-, 3-, and 4-methylphenol individually. Therefore, the ATSDR reference dose (0.1 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 3-methylphenol.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological Profiles. Last accessed (01/17/2018) at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

ATSDR (Agency for Toxic Substances and Disease Registry). 2008. Toxicological Profile for Cresols. Last accessed (01/17/2018) at http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=946&tid=196.

NTP (National Toxicology Program). 1992. NTP Report on the Toxicity Studies of Cresols (CAS NOS. 95-48-7, 108-39-4, 106-44-5) in F344/N Rat and B6C3F1 Mice (Feed Studies). NTP TOX 9. Last accessed (01/17/2018) at https://ntp.niehs.nih.gov/ntp/htdocs/st_rpts/tox009.pdf?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=tox009

NTP (National Toxicology Program). 2008. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Cresols (CAS NO. 1319-77-3) in Male F344/N Rats and Female B6C3F1 Mice (Feed Studies). NTP TR 550. NIH Publication No. 08-5891. Last accessed (01/17/2018) at http://ntp.niehs.nih.gov/?objectid=9B58ADF7-F1F6-975E-78A23152B1596409.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 1991. Voorstel voor de humaan-toxicologische onderbouwing van C-(toetsings)warden. [Proposal for the Toxicological Basis for the Determination of C-values]. RIVM Rapport 725201005. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/725201005.html

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/17/2018) at https://www.tera.org/iter/

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/17/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 1996. IPCS International Programme on Chemical Safety. Health and Safety Guide No. 100. Cresols Health and Safety Guide. Last accessed (01/17/2018) at http://www.inchem.org/documents/hsg/hsg/hsg100.htm.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 3-Methylphenol
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 3-Methylphenol (CAS Number 108-39-4)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Based on limited human data and dermal studies in animals, the data were considered inadequate derive a cancer potency value.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for 3-methylphenol is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 3-Methylphenol
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for 3-Methylphenol (CAS Number 108-39-4)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
CA EPA REL*	600 [(2)] (0.17 mg/kg/day)	1.75×10^5 (50 mg/kg/day)	NOEL	300	The reference concentration was estimated from a reference dose [based on decreased body weights and neurotoxicity (tremors, salivation, lacrimation) in rats exposed daily via gavage to 2-methylphenol in a 90-day study] using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. Study LOEL = 150 mg/kg/day.
RIVM (1991; 2001)*; TERA	170 [(3)] (0.05 mg/kg/day)	1.75×10^5 (50 mg/kg/day)	LOEL	1000	The reference concentration was estimated from a reference dose [based on decreased nervous system effects in rats exposed daily via gavage to 3-methylphenol in 90-day studies] using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. Study LOELs = 150 mg/kg/day.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.
[2]Applies to any mixture of 2-, 3-, and 4-methyphenol.
[3]According to TERA, applies to 3-methylphenol, but RIVM identifies it as the reference concentration for "methylphenols".

*****Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

2. Recommendation and Rationale

3-Methyphenol is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. A reference concentration for 3-methyphenol based on inhalation exposures is not available from the authoritative bodies listed in item number 5 (below). The CA EPA derived a reference concentration (600 mcg/m^3) for methylphenol mixtures from a reference dose for 2-methylphenol (0.17 mg/kg/day) using a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day. The

RIVM derived a reference concentration (170 mcg/m^3) for 3-methylphenol from a reference dose for methylphenols (0.05 mg/kg/day) using the same default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation as CA EPA. However, the recommended oral reference dose for 3-methylphenol is 0.1 mg/kg/day (see Oral Non-Cancer Toxicity Value Documentation for 3-methylphenol). Given that at least two authoritative bodies derived a reference concentration using exposure route extrapolation, a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the recommended reference dose. Therefore, a reference concentration of 350 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 3-methylphenol.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/12/2018) at https://oehha.ca.gov/chemicals

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 1991. Voorstel voor de humaan-toxicologische onderbouwing van C-(toetsings)warden. [Proposal for the Toxicological Basis for the Determination of C-values]. RIVM Rapport 725201005. Last accessed (01/12/2018) at http://www.rivm.nl/bibliotheek/rapporten/725201005.html

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/12/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/12/2018) at https://www.tera.org/iter/

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 3-Methylphenol
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 3-Methylphenol (CAS Number 108-39-4)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for 3-methylphenol is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 4-Methylphenol
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for 4-Methylphenol (CAS Number 106-44-5)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA HEAST (1997) Also used by: ♦ US EPA RSL	5×10^{-3}	5	NOEL	1000	Based on central nervous system toxicity (hypoactivity), respiratory distress, and maternal death in rabbits treated with 4-methylphenol on gestation days 6-18 by gavage. Study LOEL = 50 mg/kg/day.
RIVM (1991; 2001); TERA	0.05 (2)	50	LOEL	1000	Based on marginal nervous system effects in rats exposed daily via gavage to 4-methylphenol in a 90-day subchronic study or a 90-day neurotoxicity study. A study NOEL was not identified.
WHO (1996)	0.17	50	NOEL	300	Based on the results of subchronic studies that establish a NOEL of 50 mg/kg/day for all methylphenol isomers.
ATSDR*	0.1 (3)	100 (4)	LOEL	1000	Based on increased incidences of bronchiole hyperplasia of the lung and follicular degeneration of the thyroid gland in female mice exposed via the diet to a mixture containing 60% 3-methylphenol and 40% 4-methylphenol in a 2-year study. A study NOEL was not identified.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.
[2]According to TERA, applies to 3-methylphenol, but RIVM identifies it as the reference dose for "methylphenols".
[3]Applies to a 60:40 mixture of 3-methylphenol and 4-methylphenol and to 4-methylphenol alone.
[4]Based on a 60:40 mixture of 3-methylphenol and 4-methylphenol

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA HEAST derivation of the reference dose for 4-methylphenol is poorly documented and only provides the study citation, study NOEL, the type of observed effects, and the magnitude of the uncertainty factor. Moreover, deaths of the dosed female rabbits was one of the endpoints, and the use of mortality in the derivation of a reference dose is inconsistent with generally accepted risk assessment practice. The RIVM reference dose is based on marginal nervous system effects observed in rats in a 90-day gavage study. The supporting documentation for the derivation is limited. According to TERA, RIVM identified 50 mg/kg/day as a marginal effect level, and applied a total uncertainty factor of 1000. to compensate for animal to human extrapolation (10), use of a marginal effect level (10), and human variation (10). The WHO derived a reference dose by applying an uncertainty factor of 300 (for human variation (10), use of a subchronic study (10) and animal to human extrapolation (3)) to a NOEL of 50 mg/kg/day for all methyl phenol isomers based on the results of several subchronic studies. The use of an interspecies uncertainty factor of 3 rather than 10 based on "rapid and complete metabolism" is not adequately justified in their documentation. The ATSDR reference dose for a methylphenol mixture is based on a LOEL derived from a 2-year study in mice fed a 60:40 mixture of 3-methylphenol and 4-methylphenol. The ATSDR reference dose was derived using methods that are consistent with generally accepted risk assessment practices, including the use of a total uncertainty factor of 1000 to compensate for animal to human extrapolation (10), use of a LOEL (10), and human variation (10). The use of an uncertainty factor of 10 for the use of a LOEL appears appropriate given that the incidence of bronchiole hyperplasia of the lung at the LOEL was 42/50 compared to a control rate of 0/50.

The study used by ATSDR was peer-reviewed, conducted following good laboratory practices by the National Toxicology Program, and represents state-of-the-art science. It was published after US EPA/RIVM derived their reference doses for 4-methylphenol. The original reports of the studies used by RIVM could not be located on the internet or in local libraries, but based on the limited description of the similar studies in the US EPA derivations of reference doses for 2-methylphenol and 3-methylphenol, it is very unlikely that the studies used by RIVM were better than the NTP (2008) study in design, methodology, and reporting. A study based on 2 years of exposure would typically be preferred over a 90-day study as the basis of a chronic reference dose, other factors being similar. The RIVM derivations are based on a gavage study in rats, and it is possible that the pharmacokinetics and pharmacodynamics of methylphenols differ between dietary and gavage doses (ATSDR, 2008). This raises concerns given that dietary doses are more likely to mimic human chronic oral exposures at Brownfield sites than gavage doses, and other study quality factors being similar, would be preferable to gavage doses for use in deriving soil cleanup objectives for 4-methylphenol.

Although the three isomers only differ in the location of a methyl group on the parent phenol molecule, concerns could be raised about the use of a reference dose for a methylphenol mixture as the basis for a reference dose for 4-methylphenol. However, experimental evidence of animal studies on the relative toxicity of the three methylphenol isomers (2-, 3-, and 4-methylphenol) show a similar spectrum of toxicities and occasional differences in potencies for specific types of toxicity (ATSDR, 2008; NTP, 1992; WHO, 1996). Based on a series of 4-week and 13-week dietary studies, for example, the NTP (1992) concluded that 2-methylphenol may be somewhat less toxic than 3-methylphenol and 4-methylphenol, and that 4-methylphenol or a 3-/4-methylphenol mixture appears to be more irritating, resulting in proliferative lesions at contact areas, than 2-methylphenol or 3-methylphenol. According to TERA, the reference doses for 2-, 3-, and 4-methylphenol are all the same, which would indicate a similar degree of potency. ATSDR (2008) concluded that the intermediate and chronic reference doses

(i.e., minimal risk levels) based on the 60:40 mixture of 3- and 4-methylphenol also can be adopted for 2-, 3-, and 4-methylphenol individually. Therefore, the ATSDR reference dose (0.1 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 4-methylphenol.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological Profiles. Last accessed (01/17/2018) at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

NTP (National Toxicology Program). 1992. NTP Report on the Toxicity Studies of Cresols (CAS NOS. 95-48-7, 108-39-4, 106-44-5) in F344/N Rat and B6C3F1 Mice (Feed Studies). NTP TOX 9. Last accessed (01/17/2018) at https://ntp.niehs.nih.gov/ntp/htdocs/st_rpts/tox009.pdf?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=tox009

NTP (National Toxicology Program). 2008. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Cresols (CAS NO. 1319-77-3) in Male F344/N Rats and Female B6C3F1 Mice (Feed Studies). NTP TR 550. NIH Publication No. 08-5891. Last accessed (01/17/2018) at http://ntp.niehs.nih.gov/?objectid=9B58ADF7-F1F6-975E-78A23152B1596409.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 1991. Voorstel voor de humaan-toxicologische onderbouwing van C-(toetsings)warden. [Proposal for the Toxicological Basis for the Determination of C-values]. RIVM Rapport 725201005. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/725201005.html

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/17/2018) at https://www.tera.org/iter/

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/17/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 1996. IPCS International Programme on Chemical Safety. Health and Safety Guide No. 100. Cresols Health and Safety Guide. Last accessed (01/17/2018) at http://www.inchem.org/documents/hsg/hsg/hsg100.htm.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 4-Methylphenol
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 4-Methylphenol (CAS Number 106-44-5)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Based on limited human data, and dermal studies in animals, the data were considered inadequate to derive a cancer potency value.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for 4-methylphenol is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 4-Methylphenol
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for 4-Methylphenol (CAS Number 106-44-5)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
CA EPA REL*	600 [(2)] (0.17 mg/kg/day)	1.75×10^5 (50 mg/kg/day)	NOEL	300	The reference concentration was estimated from a reference dose [based on decreased body weights and neurotoxicity (tremors, salivation, lacrimation) in rats exposed daily via gavage to 2-methylphenol in a 90-day study] using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. Study LOEL = 150 mg/kg/day.
RIVM (1991; 2001)*; TERA	170 [(3)] (0.05 mg/kg/day)	1.75×10^5 (50 mg/kg/day)	LOEL	1000	The reference concentration was estimated from a reference dose [based on decreased nervous system effects in rats exposed daily via gavage to 3-methylphenol in 90-day studies] using $route_{Oral}$-to-$route_{Inhalation}$ extrapolation. Study LOELs = 150 mg/kg/day.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.
[2]Applies to any mixture of 2-, 3-, and 4-methyphenol.
[3]According to TERA, applies to 3-methylphenol, but RIVM identifies it as the reference concentration for "methylphenols".

*****Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

2. Recommendation and Rationale

4-Methyphenol is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. A reference concentration for 4-methyphenol based on inhalation exposures is not available from the authoritative bodies listed in item number 5 (below). The CA EPA derived a reference concentration (600 mcg/m^3) for methylphenol mixtures from a reference dose for 2-methyl phenol (0.17 mg/kg/day) using a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day. The

RIVM derived a reference concentration (170 mcg/m^3) for 4-methylphenol from a reference dose for methylphenols (0.05 mg/kg/day) using the same default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation as CA EPA. However, the recommended oral reference dose for 4-methylphenol is 0.1 mg/kg/day (see Oral Non-Cancer Toxicity Value Documentation for 4-methylphenol). Given that at least two authoritative bodies derived a reference concentration using exposure route extrapolation, a default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the recommended reference dose. Therefore, a reference concentration of 350 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 4-methylphenol.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/12/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 1991. Voorstel voor de humaan-toxicologische onderbouwing van C-(toetsings)warden. [Proposal for the Toxicological Basis for the Determination of C-values]. RIVM Rapport 725201005. Last accessed (01/12/2018) at http://www.rivm.nl/bibliotheek/rapporten/725201005.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/12/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/12/2018) at https://www.tera.org/iter/

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 4-Methylphenol
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 4-Methylphenol (CAS Number 106-44-5)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for 4-methylphenol is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Methyl *tert*-butyl ether
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Methyl *tert*-butyl ether (CAS Number 1634-04-4)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
NYS DOH (2000), NYS DEC (2001)	0.033	100	LOEL	3000	Based on diarrhea and changes in clinical blood chemistry parameters observed in rats exposed via corn oil gavage for 90 consecutive days to 100 mg/kg/day. Other doses were 300, 900, or 1200 mg/kg/day.
HC PSAP	0.01	100	NOEL	10,000	Based on increased relative kidney weight and changes in clinical blood chemistry parameters observed in rats in the same study as used by NYS DEC. Health Canada interpreted the study results differently from NYS DEC and identified the study LOEL as 300 mg/kg/day.
CA EPA PHG	0.01	100	NOEL	10,000	Based on increased relative kidney weight observed in rats in the same study as used by NYS DEC. CA EPA interpreted the study results differently from NYS DEC and identified the study LOEL as 300 mg/kg/day.
RIVM (2009)*	0.3	300	NOEL	1000	Based on liver and kidney toxicity observed in rats in the same study as used by NYS DEC. RIVM interpreted the study results differently from NYS DEC and identified the study LOEL as 900 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the four reference doses for methyl *tert*-butyl ether are essentially identical with respect to choice of study and species, but differed regarding the nature (NOEL or LOEL) and dose (100 or 300 mg/kg/day) of the point of departure. The NYS DOH/DEC considered the effects observed at the lowest dose to be exposure-related and judged the lowest dose (100 mg/kg/day) to be a minimal LOEL. However, HC and CA EPA identified the lowest dose in the study (100 mg/kg/day) as a NOEL, whereas RIVM identified the second lowest dose in the study (300 mg/kg/day) as a NOEL. All derivations applied a 1000-fold total uncertainty factor to account for animal-to-human extrapolation (10), the use of a subchronic study (10), and human variation (10). HC and CA EPA included an additional 10-fold uncertainty factor to account for lack of data on carcinogenicity and minimal effects at the NOEL (HC only). An additional uncertainty factor to account for a lack of carcinogenicity data is not applicable in the current context because cancer and non-cancer effects are assessed separately in the Brownfield Cleanup Program. NYS DOH/DEC provided a scientifically defensible rationale for identifying 100 mg/kg/day as a LOEL (which is lower than the LOEL identified by RIVM for liver and kidney toxicity), and used an additional 3-fold uncertainty factor to account for the use of a minimal LOEL. Therefore, the NYS DOH/DEC reference dose (0.033 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for methyl *tert*-butyl ether.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: August, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/17/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Albany, NY: Division of Water.

NYS DOH (New York State Department of Health). 2000. Toxicological Review and Criteria for Evaluation of Exposure to Methyl-*tert*-Butyl Ether. External Draft. Troy, NY: Bureau of Toxic Substance Assessment.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2009. Re-Evaluation of Some Human Toxicological Maximum Permissible Risk Levels Earlier Evaluated in the Period 1991-2001. RIVM Rapport 711701092. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701092html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry

California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Methyl *tert*-butyl ether
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Methyl *tert*-butyl ether (CAS Number 1634-04-4)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA PHG	5.6×10^{-4}	1.8×10^{-3}	multistage polynomial model, linear extrapolation to LED_{10} [2]	internal dose metrics in animals were estimated using PBPK models; then $BW^{3/4}$ [3]	Based on the geometric mean of cancer potency factor estimates obtained for the combined male rat kidney adenomas and carcinomas in a 2-year inhalation study, male rat Leydig cell tumors and combined leukemias and lymphomas in female rats in a 2-year gavage study. The estimate from the inhalation study was converted to an oral intake using a PBPK model.
NYS DOH (2000), NYS DEC (2001)	2.9×10^{-4}	3.4×10^{-3}	linearized multistage model	$BW^{3/4}$ [3]	Based on increased incidence of testicular tumors in male rats exposed by gavage in a 2-year study.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.
[2]LED_{10}: 95% lower confidence limit on the daily dose associated with a 10% increase (above background) in the incidence of tumors or cancers.
[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$.

PBPK: physiologically based pharmacokinetic.

2.Recommendation and Rationale

The CA EPA derivation of its cancer potency factor for methyl *tert*-butyl ether uses data from three studies. Two of the studies, one showing lymphomas/leukemia in female rats exposed by gavage (4 days/week) and another showing kidney tumors in male rats exposed by inhalation (6 hours/day, 5 days/week), had substantial early mortality indicating that the maximum tolerated dose may have been exceeded. This reduces confidence in the use of the studies as the partial basis of the oral cancer-based soil cleanup objective for methyl *tert*-butyl ether. There is also some uncertainty introduced by

deriving an oral cancer potency factor from an inhalation study. The basis of the NYS DOH/DEC cancer potency factor for methyl *tert*-butyl ether is an increased incidence of testicular tumors in male rats exposed via gavage 4 days/week in a 2-year study. The NYS DOH cancer potency factor is based on a study, sex, and species that did not show early mortality during the study, and is supported by other animal carcinogenicity data from oral and inhalation exposure. Moreover, it is derived for the more sensitive carcinogenic endpoint (testicular tumors). Therefore, the NYS DOH/DEC cancer potency factor (3.4×10^{-3} per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for methyl *tert*-butyl ether. The methyl *tert*-butyl ether risk specific dose calculated from this toxicity value is 2.9×10^{-4} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: March, 2005, no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Albany, NY: Division of Water.

NYS DOH (New York State Department of Health). 2000. Toxicological Review and Criteria for Evaluation of Exposure to Methyl-*tert*-Butyl Ether. External Draft. Center for Environmental Health. Troy, NY: Bureau of Toxic Substance Assessment.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Methyl *tert*-butyl ether (MTBE)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Methyl *tert*-butyl ether (MTBE) (CAS Number 1634-04-4)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL	3000	259,000	$NOEL_{HEC}$[2]	100	Based on increased absolute and relative liver and kidney weights and increased severity of spontaneous renal lesions (females), increased prostration (females), and swollen periocular tissue (males and females) exposed via inhalation for 6 hours/day, 5 days/week in a 24-month study in rats. Study $NOEL_{EXP}$ = 403 ppm (1.45×10^6 mcg/m^3); study $NOEL_{ADJ}$ = 259,000 mcg/m^3.
ATSDR	2500*	256,000	$NOEL_{HEC}$[2]	100	Based on increased incidence and severity of chronic progressive nephropathy observed in same study used by US EPA IRIS. Study $NOEL_{EXP}$ = 400 ppm (1.44×10^6 mcg/m^3); study $NOEL_{ADJ}$ = 71 ppm (256,000 mcg/m^3).
CA EPA REL	8000	260,000	$NOEL_{HEC}$[2]	30	Based on same study used by US EPA IRIS. Study $NOEL_{EXP}$ = 403 ppm (1.45×10^6 mcg/m^3); study $NOEL_{ADJ}$ = 72 ppm (260,000 mcg/m^3).
RIVM (2009)**	2600	260,000	$NOEL_{ADJ}$[3]	100	Based on same study used by US EPA IRIS. Study $NOEL_{EXP}$ = 1.44×10^6 mcg/m^3; study $NOEL_{ADJ}$ = 260,000 mcg/m^3.
HC	37	370,000	$NOEL_{HEC}$[4]	10,000	Based on neurobehavioral effects in male and female rats exposed via inhalation for 6 hours/day, 5 days/weeks in a 90-day inhalation study. Study $NOEL_{EXP}$ = 2.9×10^6 mcg/m^3; study $NOEL_{ADJ}$ = 5.2×10^5 mg/m^3.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.
[2]$NOEL_{HEC}$: human equivalent concentration (HEC) NOEL where $NOEL_{HEC} = NOEL_{ADJ}$ x 1 (default ratio for the ratio of the animal blood:air partitioning coefficients to the human blood:air partitioning coefficients for methyl *tert*-butyl ether).
[3]$NOEL_{ADJ}$: $NOEL_{EXP}$ adjusted for continuous exposure (i.e., $NOEL_{EXP}$ x 6 hours/24 hours x 5 days/7 day)
[4]The $NOEL_{ADJ}$ was also adjusted by the ratio of inhalation volume/body weight of rats [(0.11 m^3/day)/0.35 kg] to humans aged 5 to 11 years [(12 m^3/27 kg], or 5.2 x 10^5 mcg/m^3 x (0.3142/0.4444) = 3.7 x 10^5 mcg/m^3.

NOEL: no-observed-effect level; $NOEL_{EXP}$: experimental NOEL; UF: uncertainty factor.

*The ATSDR value is reported as 0.7 parts per million (ppm). For MTBE, 1 ppm = 3.61 mg/m^3.

**Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The reference concentrations for methyl *tert*-butyl ether derived by authoritative bodies from the list in item 5 (below) are based on effects on the liver, kidneys, central nervous system and periocular tissue observed in rats exposed via inhalation. The US EPA, ATSDR, CA EPA, and RIVM derivations are based on a 24-month chronic inhalation study, while the HC value was derived based on a 90-day subchronic study because the chronic study was not available at the time of the derivation. The use of a longer study as the basis of reference dose is consistent with generally accepted risk assessment practices. The US EPA, ATSDR, CA EPA, and RIVM derivations all identify the same NOEL point of departure (albeit with minor differences in dose estimates). However, the US EPA, ATSDR, and CA EPA converted the animal point-of-departure ($NOEL_{ADJ}$) to a human $NOEL_{HEC}$ using the US EPA recommended default dosimetric adjustment for extrarespiratory effects of category 3 gases. This compensates for animal-human differences in the pharmacokinetics of inhaled methyl *tert*-butyl ether. RIVM derivation does not make the default dosimetric adjustment, which would be more consistent with generally accepted risk assessment practice. The ATSDR applied a total uncertainty factor of 100 to the $NOEL_{HEC}$ to account for human variation (10) and animal-to-human extrapolation (10). This is inconsistent with generally accepted risk assessment practice because the default dosimetric adjustment for extrarespiratory effects of category 3 gases compensates for pharmacokinetic difference and thus, a 10-fold uncertainty factor for animal-to-human extrapolation is overly conservative. The CA EPA applied a total uncertainty factor of 30 to the $NOEL_{HEC}$ to account for human variation (10) and animal and human differences in sensitivity (3). The US EPA applied a total uncertainty factor of 100 to account for human variation (10), animal and human differences in sensitivity (3) and data deficiencies in the chronic study including lack of serum chemistry and urinalysis and limited reporting of motor activity/clinical signs during, exposure (3). The US EPA does not provide a clear rationale for including the database deficiencies uncertainty factor based on lack of parameters not routinely reported in chronic toxicity bioassays. Therefore, the CA EPA reference concentration (8 x 10^3 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for methyl *tert*-butyl ether.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/17/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/17/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2009. Re-Evaluation of Some Human Toxicological Maximum Permissible Risk Levels Earlier Evaluated in the Period 1991-2001. RIVM Rapport 711701092. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701092html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Methyl *tert*-butyl ether (MTBE)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Methyl *tert*-butyl ether (MTBE) (CAS Number 1634-04-4)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
Cal EPA (2002)	3.8	2.6×10^{-7}	linear extrapol. of the LED_{10} [2]	Internal dose metrics in animals were estimated with PBPK modeling; a human equivalent exposure level was derived based on $BW^{¾}$ scaling [3]	Based the geometric mean of the potency estimates obtained for male rat kidney adenomas and carcinomas combined, male rat leydig interstitial cell tumors and combined leukemias and lymphomas in female rats. Exposure was via gavage for female rats and via gavage or inhalation in male rats. Absorbed dose was assumed to be 50% by inhalation compared to ingestion.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.
[2]LED_{10} = The 95% lower confidence limit on the dose associated with a 10% increase in tumor incidence.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.

2. Recommendation and Rationale

The Cal EPA unit risk is the only available value from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the Cal EPA unit risk (2.6×10^{-7} per mcg/m^3) is the toxicity value recommended for use in the derivation of a inhalation cancer-based soil cleanup objective for methyl *tert*-butyl ether (MTBE). The methyl *tert*-butyl ether (MTBE) risk specific air concentration calculated from this toxicity value is 3.8 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2002. Air Toxics Hot Spots Program Risk Assessment Guidelines: Part II Technical Support Document for Describing Available Cancer Potency Factors. Sacramento, CA. Last accessed (01/17/2018) at http://www.oehha.ca.gov/air/cancer_guide/TSD2.html

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Naphthalene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Naphthalene (CAS Number 91-20-3)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW ♦ Cal EPA DDWEM (2000)	0.02	71	NOEL	3000	Based on mean terminal body weight decreases in male rats in a 90-day gavage study. Study LOEL = 142 mg/kg/day.
US EPA OPP*	0.1	100	NOEL	1000	Based on the same study and effects as US EPA IRIS. The reported NOEL was not adjusted for 5 days per week dosing.
RIVM (2001)	0.04	NA	NA	NA	Based on RIVM's evaluation of total petroleum hydrocarbons and its designation of naphthalene as a non-carcinogenic aromatic with 9 to 16 carbons.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor; NA: not applicable.
*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA IRIS and OPP reference doses are based on chemical-specific toxicity information for naphthalene. The RIVM value is based on a generic approach for petroleum related chemicals and is not the result of a chemical specific evaluation. The two US EPA values differ only in that US EPA OPP did not adjust the study NOEL for the 5 days per week dosing schedule and US EPA IRIS included an additional 3-fold uncertainty factor to account for database deficiencies including the lack of chronic oral toxicity and 2-generation reproductive toxicity studies. The US EPA IRIS derivation is more consistent with generally accepted risk assessment practice. Therefore, the US EPA IRIS

reference dose (0.02 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for naphthalene.

3. Review Dates

Summary table completion: February, 2004; revised January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

Cal EPA DDWEM (California Environmental Protection Agency Division of Drinking Water and Environmental Management). 2000. Memorandum: Proposed Action Level for Naphthalene. Office of Environmental Health Hazard Assessment. Sacramento, California. Last accessed (01/17/2018) at http://www.oehha.ca.gov/water/pals/index.html

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/17/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA OPP (United States Environmental Protection Agency, Office of Pesticide Programs). Pesticide Reregistration Status. Last accessed (01/17/2018) at http://www.epa.gov/opp00001/reregistration/status.htm.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Naphthalene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Naphthalene (CAS Number 91-20-3)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (2003)	--	--	--	--	Adequate human data are not available. No convincing evidence of carcinogenicity was observed in several inadequate studies in animals exposed orally, dermally, by intraperitoneal or subcutaneous injection, or by bladder implantation. Napthalene causes respiratory tumors in chronic inhalation studies in mice and rats.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for naphthalene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: February, 2004; no revision January, 2018
Toxicity value recommendation: April, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological Profile for Naphthalene/1-Methylnapthalene/2-Methylnapthalene (Draft for Public Comment). US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Naphthalene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Naphthalene (CAS Number 91-20-3)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2004)	3	9.3×10^3	LOEL	3000	Based on hyperplasia and metaplasia in respiratory and olfactory nasal epithelium and lung inflammation in mice exposed by inhalation for 6 hours/day, 5 days/week for 103 weeks.
ATSDR (2003)	3.7* (7×10^{-4} ppm)	1.05×10^3	LOEL	300	Based on the same mouse study used by US EPA IRIS (2004) and also on nasal epithelium lesions in rats exposed by inhalation 6 hours/day, 5 days/week for 105 weeks. The same experimental air concentration (10 ppm) was identified as the LOEL in both species. The point of departure was obtained from the rat data using US EPA inhalation dosimetric adjustment methods.
Cal EPA (2004)	9	9.4×10^3	LOEL	1000	Based on the same study used by US EPA IRIS (2004).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
LOEL: lowest observed effect level; UF: uncertainty factor.
*The ATSDR value is reported as 7×10^{-4} parts per million (ppm). For naphthalene, 1 ppm = 5.24 mg/m^3.

2. Recommendation and Rationale

The reference concentrations for naphthalene derived by authoritative bodies from the list in item 5 (below) are all based on observations of nasal and lung lesions in mice and rats exposed via inhalation for about 2 years. The US EPA and Cal EPA derived essentially the same LOEL point of departure from the mouse data. The US EPA described their value as representing a human equivalent concentration that incorporated a default pharmacokinetic adjustment (equal to 1) for a systemic gas when the blood:air partitioning coefficients for animals and humans are unknown. This was based on the low water solubility and reactivity of naphthalene and evidence that respiratory lesions in mice are due to absorption of naphthalene and metabolism to reactive oxygenated metabolites, rather than a direct site-of-contact mode of action. The Cal EPA's derivation cited the same information supporting a systemic mode of action, although they did not explicitly incorporate the default pharmacokinetic adjustment in their calculation of the point of departure. The ATSDR applied different dosimetry assumptions to the LOEL concentration observed in rats and mice (10 ppm in both cases), treating the nasal lesions as resulting from extrathoracic effects of a category 1 gas. Since this dosimetry treatment depends on species-specific minute volume and extra-thoracic surface area parameters, the human equivalent concentration derived from the mouse and rat LOELs differed slightly, and ATSDR chose the lower of the two values (rats) as their point of departure. There is substantial evidence that respiratory lesions in mice inhaling naphthalene are associated with oxidative metabolites that can be formed in the liver as well as the lung. Furthermore, naphthalene is not water-soluble nor is it a highly reactive site-of-contact compound, and therefore does not fit the requirements to be treated as a category 1 gas under currently-accepted dosimetry guidance. The treatment of naphthalene as a systemic (category 3) gas is more consistent with US EPA guidance on inhalation dosimetry (US EPA, 1994). The US EPA applied a total uncertainty factor of 3000, including 10-fold factors accounting for intra- and interspecies variability and the use of a LOEL. They included an additional factor of 3 to account for database deficiencies including the lack of a 2-generation reproductive toxicity study and lack of chronic inhalation toxicity data from other animal species. The Cal EPA applied a total uncertainty factor of 1000, including the same 10-fold factors as US EPA, but not including the additional factor for database deficiencies. Both derivations appear to have deviated from currently-accepted risk assessment practice in the application of a 10-fold interspecies uncertainty factor after incorporating a pharmacokinetic adjustment for systemic effects of a category 3 gas. Neither agency provides a clear rationale for this deviation, although the Cal EPA briefly mentions that it is unknown whether the reference concentration based on rodent respiratory lesions will be protective for hemolytic anemia and cataracts, which are well-known effects observed in humans exposed to naphthalene, but for which dose-duration-effect data are lacking. The criterion regarding lack of chronic inhalation data from other species stated as a basis for the additional uncertainty factor for database deficiencies applied by the US EPA no longer holds as chronic inhalation data in a second species (rats) exists and is consistent with the mouse data. Therefore, the Cal EPA reference concentration (9 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for naphthalene.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological profile for Naphthalene, 1-Methylnapthalene, 2-Methylnapthalene. Atlanta, GA: U.S. Department of Health and

Human Services, Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

Cal EPA (California Environmental Protection Agency). 2004. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Naphthalene. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. Last accessed (01/17/2018) at http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html

US EPA (United States Environmental Protection Agency). 1994. Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry. Washington DC: Office of Research and Development. EPA/600/8-90/066F.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

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5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Division of Drinking Water and Environmental Management

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Naphthalene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Naphthalene (CAS Number 91-20-3)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS	--	--	--	--	An inhalation unit risk estimate for naphthalene was not derived because of the weakness of the evidence that naphthalene may be carcinogenic in humans (observations of predominantly benign respiratory tumors in mice only at high doses).
CA EPA OEHHA* (2004) Also used by: • US EPA RSL*	0.03	3.4×10^{-5}	multistage model; linear extrapolation from the LED_{10}	body surface area[2]	Based on increased incidence of nasal respiratory epithelial adenomas and olfactory neuroblastomas in rats exposed by inhalation for 6.2 hours per day, 5 days per week for 105 weeks.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} concentration = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.

LED_{10}: 95% lower limit on effective dose at 10% increased incidence above background.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The only inhalation unit risk for naphthalene derived by an authoritative body listed below is the CA EPA OEHHA value based on increased incidence of respiratory and olfactory nasal tumors in male and female rats. Therefore the unit risk of 3.4×10^{-5} per mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for naphthalene. The naphthalene risk specific air concentration calculated from this toxicity value is 0.03 mcg/m^3.

3. Review Dates

Summary table completion: September, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA OEHHA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2004. Cover memo from Terry Tamminen, Agency Secretary, and addendum document adopting unit risk for naphthalene. Last accessed (01/17/2018) at http://oehha.ca.gov/air/hot_spots/naphth.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Nickel
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Inorganic Nickel

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
General Population					
US EPA IRIS Also used by: • US EPA RSL • US EPA ODW • US EPA HEAST (1997) • NYS DEC (1997)	0.02 (as Ni)	5	NOEL	300	Based on decreased body and organ weights observed in male and female rats in a two-year feeding study. Study LOEL = 50 mg/kg/day.
HC PSAP	0.0013 (as Ni)	1.3	LOEL	1000	Based on the LOEL for increased pup mortality in a two-generation drinking-water study in rats; a study NOEL was not identified as the LOEL also was the lowest dose tested.
CA EPA PHG	0.00112 (as Ni)	1.12	NOEL	1000	Based on NOEL for increased pup mortality identified from the combined results of three reproductive or developmental toxicity studies in rats, including the drinking water study used by HC PSAP (see text for details).
RIVM (2001)	0.05 (as Ni)	5	NOEL	100	Based on a subchronic rat dietary study. Precise identification of the critical study and effect are not provided.
TERA	0.008 (as Ni)	7.6	LOEL	1000	Based on increased incidence of albuminuria (indicating kidney glomerular dysfunction) in female rats exposed via drinking water for six months. The LOEL was the only dose tested.

WHO (2011)*	0.022 [2]	2.2	NOEL	100	Based on the NOEL in the reproductive/develop-mental study in rats used by CA EPA (i.e., follow-up study); study LOEL was not identified as the NOEL also was the highest lowest dose tested.
	0.012 [3]	0.012	LOEL	1	Based on the observed LOEL for exacerbation of eczema in a human volunteer study, using sensitized volunteers exposed via drinking water after fasting.
Child-Specific Reference Dose (chRD)					
CA EPA chRD*	0.01	1.1	NOEL	100	Based on the same study and derivation as CA EPA PHG except an additional 10-fold UF for carcinogenicity is not applied. Includes consideration of effects of exposure matrix and age on bioavailability.

[1]Agencies use different terms for the reference dose, including acceptable daily intake, tolerable daily intake, and chronic minimal risk level.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.
[2] Tolerable daily intake derived for "general toxicity" not considering nickel-sensitized individuals.
[3] Tolerable daily intake considering worst-case exposure for nickel-sensitized individuals.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The bases for the various reference doses for nickel derived from toxicity studies in rats include reduced body weights and organ weights in a chronic feeding study, reduced weight gain and blood biochemical changes in a subchronic feeding study, increased pup mortality in oral reproductive/developmental studies, and biochemical indications of kidney toxicity in a subchronic drinking water study. One reference dose value was based on data from an acute-exposure human study of nickel-sensitized volunteers exposed via drinking water after fasting.

The US EPA IRIS derived its reference dose based on a NOEL (5 mg/kg/day) from a chronic rat feeding study and a total uncertainty factor of 300. US EPA IRIS used uncertainty factors of 10 each to account for animal-to-human and human variability in its derivation. In addition, a factor of 3 was included to account for a limited database and earlier studies, including one used by HC (see studies discussed below), showing some effect of maternal nickel exposure on pup survival, and thus, the potential for reproductive/developmental toxicity at non-maternally-toxic doses.

The HC PSAP value is based on a LOEL (1.3 mg/kg/day) for increased pup mortality in a two-generation dietary study, where parental and offspring generations were exposed to approximately 0, 1.3, 6.8, or 32 mg/kg/day. The LOEL for pup mortality in the first generation of pups (LOEL = 32 mg/kg/day, highest dose tested) differed from the LOEL for pup mortality in the second generation (LOEL = 1.3 mg/kg/day, lowest does tested), even thought there was no effect at mid-dose, but an

effect at the highest dose. HC PSAP used the lower LOEL, and a total uncertainty factor of 1000 (to account for animal-to-human, human variability, and the use of a LOEL) to obtain its reference dose.

The CA EPA PHG reference dose derivation for nickel included data from the study used by HC PSAP (LOEL = 1.3 mg/kg/day) and data from more recent reproductive/developmental toxicity studies not available at the time the US EPA IRIS or HC PSAP conducted its assessments. The two more recent studies were done sequentially by the same researchers as a small dose-ranging study and then a larger follow-up study. The dose-ranging developmental toxicity study identified a LOEL (2.23 mg/kg/day, the lowest non-zero dose tested) for increased pup mortality. A NOEL was not identified. The follow-up two-generation study used more animals per group and had four non-zero dose groups (0.223, 0.558, 1.12, and 2.23 mg/kg/day), with the highest dose equal to the lowest non-zero dose in the first study (i.e., 2.23 mg/kg/day). No effects on pup survival or any other reproductive/developmental effects were observed at any dose (NOEL = 2.23 mg/kg/day, highest dose tested) in the follow-up study.

The CA EPA reviewed the combined results of the three studies (see table below) and identified an overall NOEL for development/reproductive effects of 1.12 mg/kg/day from the follow-up study (the second highest dose) because the true NOEL from the follow-up study (the highest dose of 2.23 mg/kg/day) was higher than the LOEL (1.3 mg/kg/day) from the two-generation study[3]. CA EPA applied a total uncertainty factor of 1000 to this dose to account for animal-to-human (10-fold), human variability (10-fold) and a 10-fold factor to compensate for the potential carcinogenicity of soluble nickel by the oral route, after determining that a quantitative assessment of oral cancer potency of nickel was not possible.

Study	Doses (mg/kg/day)	NOEL (mg/kg/day)	LOEL (mg/kg/day)
Two-generation study	0, 1.3, 6.8, 32	none	1.3
Range finding study	0, 2.23, 4.48, 6.60, 11.15, 16.72	none	2.23
Follow-up study	0, 0.223, 0.558, 1.12, 2.23	2.23	none
All studies		1.12	2.23

The basis for RIVM's reference dose is only described as a "semi-chronic experiment with rats exposed to nickel-sulfate in the diet." A total uncertainty factor of 100 is applied to the NOEL (5 mg/kg/day) to obtain the reference dose, but no further details of the derivation are provided. Consequently, the RIVM reference dose is not considered further as the basis for an oral non-cancer-based soil cleanup objective for nickel.

TERA based its derivation on a subchronic drinking water study where a biochemical indication of functional kidney toxicity was observed in male and female rats at the only non-zero dose tested. TERA considered the observed changes "small but biologically significant" and the difference was statistically significant from controls in female rats. A total uncertainty factor of 1000 was applied to the LOEL (7.6 mg/kg/day) to derive the TERA reference dose. It was composed of a 10-fold factor each for animal-to-human extrapolation and human variability and a 10-fold factor to collectively account for the use of a subchronic study, the use of a minimal LOEL, and an incomplete database. However, the TERA derivation was based on a one dose study, which precluded dose-response assessment. Moreover, TERA identified several interpretation issues regarding their identified critical effect: Only a single indication of kidney toxicity was observed; although statistically significant (in females, in males the NOEL dose was 6.9 mg/kg/day), the increases were not large for the affected

[3] Even though confidence that 1.3 mg/kg/day is a true LOEL (i.e., not a false positive) is not strong, since no effects were seen at the next highest dose (6.8 mg/kg/day).

endpoint; no baseline comparative data for the quantitative endpoint were provided; the supporting data for kidney toxicity as the critical endpoint for nickel exposure is weak (e.g., kidney histopathology has not been observed at lethal doses in chronic studies); and interpretation of the results was complicated by considerable variability in response among control and exposed animals. These issues raise substantial uncertainty about whether this dose should be considered an effect level. Thus, the TERA reference dose is not considered further as the basis for an oral non-cancer-based soil cleanup objective for nickel.

WHO (2011) derived two nickel reference doses. The "general toxicity" value is based on the NOEL (2.23 mg/kg/day) from the reproductive/developmental toxicity "follow-up" study used by CA EPA PHG and uncertainty factors of 10 each to account for animal-to-human and human variability. WHO also derived a second reference dose intended to be protective of the exacerbation of eczema in nickel-sensitized individuals. It was based on an observed LOEL (0.012 mg/kg/day) in a human-volunteer provocation study, where fasted nickel-sensitized patients were exposed to a single dose of nickel in drinking water. WHO applied a total uncertainty factor of 1 to this LOEL to derive this reference dose. An uncertainty factor accounting for human variability was not considered necessary because the study participants represented a highly sensitive population. WHO also considered the study design, which used a drinking water exposure on an empty stomach to maximize nickel GI absorption, to represent a worst-case exposure scenario for deriving a reference dose for total oral exposure. WHO based its recommended drinking water guideline value on the lower of the two reference doses.

The WHO reference dose based on exacerbation of eczema in sensitized patients is based on a well-designed and conducted study but is primarily relevant to acute exposures. WHO noted that the experimental protocol exposing sensitized patients to nickel in drinking water on an empty stomach represents a worst-case exposure scenario. While this may be a reasonable basis to establish a health-protective exposure guideline for drinking water, this value is less relevant to scenarios involving typical meal consumption and chronic soil exposures, where nickel bioavailability is expected to be significantly lower. Thus, this WHO reference dose is not considered further as the basis for an oral non-cancer-based soil cleanup objective for nickel.

CA EPA has formally developed a program to derive reference doses for evaluating childhood exposures to contaminants in and around schools. This program stems from the possibility that children may be more sensitive than adults to contaminant exposures. CA EPA bases child-specific reference doses (chRD), when possible, on studies in young animals or children rather than on studies based on adult animals or humans and the use of an uncertainty factor to compensate for typically unknown adult-child differences in pharmacokinetics and pharmacodynamics. The CA EPA chRD assessment re-considered the available data for nickel toxicity and concluded the critical effect and NOEL point of departure used for the CA EPA PHG assessment were appropriate for derivation of a child-specific reference dose. CA EPA considered whether a child-specific oral absorption factor should be applied to the PHG (which is specific to drinking water). They noted that gastrointestinal (GI) nickel absorption from water is about 10-fold greater than from food. Assuming that the GI absorption from food and from soil are equivalent (and the absorption from water 10-fold greater than from soil), CA EPA concluded that an absorption factor for the effect of exposure matrix (soil) would be appropriate. However, they also noted that data indicate child GI absorption of nickel could be approximately 11.8 times higher than adult GI absorption. Considering the retardation of absorption by the soil matrix and the higher GI absorption in children, CA EPA concluded that an absorption factor was not required to adjust the PHG for a soil-based child-specific reference dose. CA EPA also noted that the PHG included an extra uncertainty factor to account for database deficiencies for carcinogenic effects via the oral route. However, since the CA EPA chRD by definition addresses only non-cancer endpoints, they did not apply a cancer database uncertainty factor to derive the chRD.

General risk assessment practice would typically choose as the basis of a reference dose the lowest LOEL from a collection of equally valid LOELs and NOELs, if the LOELs are lower than the identified NOELs. The study used by HC PSAP has the lowest LOEL (1.3 mg/kg/day) among the numerous subchronic, chronic and reproductive/developmental oral-dosing studies available for nickel, but it is higher than the US EPA NOEL (5 mg/kg/day) for decreased body and organ weights. Thus, it would typically be selected as the basis of the reference dose for nickel. However, that study and the two more-recent studies used by the CA EPA and WHO lack convincing evidence of a clear dose-response in the dose range below about 5 mg/kg/day. The equivocal dose-response at the lowest doses from the three reproductive studies suggests that doses below about 2 mg/kg/day are as likely to have been NOELs as effect levels, suggesting that the effects observed at 1.3 mg/kg/day and 2.23 mg/kg/day could have been due to chance. Given the uncertainty regarding the location of a reproductive/developmental NOEL, and thus, our reduced confidence in a derived reference dose based on reproductive/developmental effects, the two CA EPA reference doses (general and childhood) and the WHO animal-based reference doses are not considered further as the basis for an oral non-cancer-based soil cleanup objective for nickel. Moreover, we note that the three-fold uncertainty factor for database uncertainties that US EPA applied to its NOEL (5 mg/kg/day/3 = 1.7 mg/kg/day) based on decreased body and organ weights compensates for this uncertainty in the developmental/reproductive data.

Overall, the US EPA IRIS derivation appears to be based on the most reliable chronic dose-response data and adequately accounts for uncertainties in the available reproductive/developmental toxicity information. Therefore, the US EPA reference dose (0.02 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for nickel.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/18/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

CA EPA chRD (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Child-Specific Reference Doses. Last accessed (01/18/2018) at http://www.oehha.ca.gov/public_info/public/kids/chrds.html.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/18/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Nickel and Nickel Compounds. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (8/18/2015) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/18/2018) at https://www.tera.org/iter/

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/18/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/18/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/18/2018) at http://water.epa.gov/action/advisories/drinking/upload/dwstandards2012.pdf.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/18/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Nickel
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Nickel

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Health Canada (1994)	--	--	--	--	Several nickel compounds have been evaluated for carcinogencity. The US EPA has classified nickel subsulfide and nickel refinery dust as known human carcinogens based on occupational epidemiological data and nickel carbonyl as a probable human carcinogen based on rat inhalation and injection studies. Health Canada classifies oxidic, sulfidic and soluble nickel compounds as carcinogenic to humans. However, no quantatitive assessments for oral exposure have been made.
Cal EPA (2004) Cal EPA (2003)	8.0×10^{-5} (nickel refinery dust total intake in mg/d)[2] -- 4.0×10^{-5} (nickel subsulfide total intake in mg/d)[2]	-- 1.7	--	--	Basis of values cited by Cal EPA in a table in the 1987 US EPA Health Assessment Document for beryllium without further details.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

[2]Risk-specific intakes were originally reported in mcg/d for a 1 in 10^5 lifetime excess cancer risk (CA EPA, 2003) and were re-scaled to the 1 in 10^6 total intake in mg/d by dividing by 10^4.

2. Recommendation and Rationale

The US EPA and Health Canada have both evaluated several nickel compounds and classes of compounds for carcinogenicity. Both agencies consider nickel refinery dust and its major component, nickel subsulfide as known human carcinogens based on occupational inhalation exposure. Oral cancer potency factors are not derived for nickel by US EPA or Health Canada, but US EPA has derived inhalation cancer unit risk values (the excess cancer risk associated with lifetime continuous inhalation of the chemical at a unit concentration of 1 mcg/m^3 in air) for nickel refinery dust and nickel subsulfide. The Cal EPA has apparently chosen to apply those unit risks directly to assessment of oral cancer risk by converting the unit risk to a cancer potency factor assuming a 70 kg adult breathes 20 m^3 of air per day for a lifetime. This simple route-extrapolation calculation yields the 1.7 $(mg/kg/d)^{-1}$ cancer potency factor for nickel subsulfide and the 8.0 x 10^{-5} mg/d 1-in-10^6 risk-specific total intake for nickel refinery dust reported in Cal EPA (2004). However, human and animal evidence suggests nickel acts primarily as a site-of-contact (i.e., nose and lung when inhaled in occupational studies) or injection site (in animal studies) carcinogen, so the application of a direct route extrapolation to oral exposure in the absence of data detailing relative route-specific deposition, pharmacokinetics or local or systemic potency is not well justified. The Cal EPA (2001) concluded that suitable data to perform a quantitative oral cancer assessment were not available when deriving a drinking water public health goal for nickel. They noted that human data only indicated increased incidence of site-of-contact tumors with inhalation exposure, even though serum nickel levels were elevated in exposed workers, and that all four published chronic drinking water or dietary animal studies failed to show evidence of increased tumor incidence in exposed animals. Therefore, an oral cancer potency value for nickel is not identified for use in setting brownfield soil cleanup objectives.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2001. Public health goals for chemicals in drinking water. Nickel. Office of Environmental Health Hazard Assessment. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

Cal EPA (California Environmental Protection Agency). 2003. Proposition 65 status report safe harbor levels: No significant risk levels for carcinogens and maximum allowable dose levels for chemicals causing reproductive toxicity reproductive and cancer hazard. Office of Environmental Health Hazard Assessment. Last accessed (01/17/2018) at https://oehha.ca.gov/proposition-65/general-info/current-proposition-65-no-significant-risk-levels-nsrls-maximum

Cal EPA (California Environmental Protection Agency). 2004. Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. Last accessed (01/18/2018) at https://oehha.ca.gov/chemicals

Health Canada, Environment Canada. 1994. Priority Substances List Assessment Report: Nickel and its compounds. Ottawa, Ministry of Public Works and Government Services. Last accessed (01/19/2018) at https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/canadian-environmental-protection-act-priority-substances-list-assessment-report-nickel-compounds.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Nickel
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Reference Concentrations for Inorganic Nickel

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Concentration (mcg/m^3)	Basis		
ATSDR (2003)	0.09	2.7	HEC_{NOEL}[2]	30	Based on fibrosis and inflammation of the lungs in rats exposed to nickel sulfate hexahydrate by inhalation for 6 hours/day, 5 days/week for 2 years. Study LOEL = 11 mcg/m^3.
CA EPA (2012)	0.014	1.4	HEC_{BMDL05}[2]	100	Based on the same study used by ATSDR (2003). This reference concentration applies to all particulate nickel forms except nickel oxide.
	0.02	2.0	HEC_{BMDL05}[2]	100	Based on pathological changes in the lungs of mice exposed by inhalation to nickel oxide for 6 hours/day, 5 days/weeks for 104 weeks. Study LOEL = 1 mg/m^3
NYS DOH (1989)	0.02	20	NOEL	1000	Based on chronic pulmonary inflammation in rats exposed by inhalation for 6 hours/day, 5 days/week for 13 weeks. The study LOEL was 40 mcg/m^3.

HC PSAP (1996) TERA (2004)	range of values from 3.5×10^{-3} to 0.018 depending on form of Ni	range of values from 3.5 to 18 depending on form of Ni	NOEL or minimal LOEL	1000	TERA (2004) reports several values from Health Canada for different forms of inorganic nickel all based on respiratory effects in rodents in a subchronic inhalation study. Health Canada (1994) bases its evaluation of nickel on carcinogenicity and does not actually report a reference concentration for any form, although they note that the lowest LOEL in animals for non-cancer effects is derived from the same study used by NYS DOH and is reported by Health Canada as 0.02 mg/m^3 (= 3.5×10^{-3} mg/m^3 adjusted for continuous exposure). Details of the values presented in TERA (2004) are not available.
TERA (2004)	0.2	1.7	$BMCL_{10}$ [3]	10	Based on the same study used by ATSDR (2003). This value is presented by TERA (2004) for nickel chloride, nickel sulfate and soluble nickel compounds not otherwise classified.
RIVM (2001)	0.05	5	NOEL	100	Based on the same study used by ATSDR (2003). Limited information on derivation available.

[1]Agencies use different terms for the reference concentration, including tolerable concentration in air.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

[2]HEC_{NOEL} and HEC_{BMCL05}: the human equivalent air concentration (HEC) at which the human internal dose equals the rat internal dose at the NOEL or $BMCL_{05}$. The $BMCL_{05}$ is the 95% lower confidence limit on the benchmark air concentration associated with a 5% increase (relative to controls) in the incidence of an adverse effect.

[3]$BMCL_{10}$: The 95% lower confidence limit on the benchmark air concentration associated with a 10% increase (relative to controls) in the incidence of an adverse effect.

2. Recommendation and Rationale

The reference concentrations for inorganic nickel derived by authoritative bodies from the list in item 5 (below) are all primarily based on lung toxicity observed in rats exposed via inhalation to nickel sulfate hexahydrate aerosols. One value specific to nickel oxide has also been derived that is based on lung, lymph node and adrenal effects in rats exposed by inhalation to nickel oxide aerosols. The values based on nickel sulfate exposure in rats are all derived from either a 13-week study (NYS DOH and Health Canada values) or a 2-year study (ATSDR, CA EPA (other than nickel oxide), TERA and RIVM values). The two studies reported similar effects in the lungs, but the chronic study identified a lower LOEL and is the more suitable study on which to base a chronic inhalation reference concentration. Therefore, the NYS DOH and Health Canada values are not considered further.

The chronic rat study tested different forms of nickel in parallel experiments, and CA EPA chose to derive two separate reference concentrations based on its conclusion that, although the effects of nickel inhalation in rats were similar regardless of whether soluble (nickel sulfate) or insoluble (nickel oxide) forms were involved, nickel oxide produced less severe effects (e.g., inflammation but no lung fibrosis observed) and a higher LOEL dose was identified, suggesting that nickel oxide is less potent than other nickel compounds. However, information of the chemical form of nickel (sulfate or oxide or some other form) in the soil) may seldom be available as part of the evaluation of nickel soil contamination. In the absence of data on the nickel form found in soil and the observation that nickel sulfate appears to be a more potent respiratory tract toxicant than nickel oxide, the CA EPA nickel oxide value will not be considered further.

The four remaining derivations (RIVM, TERA, ATSDR and CA EPA) estimated human equivalent concentrations (HECs) from the same two-year inhalation study of nickel sulfate in rats. The HEC derived by RIVM only accounts for the discontinuous exposure regime and makes no pharmacokinetic adjustment for particle deposition in the lung, and is not considered further. ATSDR calculated an HEC at the NOEL, while TERA calculated an HEC at a modeled benchmark air concentration (a $BMCL_{10}$). Both applied similar pharmacokinetic adjustments based on regional deposited dose ratios to account for relative particulate deposition in the pulmonary region of the respiratory system in rats and humans. ATSDR applied a total uncertainty factor of 30, including 10-fold to account for intraspecies variability and 3-fold to account for interspecies variability. TERA applied the same 10-fold factor for intraspecies variability, but argued that the 3-fold factor for interspecies variability beyond the pharmacokinetic adjustment was unnecessary, based on a single occupational study where minimal effects were observed by x-ray in lungs of nickel workers. The estimated minimal LOEL in workers was approximately 10- to 100-fold higher than the $BMCL_{10}$ from the rat study. This was interpreted as evidence that rats are more sensitive to the non-cancer effects of nickel inhalation exposure than humans. However, TERA points out that there are several limitations in the occupational study that raise questions about its sensitivity, including “highly approximate” exposure estimates, mixed exposure to soluble and insoluble forms of nickel and substantial variation in interpretation of the x-rays. The weaknesses in this study make its use as the basis for deviating from the default uncertainty factor for interspecies variability questionable, and the TERA value is not considered further.

The CA EPA calculated an HEC at a modeled benchmark air concentration (a $BMCL_{05}$). The animal air concentration was converted to an HEC using dosimetric adjustment factors obtained from a well-documented, peer-reviewed and validated multipathway particle dosimetry model that modelled lung deposition in adult rats, and extrapolated them to humans at five different ages (3 months, 3 years, 9 years, 14 years and 21 years). CA EPA applied a total uncertainty factor of 100 to the HEC, including 3-fold to account for interspecies variability and 30-fold to account for intraspecies variability. The

additional factor of 3 (beyond the default of 10) to account for intraspecies differences was applied to address potential increased sensitivity of infants and children (relative to adults) to continuous exposures to airborne nickel particles.

The CA EPA derivation is preferred over the ATSDR derivation because CA EPA used more scientifically robust dosimetric adjustment factors to extrapolate animal inhaled doses to humans than did ATSDR. The CA EPA derivation also is preferred over the ATSDR derivation because it calculates an HEC from a modeled benchmark air concentration (rather than a NOEL). Therefore, the CA EPA reference concentration (0.014 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for inorganic nickel.

3. Review Dates

Summary table completion: September, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/16/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2012. Notice of Adoption of Revised Reference Exposure Levels for Nickel and Nickel Compounds. Last accessed (01/16/2018) at https://oehha.ca.gov/air/crnr/notice-adoption-revised-reference-exposure-levels-nickel-and-nickel-compounds.

HC PSAP (Health Canada). 1996. Priority Substances Assessment Program. Health-Based Tolerable Daily Intakes/Concentrations and Tumorigenic Doses/ Concentrations for Priority Substances. Cat. H46-2/96-194E. Last accessed (01/16/2018) at http://publications.gc.ca/site/eng/411636/publication.html

NYSDOH (New York State Department of Health). 1989. Ambient Air Criteria Document for Nickel. Albany NY: Bureau of Toxic Substance Assessment.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/16/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/16/2018) at http://www.tera.org/iter/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)

New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Nickel
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Nickel

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • US EPA HEAST (1997)	4.2×10^{-3} (nickel refinery dust) 2.1×10^{-3} (nickel subsulfide)	2.4×10^{-4} (nickel refinery dust) 4.8×10^{-4} (nickel subsulfide)	Additive and multiplicative excess risk models	--	Based on several studies showing increased incidence of lung cancer in workers exposed by inhalation to nickel refinery dust. Approximately 50% of nickel refinery dust is assumed to be nickel subsulfide.
Cal EPA (2002) Cal EPA (2004)	3.9×10^{-3} (nickel refinery dust) 2.0×10^{-3} (nickel subsulfide)	2.6×10^{-4} (nickel refinery dust) 4.9×10^{-4} (nickel subsulfide)	relative risk model	--	Based on data from some of the same occupational studies as used by US EPA.
NYS DOH (1989)	2×10^{-4} (nickel subsulfide)	--[3]	linearized multistage model	body surface area[2]	Based on the combined incidence of lung adenomas and adenocarcinomas in rats exposed by inhalation 6 hours/day, 5 days/week for 78 weeks.

Health Canada (1994)	40 – 1000 reported as a TC_{05} [2]; linear equivalent risk specific concentration range = 8×10^{-4} to 2×10^{-2} (nickel refinery dust) 70 reported as a TC_{05} [2]; linear equivalent risk specific concentration = 1.4×10^{-3} (soluble nickel compounds)	--[3]	not stated	not stated	Based on data from some of the same occupational studies as used by US EPA. Complete details of the extrapolation model were not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} concentration = 1×10^{-6} / cancer potency factor.
[2]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.
[3] The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported, but would be equal to 1×10^{-6} divided by the 10^{-6} risk-specific concentration.

2. Recommendation and Rationale

The inhalation unit risks derived by authoritative bodies from the list in item 5 (below) are based on increased incidence of lung tumors in human occupational studies or in rats exposed by inhalation for 78 weeks. Health Canada derived a range of inhalation risk-specific concentrations from cohorts where the exposure information was for refinery dust and a separate risk-specific concentration for another cohort where nickel species information was available. However, they only reported maximum likelihood TC_{05}s that do not provide lower-bound estimates on the risk specific concentrations. The US EPA IRIS derivations for nickel refinery dust are based on occupational data from several studies of lung cancer in nickel workers. The Cal EPA considered all of the same studies, but concluded that data from only one of the cohorts was suitable for derivation of a unit risk. Both agencies derived separate unit risks for nickel refinery dust and nickel subsulfide. The US EPA IRIS makes an explicit assumption that refinery dust is composed of approximately 50% nickel subsulfide, and that nickel subsulfide is the primary carcinogenic component, so that the nickel subsulfide unit risk is 2-fold higher than the nickel refinery dust unit risk. The same numerical relationship is true for the Cal EPA unit risks, but details of the nickel subsulfide unit risk (which is based on a Proposition 65 No Significant Risk Level) are not available. Although the US EPA and Cal EPA derivations differ in the details of the dose-response modeling, the unit risk values are nearly identical. The NYS DOH derived a unit risk based on lung tumors in a rat inhalation study with nickel subsulfide. The NYS DOH value is based on older default interspecies extrapolation methods that are no longer consistent with currently-accepted risk assessment practice. A risk-specific concentration based on human equivalent concentration estimates reflecting

pharmacokinetic adjustment for relative particulate deposition in the lung would be expected to be higher than the NYS DOH value. In addition, a value based on human data is typically chosen over values based on animal studies if such data are available and adequate. As a mid-point from a range of values estimated from several different occupational cohort studies, the US EPA IRIS value represents a robust unit risk estimate from human data. The unit risk value based on nickel subsulfide is chosen in the absence of a site-specific material (such as nickel refinery dust) for which the nickel subsulfide contribution is known. Therefore, the US EPA IRIS unit risk (4.8×10^{-4} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for nickel. The nickel risk specific air concentration calculated from this toxicity value is 2.1×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency), 2002. Air Toxics Hot Spot Program Risk Assessment Guideline. Part II. Technical Support Documentation for Describing Available Cancer Potency Factors. Sacramento, CA: Office of Environmental Health Hazard Assessment. Last accessed (01/19/2018) at http://www.oehha.ca.gov/air/cancer_guide/TSD2.html.

Cal EPA (California Environmental Protection Agency), 2004. Toxicity Criteria Database. Nickel subsulfide and Nickel refinery dust. Office of Environmental Health Hazard Assessment. Last accessed (01/17/2018) at https://oehha.ca.gov/chemicals

Health Canada, Environment Canada. 1993. Priority Substances List Assessment Report: Hexachlorobenzene. Ottawa, Ministry of Public Works and Government Services. Last accessed (01/15/2018) at https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/canadian-environmental-protection-act-1999-priority-substances-list-assessment-report-hexachlorobenzene.html

NYS DOH (New York State Department of Health) 1989. Ambient Air Criteria Document: Nickel. Albany NY: Bureau of Toxic Substance Assessment.

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1.
Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Division of Drinking Water and Environmental Management
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Nitrobenzene*
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Nitrobenzene (CAS Number 98-95-3)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL	2×10^{-3}	1.8	$BMDL_{1SD}$[(2)]	1000	Based on increased methemoglobin levels in male rats exposed via gavage each day in a 90-day study.
NYS DEC (1997)	6×10^{-4}	0.6	LOEL[3]	1000	Based on bile duct inflammation and splenic congestion in male rats exposed via inhalation 6 hours/day, 5 days/week in a 2-year study. Study $LOEL_{EXP}$ = 5 mg/m^3, which was the lowest exposure level tested.
WHO (2009, 2011)	1.3×10^{-3}	0.13	$BMDL_{10}$[(4,5)]	100	Based on the increased incidence of pigmentation of nasal epithelium and extramedullary haematopoiesis in the spleen of rats exposed via inhalation for 6 hours/day, 5 days/week in a 2-year study. Study $LOEL_{EXP}$ (nasal and spleen effects) = 5 mg/m^3, which was the lowest exposure level tested.
	7.5×10^{-3}	0.75	NOEL[6]	100	Based on the increased incidence of eosinophilic foci and centrilobular hepatocytomegaly in the livers of rats exposed via inhalation for 6 hours/day, 5 days/week in a 2-year study. Study $NOEL_{EXP}$ and $LOEL_{EXP}$ (liver effects) = 5 mg/m^3 and 25 mg/m^3, respectively.
	1.0×10^{-2}	1.0	$BMDL_{10}$[(4,7)]	100	

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]$BMDL_{1SD}$: 95% lower confidence limit on benchmark dose (BMD) corresponding to a change in the mean equal to one standard deviation (SD) of the control mean.

[3]LOEL (mg/kg/day) = [5 mg/m^3 ($LOEL_{EXP}$) x 6 hours/24 hours x 5 days/7 days x 0.51 m^3/day (daily respiration volume of rats) x 0.8 (absorption fraction of inhaled dose)]/0.65 kg (mean body weight).

[4]$BMDL_{10}$: The lower 95% confidence limit on the benchmark dose (BMD) associated with a 10% change (relative to the control mean) in the mean incidence of an adverse effect.

[5]$BMDL_{10}$ (mg/kg/day) = [0.88 mg/m^3 ($BMDL_{10}$) x 6 hours/24 hours x 5 days/7 days x 0.29 m^3/day (daily respiration volume of rats) x 1 (absorption fraction of inhaled dose)]/0.35 kg (mean body weight).

[6]NOEL (mg/kg/day) = [5 mg/m^3 ($NOEL_{EXP}$) x 6 hours/24 hours x 5 days/7 days x 0.29 m^3/day (daily respiration volume of rats) x 1 (absorption fraction of inhaled dose)]/0.35 kg (mean body weight).

[7]$BMDL_{10}$ (mg/kg/day) = [7.1 mg/m^3 ($BMDL_{10}$) x 6 hours/24 hours x 5 days/7 days x 0.29 m^3/day (daily respiration volume of rats) x 1 (absorption fraction of inhaled dose)]/0.35 kg (mean body weight).

NOEL: no-observed-effect level; $NOEL_{EXP}$: experimental NOEL; LOEL: lowest-observed-effect level; $LOEL_{EXP}$: experimental LOEL.

*Nitrobenzene is a new priority contaminant and this is a new fact sheet. Nitrobenzene was not identified as a priority contaminant in the 2006 Technical Support Document for the Development of Soil Cleanup Objectives in the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA reference dose for nitrobenzene is based on a 90-day oral study in rats. The NYS DEC and WHO reference doses are based on a 2-year inhalation study in rats. In general, an oral study is a more appropriate basis for an oral reference dose than an inhalation study, unless it is a scientifically poorer study, because of the uncertainties in route$_{Inhalation}$-to-route$_{Oral}$ extrapolations. Although the oral study was only 90 days long, the US EPA's confidence in the scientific quality of the study was rated "high," and its use in the derivation of the reference dose is well documented and peer-reviewed. The derivation is consistent with generally accepted risk assessment practices for high to low dose and animal to human extrapolations of noncancer effects, including the use of a 1000-fold uncertainty factor to compensate for animal to human extrapolation (10), the use of a subchronic study (3), human variation (10) and database deficiencies (3) given evidence of male reproductive toxicity and the lack of an oral multigenerational reproductive toxicity study. The US EPA (2009) provided a scientifically sound and well-documented rationale for the use of a 3-fold uncertainty factor (rather than 10) to compensate for the use a subchronic study. Therefore, the US EPA reference dose (2×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for nitrobenzene.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS DEC (New York State Department of Environmental Conservation). 1997. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Nitrobenzene. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

WHO (World Health Organization). 2009. Nitrobenzene in Drinking-Water. Background Document for Development of WHO Guidelines for Drinking-Water Quality. WHO/HSE/WSH/09.01/4. Last accessed (01/17/2018) at http://www.who.int/water_sanitation_health/dwq/chemicals/en/index.html.

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/17/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html.

6. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Nitrobenzene*
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Nitrobenzene (CAS Number 98-95-3)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
NYS DEC (1997)	1.2×10^{-5}	0.084	linearized multistage model	animal inhaled dose [(2)], $BW^{¾}$ [(3)]	Based on increased incidence of hepatocellular adenoma and carcinoma in male rats exposed via inhalation 6 hours/day, 5 days/week in a 2-year study.
WHO (2009, 2011)	2.7×10^{-5}	0.037	unspecified model used to estimate $BMDL_{10}$ [(5)]	human inhaled dose calculated from experimental air concentrations, adjusted for continuous exposure [(4)]	Based on combined incidence of liver, thyroid, and kidney tumors in male rats exposed via inhalation for 6 hours/day, 5 days/week in a 2-year study.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.
[2]Inhaled dose (mg/kg/day) = [X mg/m^3 (experimental air levels) x 6 hours/24 hours x 5 days/7 days x 0.35 m^3/day (daily respiration volume of rats) x 0.8 (absorption fraction of inhaled dose)]/0.38 kg (mean body weight).
[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$.
[4]Human inhaled dose (mg/kg/day) = [X mg/m^3 (experimental air level) x 6 hours/24 hours x 5 days/7 days x 20 m^3/day (daily respiration volume of humans) x 1 (absorption fraction of inhaled dose)]/70 kg (mean body weight).
[5]$BMDL_{10}$: 95% lower confidence limit of the benchmark dose (BMD) associated with a 10% increase (relative to controls) in the incidence of tumors.

*Nitrobenzene is a new priority contaminant and this is a new fact sheet. Nitrobenzene was not identified as a priority contaminant in the 2006 Technical Support Document for the Development of Soil Cleanup Objectives in the New York State Brownfield Cleanup Program.

2.Recommendation and Rationale

Nitrobenzene is a toxicant that is expected to be absorbed into the body and cause systemic cancer effects after oral or inhalation exposure. The NYS DEC and WHO cancer potency factors for nitrobenzene are the only available values from an authoritative body listed in item 5 (below). Both agencies based their cancer potency factor on the same 2-year inhalation study in rats. Neither agency calculated an inhalation unit risk, but each used a similar, but different, default route$_{Inhalation}$-to-route $_{Oral}$ extrapolation method. The DEC route-to-route extrapolation method is inconsistent with the pharmacokinetics of a category 2 gas with systemic toxicity such as nitrobenzene (see Inhalation Toxicity Value Documentation for Nitrobenzene). Thus, the DEC cancer potency factor was not considered further in the derivation. The WHO derivation of a unit risk was determined to be inferior to

a unit risk derived by US EPA, and the US EPA unit risk (4×10^{-5} per mcg/m^3), rather than the WHO unit risk (3.1×10^{-5} per mcg/m^3), was selected as the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for nitrobenzene (see Inhalation Toxicity Value Documentation for Nitrobenzene).

In the absence of adequate data to derive an oral cancer potency factor from oral exposures, a default $route_{Inhalation}$-to-$route_{Oral}$ extrapolation, assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day, was used to derive a cancer potency factor (0.14 per mg/kg/day) from the recommended unit risk (4×10^{-5} per mcg/m^3). Therefore, the cancer potency factor of 0.14 per mg/kg/day is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for nitrobenzene. The nitrobenzene risk-specific dose calculated from this toxicity value is 7.1×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table and Recommendations and Rationale

NRC (National Research Council, Committee on Risk Assessment of Hazardous Air Pollutants). 1994. Science and Judgment in Risk Assessment. Washington, DC: National Academy Press.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2009. Nitrobenzene in Drinking-Water. Background Document for Development of WHO Guidelines for Drinking-Water Quality. WHO/HSE/WSH/09.01/4. Last accessed (01/15/2018) at http://www.who.int/water_sanitation_health/dwq/chemicals/en/index.html.

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/15/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables

Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Nitrobenzene*
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Nitrobenzene (CAS Number 98-95-3)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL	9	260	$BMCL_{10\text{-}HEC}$[2]	30	Based on bronchiolization of the alveoli and olfactory degeneration in mice exposed via inhalation for 6 hours/day, 5 days/week in a 2-year study.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

[2]$BMCL_{10\text{-}HEC}$: the human equivalent concentration (HEC) associated with the 95% lower confidence limit of the benchmark air concentration (BMC) associated with a 10% increase in the incidence of either lesion in animals. It was calculated from the animal adjusted $BMCL_{10}$ (i.e., $BMCL_{10\text{-}ADJ}$) using US EPA recommended methods for pulmonary effects of a category 2 gas, where $BMCL_{10\text{-}ADJ}$ equals the $BMCL_{10\text{-}EXP}$ x 6 hours/24 hours x 5 days/7 days.

$BMCL_{10\text{-}EXP}$: experimental $BMCL_{10}$; UF: uncertainty factor.

*Nitrobenzene is a new priority contaminant and this is a new fact sheet. Nitrobenzene was not identified as a priority contaminant in the 2006 Technical Support Document for the Development of Soil Cleanup Objectives in the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA reference concentration for nitrobenzene is the only available value from an authoritative body listed in item 5 (below). Nitrobenzene is a category 2 gas and the animal point of departure ($BMCL_{10}$) was converted to a human $BMCL_{10\text{-}HEC}$ using the US EPA recommended dosimetric adjustment for pulmonary effects of a category 2 gas. This compensates for animal-human differences in the pharmacokinetics of inhaled nitrobenzene. US EPA applied a 30-fold uncertainty factor to compensate for animal to human differences in sensitivity (3) and human variation (10). The derivation is well documented and peer-reviewed and is consistent with generally accepted risk assessment practices for high to low dose and animal to human extrapolations. Therefore, the US EPA reference concentration (9 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for nitrobenzene.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table and Recommendation and Rationale

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Nitrobenzene*
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for Nitrobenzene (CAS Number 98-95-3)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ♦ US EPA RSL	0.025	4×10^{-5}	multistage model, linear extrapolation from the $LEC_{10\text{-}HEC}$[3]	dosimetry for extrarespiratory effects of category 2 gas, adjusted for continuous exposure[2]	Based on combined incidence of liver, thyroid and kidney tumors in male rats exposed via inhalation for 6 hours/day, 5 days/week in a 2-year study.
WHO (2003, 2011)	0.032	3.1×10^{-5} (5)	linearized multistage model	human inhaled dose calculated from experimental air concentrations, adjusted for continuous exposure[4]	Based on the combined incidence of liver, thyroid and kidney tumors in male rats exposed via inhalation for 6 hours/day, 5 days/week in a 2-year study

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million, where 1×10^{-6} air concentration = 1×10^{-6}/cancer unit risk.

[2]Human equivalent concentration (HEC) = X mg/m^3 (experimental air level) x 6 hours/24 hours x 5 days/7 days x 1 (default ratio for the ratio of the animal blood:air partitioning coefficient to the human blood:air partitioning coefficient for nitrobenzene).

[3]$LEC_{10\text{-}HEC}$: The HEC associated with the 95% lower confidence limit on the effective air concentration (EC) associated with a 10% increase (above controls) in the incidence of tumors in animals.

[4]Human inhaled dose (mg/kg/day) = [X mg/m^3 (experimental air level) x 6 hours/24 hours x 5 days/7 days x 20 m^3/day (daily respiration volume of humans) x 1 (absorption fraction of inhaled dose)]/70 kg (mean body weight).

[5]A unit risk was not recommended by WHO, but was calculated from the recommended inhalation cancer potency factor of 0.11 $(mg/kg/day)^{-1}$.

*Nitrobenzene is a new priority contaminant and this is a new fact sheet. Nitrobenzene was not identified as a priority contaminant in the 2006 Technical Support Document for the Development of Soil Cleanup Objectives in the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA and WHO unit risks for nitrobenzene are based on the same cancer endpoints (liver, thyroid, and kidney tumors in male rats) from the same 2-year inhalation study. Both used a multistage model to estimate a point of departure. Nitrobenzene is a category 2 gas and the US EPA based the animal to human extrapolation on the agency's recommended method for extrarespiratory (i.e., systemic) effects of a category 2 gas. The WHO apparently converted the animal experimental

concentrations (adjusted for continuous exposure) to human equivalent inhaled doses using human body weights and daily inhalation rates. Although this approach is conceptually flawed given our understanding of the pharmacokinetic of Category 2 gases in animals and humans, it gives essentially the same results as the US EPA's recommended interspecies extrapolation method for extrarespiratory (i.e., systemic) effects of a category 2 gas.

The US EPA unit risk is based on summing the risk estimates from each separate tumor type rather than on a unit risk based on tumor-bearing animals (i.e., animals with one or more tumor types caused by the chemical). This approach is consistent with the recommendation of National Research Council (NRC, 1994), which concluded that an approach based on counts of tumor-bearing animals would tend to underestimate overall risk when tumor types occur independently. The WHO unit risk apparently is based on the incidence of tumor-bearing animals at each exposure level, although it is unclear how the WHO obtained their incidence data.

The US EPA unit risk derivation was peer-reviewed and well documented. It is consistent with generally accepted risk assessment practices for high-to-low-dose and animal-to-human extrapolations. Therefore, the US EPA unit risk (4×10^{-5} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for nitrobenzene. The nitrobenzene risk specific air concentration calculated from this toxicity value is 0.025 mcg/m^3.

3. Review Dates

Summary table completion: January, 2018
Toxicity value recommendation: January, 2018

4. References for Summary Table and Recommendations and Rationale

NRC (National Research Council, Committee on Risk Assessment of Hazardous Air Pollutants). 1994. Science and Judgment in Risk Assessment. Washington, DC: National Academy Press.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2003. Environmental Health Criteria 230. Nitrobenzene. Last accessed (01/15/2018) at http://www.who.int/ipcs/publications/ehc/ehc_230/en/index.html.

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/15/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation

New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization
Public Health & Environmental Protection, Netherlands

Chemical Name: Pentachlorophenol
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Pentachlorophenol (CAS Number 87-86-5)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
General Population					
US EPA IRIS* Also used by: • US EPA RSL* • US EPA ODW* • US EPA OPP*	5×10^{-3}	1.5	LOEL	300	Based on liver lesions including pigmentation, inflammation, cytoplasmic vacuolation and minimal necrosis in dogs exposed orally for one year. The lowest dose was considered a minimal LOEL because of progression in severity and incidence with dose.
US EPA HEAST (1997)	0.03	3	NOEL	100	Based on pigmentation in the liver and kidneys of male and female rats in a 2-year feeding study. Study LOEL = 10 mg/kg/day.
ATSDR	1×10^{-3}	1	LOEL	1000	Based on decreased thyroid hormone concentrations and decreased relative thyroid weight in a multigeneration reproduction feeding study in minks. The LOEL was the only dose tested.
CA EPA PHG*	1×10^{-3}	1	LOEL	1000	Based on the same study used by ATSDR and a two-generation feeding study in sheep with the same LOEL that also showed evidence of disruption of thyroid function.
RIVM (2001)	3×10^{-3}	1	LOEL	300	Based on the same study reviewed in ATSDR.
HC DWQ	6×10^{-3}	3	NOEL	500	Based on reduction in mean adult body weight in female rats exposed prior to mating, during mating and gestation

					and throughout lactation, and on decreased survival in neonates among their litters. Study LOEL = 30 mg/kg/day. The NOEL is consistent with a NOEL for liver and kidney effects in a limited chronic study.
Child-Specific Reference Dose (chRD)					
CA EPA chRD*	1×10^{-3}	1	LOEL	1000	Based on the same study used by ATSDR and a two-generation feeding study in sheep with the same LOEL that also showed evidence of disruption of thyroid function.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.

NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The bases for the various reference doses for pentachlorophenol include adult body weight gain reduction and decreased neonate survival in rats; blood, liver and kidney effects in rats; liver effects in dogs and thyroid effects in mink and sheep. The US EPA IRIS value is based on a LOEL in a chronic dog oral exposure study. CA EPA, ATSDR and RIVM used a LOEL from a multigeneration reproductive study in mink (CA EPA also noted a similar two-generation study in sheep that gave the same LOEL for thyroid effects). US EPA HEAST cited a NOEL for liver and kidney effects from a chronic rat feeding study. Health Canada used a NOEL from a developmental toxicity study that is equivalent to this chronic rat NOEL to derive its reference dose. The mink and dog LOEL values are approximately the same as the subchronic rat NOEL and are 2- to 3-fold lower than the chronic rat NOEL and the developmental rat NOEL, indicating that the chronic and developmental rat NOELs may not be sufficiently health protective of the effects seen in the multigeneration study in mink or the chronic dog study. The dog study included three dose groups plus the control group, but was limited by small numbers of animals (4 per sex) per dose group. The multigeneration mink and sheep studies are limited by only having one dose group plus a control group. US EPA considered the observed liver effects at the LOEL to be minimal toxic effects and so reduced the uncertainty factor accounting for use of LOEL from 10 to 3. ATSDR and CA EPA used a total uncertainty factor of 1000 to account for animal-to-human and human variability and extrapolation from a LOEL, while RIVM used a total uncertainty factor of 300, only applying a factor of 3 to account for the use of what they concluded was a minimal LOEL. Thyroid effects were seen in the parent and offspring generations in the study, and in both sexes, and so should not be considered minimal. The LOEL from the multigeneration mink and sheep studies is slightly lower than the dog LOEL. Therefore, the ATSDR reference dose (1×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for pentachlorophenol.

CA EPA has developed a program to derive reference doses for evaluating childhood exposures to contaminants in and around schools. This program stems from the possibility that children may be more

sensitive than adults to contaminant exposures. CA EPA bases child-specific reference doses (chRD), when possible, on studies in young animals or children rather than on studies based on adult animal or humans and the use of an uncertainty factor to compensate for typically unknown adult-child differences in pharmacokinetics and pharmacodynamics. CA EPA derived its chRD for pentachlorophenol based on the same study in sheep as was used by ATSDR to derive their reference dose for the general population, and using the same uncertainty factors. The chRD is equivalent to the ATSDR value (1 x 10^{-3} mg/kg/day), and is the only child-specific toxicity value derived by an authoritative body in item 5 (below) and is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for pentachlorophenol involving child exposure. However, since the reference doses are identical, a separate child-specific reference dose for pentachlorophenol is not needed.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: August, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/18/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/18/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

CA EPA chRD (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Child-Specific Reference Doses. Last accessed (01/18/2018) at http://www.oehha.ca.gov/public_info/public/kids/chrds.html.

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/18/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/18/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/18/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/18/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/18/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA OPP (United States Environmental Protection Agency, Office of Pesticide Programs). Pesticide Reregistration Status. Last accessed (01/18/2018) at http://www.epa.gov/opp00001/reregistration/status.htm.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Pentachlorophenol (PCP)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for PCP (CAS Number 87-86-5)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS* Also used by: ◆ US EPA RSL*	2.5×10^{-6}	0.4	linear extrapolation from LED_{10} [2]	$BW^{¾}$ [3]	Based on increased incidence of liver and adrenal gland tumors in male mice exposed via the diet for 2 years to technical PCP; recommended value based on the sum of the risk estimates from each separate tumor type, and not on the incidence of animals with one or more tumors.
US EPA OPP	1.4×10^{-5}	0.07	linearized multistage model, extra risk	$BW^{¾}$ [3]	Based on increases in the pooled incidence of liver, adrenal gland and vascular tumors in female mice exposed via the diet for 2 years to technical PCP or to a commercial PCP product (Dowicide EC-7); recommended value was the geometric mean of two values.
CA EPA PHG	1.2×10^{-5} ---- 1.2×10^{-5}	0.0834 ---- 0.0811	linearized multistage model, extra risk ---- linear extrapolation from LED_{10} [2]	$BW^{¾}$ [3] ---- $BW^{¾}$ [4]	Based on increased incidence of liver tumors in male mice exposed via the diet for 2 years to commercial PCP product (Dowicide EC-7).

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.
[2]LED_{10} = lower bound on the dose associated with 10% increase in the incidence of tumors.
[3]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[4]Factor for dose adjustment from animal to humans was not provided, but likely to be $BW^{¾}$ based on statements in the CA EPA document and the similarity of the two cancer potency estimates derived by CA EPA from the same dose-response data.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The cancer potency factors for pentachlorophenol (PCP) derived by authoritative bodies were all based on tumor incidence data for male or female mice from two NTP dietary studies using two different PCP technical-grade mixtures [a composite lot of technical-grade PCP and a commercial product (Dowicide EC-7)].[4]

Dietary exposures to PCP mixtures induced multiple tumor types/sites in mice. The estimation of human risk based on only one tumor type/site induced by PCP may underestimate the overall carcinogenic potential of PCP (NRC, 1994). As noted by the US EPA (2010), there are two ways to assess the total risk from multiple tumors types/sites: "analyzing the incidences of tumor-bearing animals or combining the potencies associated with significantly elevated tumors at each site." US EPA (2010) went on to note.

> The NRC (1994) concluded that an approach based on counts of animals with one or more tumors would tend to underestimate overall risk when tumor types occur independently, and that an approach based on combining the risk estimates from each separate tumor type should be used.

Only the US EPA IRIS used the latter approach in its derivation of a cancer potency factor for technical PCP.[5] The estimation of risk based on the incidence of mice with one or more tumor types/sites (US EPA OPP derivation) or on mice with only one tumor type/site (CA EPA PHG derivation) may underestimate the overall carcinogenic potential of a chemical (i.e., technical PCP). Thus, we did not consider further the US EPA OPP or the CA EPA cancer potency factors as potential toxicity values for use in the derivation of an oral cancer-based soil cleanup objective for PCP.

The US EPA IRIS derived a cancer potency of 0.4 $(mg/kg/day)^{-1}$ based on the male mouse tumors (liver and adrenal gland) observed in the NTP study with technical PCP. The US EPA IRIS Program (US EPA, 2010) was concerned that the presence of contaminants in the technical PCP and Dowicide EC-7 (see footnote 1) could have contributed to the carcinogenicity of the PCP formulations. However, the US EPA (2010) noted.

> … the degree of influence of the contaminants on the cancer potency of either formulation (e.g., whether these contaminants resulted in an over- or underestimation of the potency of PCP alone) cannot be determined. Therefore, in the absence of information to indicate the formulation which best represents PCP carcinogenicity, EPA selected the most sensitive cancer risk estimate, the slope factor of 4×10^{-1} $(mg/kg\text{-}day)^{-1}$ derived for technical pentachlorophenol, which is the higher cancer potency of the two formulations, to represent the cancer risk estimate for PCP.

The US EPA IRIS derivation reflects generally-accepted risk assessment practices for inter-species and high-to-low dose extrapolations and for estimating cancer risk from multiple tumor types/sites and also represents a more health-protective cancer potency value than the other assessments. Therefore, the US EPA IRIS cancer potency factor (0.4 per mg/kg/day) is the toxicity value recommended for use in the

[4] The NTP (1989) determined that the technical PCP formulation was approximately 90% PCP, 4% tetrachlorophenol, 6% chlorohydroxydiphenyl ethers, with trace amounts of chlorinated dibenzo-*p*-dioxins and dibenzofurans; the EC-7 formulation was approximately 91% PCP, 9% tetrachlorophenol, 4% chlorohydroxydiphenyl ethers, with trace amounts of chlorinated dibenzo-*p*-dioxins and dibenzofurans.

[5] As noted by the US EPA (2010) "This approach assumes independence of tumors. This is a reasonable assumption since NRC (1994) stated that '…a general assumption of statistical independence of tumor-type occurrences within animals is not likely to introduce substantial error in assessing carcinogenic potency.' "

derivation of an oral cancer-based soil cleanup objective for PCP. The PCP risk specific dose calculated from this toxicity value is
2.5×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/15/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

NRC (National Research Council). 1994. Science and Judgment in Risk Assessment. Washington, DC: National Academy Press.

US EPA (United States Environmental Protection Agency). 2010. Toxicological Review of Pentachlorophenol (CAS No. 87-86-5) in Support of Summary Information on the Integrated Risk Information System (IRIS). EPA/635/R-09/004F. Last accessed (01/15/2018) at http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showSubstanceList&list_type=alpha&view=P.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA OPP (United States Environmental Protection Agency, Office of Pesticide Programs). Pesticide Reregistration Status. Last accessed (01/15/2018) at http://www.epa.gov/opp00001/reregistration/status.htm.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Pentachlorophenol
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Pentachlorophenol (CAS Number 87-86-5)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for pentachlorophenol is not available from the authoritative bodies listed in item number 5 (below). Pentachlorophenol is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for pentachlorophenol is 1.0×10^{-3} mg/kg/day. Therefore, a reference concentration of 3.5 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for pentachlorophenol.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Pentachlorophenol (PCP)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for PCP (CAS Number 87-86-5)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA CPF* Also used by: • US EPA RSL*	0.2	5.1×10^{-6} (2)	linearized multistage model	$BW^{¾}$ (3)	Route-specific data suitable for derivation of a chemical-specific inhalation unit risk are not available. The unit risk is based on a route-to-route extrapolation from an oral cancer potency factor based on the increased incidence of liver tumors in male mice exposed via the diet for 2 years to a commercial PCP product.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration = 1×10^{-6} /unit risk.

[2] Value from table in Appendix A of CA EPA cancer potency factor technical support document; Appendix B gives the unit risk as 4.6×10^{-6} $(mcg/m^3)^{-1}$, but that value is not consistent with the stated cancer potency factor $(0.018\ (mg/kg/d)^{-1})$ given in both appendices.

[3]Factor for dose adjustment from animal to humans is $(\text{animal body weight/human body weight})^{0.25}$.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

An inhalation unit risk for PCP based on inhalation data is not available from the authoritative bodies listed in item number 5 (below). PCP is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral cancer potency factor based on cancer effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day can be used to derive a unit risk from an oral cancer potency factor.

CA EPA CPF derived a unit risk by applying a default route-to-route extrapolation (70 kg adult breathing 20 m^3 of air per day) to an oral cancer potency factor based on the increased incidence of liver tumors in male mice exposed via the diet for 2 years to a commercial PCP product (Dowicide EC-7) (see Pentachlorophenol Oral Cancer Toxicity Value Documentation). However, this cancer potency factor was not chosen as the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for PCP. Instead, an oral cancer potency factor (0.4 per mg/kg/day) derived by the US EPA IRIS program was recommended for use in the derivation of an oral cancer-based soil cleanup

objective for PCP (see Pentachlorophenol Oral Cancer Toxicity Value Documentation). Thus, we used the default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation, assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day, to derive an inhalation unit risk from the recommended oral cancer potency factor. Therefore, a unit risk of 1.14×10^{-4} per mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for PCP. The risk specific air concentration calculated from this toxicity value is 8.8×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines Part II: Technical Support Document for Cancer Potency Factors. Last accessed (01/17/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Perfluorooctanoic Acid (PFOA)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for PFOA (CAS Number 335-67-1)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
NYS DEC (2019)	1.5×10^{-6}	4.6×10^{-4}	HED_{LOEL}[2]	300	Based on increased liver weight in offspring of mice exposed by gavage on gestational days 1 to 17. LOEL = 0.3 mg/kg/day.
US EPA (2016)	2.0×10^{-5}	5.3×10^{-3}	HED_{LOEL}[3]	300	Based on decreased bone formation and accelerated male puberty in offspring of mice exposed by gavage on gestational days 1 to 17. LOEL = 1 mg/kg/day.
MDH (2018)	1.8×10^{-5}	5.3×10^{-3}	HED_{LOEL}	300	Based on the same study, effects, and point of departure as US EPA (2016).
NJ DEP (2019)	2.0×10^{-6}	6.1×10^{-4}	$BMSL_{10}$ [4,5]	300	Based on increased relative liver weights in adult mice exposed to a mixture of linear and branched isomers of PFOA by gavage for 14 days. NOEL = 0.3 mg/kg/day; LOEL = 1 mg/kg/day.
CA EPA (2019)	4.5×10^{-7}	1.4×10^{-4}	SL_{LOEL}[6]	300	Based on hepatic mitochondrial membrane potential changes, increased apoptosis, and oxidative DNA damage in female mice exposed by gavage for 28 days. LOEL = 0.05 mg/kg/day.
Health Canada (2018)	2.1×10^{-5}	5.2×10^{-4}	HED_{BMDL10}[7]	25	Based on hepatocellular hypertrophy and increased liver weight in rats exposed in the diet for 13 weeks. NOEL = 0.06 mg/kg/day; LOEL = 0.64 mg/kg/day.
EFSA (2018)	9×10^{-7}	9×10^{-7}	$BMSL_{05}$[8]	1	Based on increased total serum cholesterol in epidemiological studies.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]The HED_{LOEL} is the human exposure at which the human internal dose equals the animal internal dose at the animal LOEL. HED_{LOEL} = PFOA serum concentration x PFOA clearance = 4.98 mg/L x 0.000092 L/kg-day = 0.00046

mg/kg/day. PFOA clearance = (ln2/PFOA half-life) x volume of distribution = (0.693/1277.5 days) x 0.17 L/kg = 0.000092 L/kg-day.

[3]HED_{LOEL} = PFOA serum concentration x PFOA clearance = 38 mg/L x 0.00014 L/kg-day = 0.0053 mg/kg/day. PFOA clearance = (ln2/PFOA half-life) x volume of distribution = (0.693/839.5 days) x 0.17 L/kg = 0.00014 L/kg-day.

[4]The $BMSL_{10}$ or benchmark serum level, is the 95% lower confidence limit on the serum level corresponding to a 10% increase (relative to controls) in the incidence of an adverse effect.

[5]PFOA serum concentration / uncertainty factors = 4.35 mg/L / 300 = 0.0145 mg/L. Reference dose = PFOA serum concentration x PFOA clearance = 0.0145 mg/L x 0.00014 L/kg-day = 2.0 x 10^{-6} mg/kg-day. The PFOA serum concentration of 4.35 mg/L can also be multiplied by the same clearance factor to result in a corresponding administered human equivalent dose of 0.00061 mg/kg-day.

[6]SL_{LOEL} = serum level at the lowest observed effect level. PFOA serum concentration / uncertainty factors = 0.97 mg/L / 300 = 0.0032 mg/L. Reference dose = PFOA serum concentration x PFOA clearance = 0.0032 mg/L x 0.00014 L/kg-day = 4.5 x 10^{-7} mg/kg-day. The PFOA serum concentration of 0.97 mg/L can also be multiplied by the same clearance factor to result in a corresponding human equivalent dose of 0.00014 mg/kg-day.

[7]The HED_{BMDL10} is the human exposure at which the human internal dose equals the animal internal dose at the 95% lower confidence limit on the benchmark dose (BMDL) corresponding to a 10% increase (relative to controls) in the incidence of an adverse effect. HED_{BMDL10} = $BMDL_{10}$ / AK_{UF} = 0.05 mg/kg-day / 96 = 0.000521 mg/kg-day.

[8]The $BMSL_{05}$ or benchmark serum level, is the 95% lower confidence limit on the serum level corresponding to a 5% increase (relative to controls) in the incidence of an effect.

mg/kg/day: milligrams per kilogram per day; NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor; HED: human equivalent dose; BMDL: benchmark dose level: BMSL: benchmark serum level; SL: serum level.

2. Recommendation and Rationale

The United States Environmental Protection Agency (US EPA), Minnesota Department of Health (MDH), New Jersey Department of Environmental Protection (NJ DEP), California Environmental Protection Agency, Health Canada, European Food Safety Authority Panel on Contaminants in the Food Chain (EFSA CONTAM), and the New York State Department of Environmental Conservation (NYS DEC) all derived reference doses for PFOA.

The European Food Safety Authority Panel on Contaminants in the Food Chain (EFSA CONTAM 2018) tolerable daily intake (TDI) is the only value based on epidemiology studies. EFSA CONTAM's TDI is based on increased total serum cholesterol in human epidemiological studies as part of a scientific opinion on the risks of PFOA in food. In general, cross-sectional studies such as those used by EFSA CONTAM in a weight of evidence approach don't provide sufficient evidence on their own to establish causality. There is also no clear consensus among health agencies about whether the limitations of these cross-sectional studies preclude their use for quantitative risk assessment (NJ DWQI 2017; ATSDR 2018). Further, the TDI is based on a risk factor (increased serum cholesterol) rather than an adverse effect. Based on these uncertainties, the EFSA CONTAM TDI is not considered further as the basis for a noncancer PFOA soil cleanup objective.

The US EPA (2016) reference dose is based on a developmental toxicity study in mice exposed to PFOA on gestational days 1 to 17 (Lau et al. 2006). The US EPA used a pharmacokinetic model to predict average PFOA serum concentrations from administered doses. The serum concentration at the LOEL was converted to a human equivalent dose using a human one-compartment pharmacokinetic model. Uncertainty factors of 10 for human variation, 3 for pharmacodynamic differences between animals and humans, and 10 for use of a LOEL (total uncertainty factor of 300) were applied to the point of departure to obtain the reference dose of 2 x 10^{-5} mg/kg/day. The MDH (2018) used the same study, toxicological endpoint, and point of departure as the US EPA to derive a numerically similar reference dose. Like the US EPA, a total uncertainty factor of 300 was applied to the point of departure, but a

lower uncertainty factor for use of a LOEL (3 instead of 10) was applied, and an addition uncertainty factor for database incompleteness (3) was added.

Health Canada (2018) based its reference dose on hepatocellular hypertrophy in male rats exposed to PFOA for 13 weeks in the diet (Perkins et al. 2004). Benchmark dose modeling of administered doses was conducted to obtain the lower bound on the dose associated with a 10% response (0.05 mg/kg/day). This dose was adjusted through application of a species and dose range-specific toxicokinetic uncertainty factor of 96 to obtain a human equivalent dose. A total uncertainty factor of 25 (2.5 for toxicodynamic differences and 10 for human variation) was then applied to obtain the reference dose of 2.1×10^{-5} mg/kg/day.

The NJ DEP (2019) derived a reference dose based on liver toxicity (increased relative liver weights) in adult mice exposed to a mixture of linear and branched isomers of PFOA for 14 days (Loveless et al. 2006). Measured PFOA serum levels at each dose were used to obtain the lower bound on the modeled serum level corresponding to a 10% response in increased liver weight (4.35 mg/L) which was used as the point of departure. A total uncertainty factor of 300 (10 for human variation, 10 for database incompleteness, and 3 for pharmacodynamic differences between animals and humans) was applied to obtain a target human serum level of 0.0145 mg/L, which was converted to the reference dose of 2×10^{-6} mg/kg/day using the same one-compartment pharmacokinetic model used by the US EPA (2016).

The NYS DEC (2019) derived a reference dose based on increased liver weights observed in the offspring of mice exposed during days 1 to 17 of gestation (Macon et al. 2011). Measured serum PFOA levels at the LOEL were used as the basis of the point of departure. A human equivalent dose of 0.0046 mg/kg/day was calculated from the serum level at the LOEL using a human one compartment model. A total UF of 300, which included factors of 3 for use of a LOEL, 3 for interspecies pharmacodynamic differences, 10 for variability in humans, and 3 for database deficiencies (to account for limited evidence for effects on the liver and on mammary gland development at PFOA exposures lower than 0.3 mg/kg-day [Macon et al., 2011; Tucker et al., 2015; Quist et al., 2015]), was applied to obtain the reference dose of 1.5×10^{-6} mg/kg/day.

The CA EPA (2019) based its acceptable daily dose (equivalent to a reference dose) on hepatocellular effects observed in mice (changes in mitochondrial membrane potential, oxidative stress with DNA damage, and apoptosis) exposed for 28 days (Li et al. 2017). A total uncertainty factor of 300 (3 for interspecies extrapolation, 10 for human variation, 3 for LOEL to NOEL extrapolation, and 3 for potential developmental toxicity at the point of departure) was applied to the measured serum level at the LOEL (0.97 mg/L) to obtain a target human serum concentration of 0.0032 mg/L. The CA EPA then used the human single compartment pharmacokinetic model used by the US EPA (2016) to convert the target serum concentration to a reference dose of 4.5×10^{-7} mg/kg/day.

The reference doses derived by the US EPA, the MDH, and Health Canada are based on studies that identify a LOEL at a higher administered dose than the studies used by the NYS DEC and CA EPA, which suggest a more sensitive toxicological endpoint for the latter derivations. The CA EPA derivation is based on a LOEL for effects on morphology and function of hepatic mitochondria, and evidence for DNA damage and apoptosis, which are sensitive and subtle upstream changes that may or may not lead to gross functional or morphological adverse effects. The Li et al. (2017) study reported gross morphological changes at the same general administered dose in mice (hepatic hypertrophy at 0.5 mg/kg/day) as the maternal dose in the Macon et al. (2011) study that increased relative liver weights in the offspring (0.3 mg/kg/day). The CA EPA derivation also uses an additional uncertainty factor of 3 to account for the possibility that developmental effects could occur at the LOEL, based on a study reporting reduced body weights on postnatal day 4 in the offspring of mice exposed to 0.01 mg/kg/day for 11 weeks prior and during mating, and throughout gestation and lactation (van Esterick et al. 2016).

Comparison of exposures in this study on an internal dose basis to those of other studies is not possible since PFOA serum levels, the preferred dose metric for PFOA, were not measured. Based on these uncertainties, the sensitive nature of the effects and the minimal LOEL on which the reference dose is based, an extra uncertainty factor for database uncertainties may not be necessary to provide adequate protection against adverse effects. Removal of this uncertainty factor would render a reference dose similar to those derived by the NYS DEC and NJ DEP. The NJ DEP and NYS DEC derived similar reference doses, based respectively on increased liver weights in adult mice exposed 14 days (Loveless et al. 2006) and in the offspring of dams exposed gestationally (Macon et al. 2011). Both studies measured serum PFOA levels, which is the preferred dose metric for evaluating exposure. The NYS DEC derivation is based on a study that reported effects at a lower administered dose (0.3 mg/kg/day compared to 1 mg/kg/day) during early lifestages, which represents a particularly vulnerable window for PFOA toxicity in humans. Based on these considerations, the NYS DEC reference dose (1.5×10^{-6} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for PFOA.

3. Review Dates

Summary table completion: January 2020
Toxicity value recommendation: January 2020

4. References for Summary Table and Recommendation and Rationale

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NJ DEP (New Jersey Department of Environmental Protection). 2019. Technical Support Document: Interim Specific Ground Water Criterion for Perfluorooctanoic Acid (PFOA, C8) (CAS #: 335-67-1; Chemical Structure: CF3(CF2)6COOH). Division of Science and Research. Last accessed (04/10/2019) at https://www.nj.gov/dep/dsr/supportdocs/PFOA_TSD.pdf.

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5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
Maine Center for Disease Control and Prevention
Minnesota Department of Health
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New Jersey Department of Environmental Protection
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
  Integrated Risk Information System
  Office of Drinking Water

Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
Health Effects Assessment Summary Tables
Provisional Peer Reviewed Toxicity Values
Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Perfluorooctanoic Acid (PFOA)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for PFOA (CAS Number 335-67-1)

Agency	Risk-Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
NYS DEC (2019)	1.9×10^{-7}	5.3	Linearized multistage model with linear extrapolation from a $BMSL_{10}$ (2)	Single compartment human PBPK model [3]	Based on Leydig cell tumors in male rats exposed via the diet for two years. Area under the curve PFOA serum concentrations were estimated from administered doses using the rat PBPK model of Tardiff et al. (2009).
US EPA (2016)	1.4×10^{-5}	0.07	Linearized multistage model with linear extrapolation from a $BMDL_{04}$ (4)	$BW^{¾}$ (5)	Based on the same study and tumor incidence used by NYS DEC. A $BMDL_{04}$ was modeled based on administered doses.
NJ DEP (2019)	4×10^{-7}	2.5	Gamma and log logistic dose-response models with linear extrapolation from the average $BMDL_{05}$ (6)	Pharmacokinetic (PK) factor based on the ratio of serum half-lives in humans and male rats [7]	Based on the same study and tumor incidence used by NYS DEC. Administered doses were modeled to $BMDL_{05}$ values. An average $BMDL_{05}$ from two different models was used.
CA EPA (2019)	7.0×10^{-9}	143	Linear multistage model with linear extrapolation from $BMDL_{05}$ (6)	Single compartment human PBPK model and $BW^{1/8}$ adjustment [8]	Based on the combination of hepatocellular adenomas or carcinomas and pancreatic acinar cell adenomas or carcinomas in male rats exposed in the diet for 107 weeks. A $BMDL_{05}$ was modeled based on human equivalent doses.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2]The $BMSL_{10}$ is the 95% lower confidence limit on the serum level corresponding to a 10% increase (relative to controls) in the incidence of tumors.

[3]Human equivalent dose = $BMSL_{10}$ x PFOA clearance = 203 mg/L x 0.000092 L/kg-day = 1.9 x 10^{-2} mg/kg/day. One-in-one million dose = 1.9 x 10^{-2} mg/kg/day / 100,000 = 1.9 x 10^{-7} mg/kg/day. PFOA clearance = (ln2/PFOA half-life) x volume of distribution = (0.693/1277.5 days) x 0.17 L/kg = 0.000092 L/kg-day.

[4]The $BMDL_{04}$ is the 95% lower confidence limit on the benchmark dose corresponding to a 4% increase (relative to controls) in the incidence of tumors.

[5]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$. One-in-one million dose = 0.58 mg/kg/day / 40,000 = 1.4 x 10^{-5} mg/kg/day.

[6] The $BMDL_{05}$ is the 95% lower confidence limit on the benchmark dose corresponding to a 5% increase (relative to controls) in the incidence of tumors.

[7]Human equivalent dose = $BMDL_{05}$ / pharmacokinetic factor = 2.36 mg/kg/day /120 = 0.02 mg/kg/day. One-in-one million dose = 0.02 mg/kg/day / 50,000 = 4.0 x 10^{-7} mg/kg/day. Pharmacokinetic factor = serum half life (humans) / serum half life (rats) = 840 days / 7 days = 120.

[8]Human equivalent doses calculated from each measured serum concentrations using PFOA clearance of 0.00014 L/kg-day (US EPA 2016). PFOA clearance = (ln2/PFOA half-life) x volume of distribution = (0.693/839.5 days) x 0.17 L/kg = 0.00014 L/kg-day. Factor for dose adjustment for pharmacodynamic differences is (animal body weight/human body weight)$^{0.125}$. One-in-one million dose = 3.5 x 10^{-4} mg/kg/day / 50,000 = 7.0 x 10^{-9} mg/kg/day.

mg/kg/day: milligrams per kilogram per day; PBPK: physiologically-based pharmacokinetic; BMSL: lower bound on benchmark serum concentration; BMDL: lower bound on benchmark dose; mg/L: milligrams per liter; L/kg-day: liters per kilogram per day.

3. Recommendation and Rationale

The cancer potency factors derived for PFOA by the New York State Department of Envirnmental Conservation (NYS DEC), the United States Environmental Protection Agency (US EPA) and the New Jersey Department of Environmental Protection (NJ DEP) are based on an increased incidence of Leydig cell tumors (also called testicular interstitial cell tumors) in male rats reported in a two-year dietary study (Sibinski 1987; Butenhoff et al. 2012). The US EPA (2016) modeled a $BMDL_{04}$ based on administered doses, and then used a default allometric scaling approach (i.e., $BW^{3/4}$ scaling) to calculate a human equivalent dose, followed by linear extrapolation to a dose corresponding to an increased lifetime risk of one-in-one million. The use of default allometric scaling in the US EPA (2016) derivation to calculate a human equivalent dose for PFOA is not a preferred interspecies extrapolation method because it does not adequately adjust for the large pharmacokinetic differences in PFOA serum clearance between animals and humans (as compared with available pharmacokinetic models), which could potentially underestimate the cancer potency.

The NJ DEP (2017) used dose response modeling to obtain a $BMDL_{05}$ based on administered doses followed by linear extrapolation to the one-in-one million dose, which was converted to a human equivalent dose using a pharmacokinetic adjustment factor based on the ratio of half-lives for humans and male rats. The NYS DEC cancer potency factor is based on the work of Tardiff et al. (2009), who used a pharmacokinetic model (Tan et al. 2008) to convert the administered experimental doses reported in Butenhoff et al. (2012) to rat PFOA plasma concentrations. Tardiff et al (2009) then used the linearized multistage model to estimate the PFOA concentration in plasma associated with a 10% tumor incidence rate. The NYS DEC then converted to a human equivalent dose using a human one compartment pharmacokinetic model, followed by linear extrapolation to the one-in-one million dose. The NYS DEC and NJ DEP (2019) derivations are comparable, with the NYS DEC derivation being preferred because it uses an internal dose metric (i.e., serum PFOA levels) as the point of departure.

The California Environmental Protection Agency (CA EPA) cancer potency factor is based on the combined incidence of hepatocellular adenomas or carcinomas and pancreatic acinar cell adenomas or carcinomas reported in a National Toxicology Program two-year dietary study in rats (NTP 2019). A draft report of the NTP study has been released for peer review, but has not yet been finalized. There are

also apparent discrepancies in the tumor incidences used in the CA EPA derivation and those reported in the draft NTP report. Finally, the CA EPA derivation applies an additional pharmacodynamic adjustment factor to the human equivalent dose which suggests a greater sensitivity of humans to the carcinogenic effects of PFOA (compared to rats), but the documentation provides no detailed justification for this assumption. Given the draft status of the NTP report, and the uncertainty regarding tumor incidence and the use of a pharmacodynamic adjustment factor, the CA EPA estimate of potency is not used as the basis for a PFOA soil cleanup objective. Therefore, the NYS DEC cancer potency factor (5.3 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for PFOA. The PFOA risk specific dose calculated from this toxicity value is 1.9×10^{-7} mg/kg/day.

4. Review Dates

Summary table completion: January 2020
Toxicity value recommendation: January 2020

5. References for Summary Table and Recommendation and Rationale

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NJ DEP (New Jersey Department of Environmental Protection). 2019. Technical Support Document: Interim Specific Ground Water Criterion for Perfluorooctanoic Acid (PFOA, C8) (CAS #: 335-67-1; Chemical Structure: CF3(CF2)6COOH). Division of Science and Research. Last accessed (04/10/2019) at https://www.nj.gov/dep/dsr/supportdocs/PFOA_TSD.pdf.

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6. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Perfluorooctanoic Acid (PFOA)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for PFOA (CAS Number 335-67-1)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for PFOA is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

PFOA is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the recommended reference dose based on systemic effects (1.5×10^{-6} mg/kg/day; see Oral Non-Cancer Toxicity Value Documentation). Therefore, a reference concentration of 5.2×10^{-3} mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for PFOA.

3. Review Dates

Summary table completion: January 2020
Toxicity value recommendation: January 2020

4. References for Summary Table and Recommendation and

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System

Office of Drinking Water
Office of Pesticide Programs
Office of Superfund Remediation and Technology Innovation
Health Effects Assessment Summary Tables
Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Perfluorooctanoic Acid (PFOA)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for PFOA (CAS Number 335-67-1)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
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[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} concentration), where 1×10^{-6} air concentration = 1×10^{-6} /unit risk.

2. Recommendation and Rationale

PFOA is a toxicant that is expected to be absorbed into the body and cause systemic cancer effects after oral or inhalation exposure. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day was used to derive a unit risk from the recommended cancer potency factor. The recommended oral cancer potency factor for PFOA is 5.3 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for PFOA). Therefore, a unit risk of 1.5×10^{-3} per mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for PFOA. The risk specific air concentration calculated from this toxicity value is 6.6×10^{-4} mcg/m^3.

3. Review Dates

Summary table completion: January 2020
Toxicity value recommendation: January 2020

4. References for Summary Table and Recommendation and Rationale

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation

New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Perfluorooctanesulfonic Acid (PFOS)
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for PFOS (CAS Number 1763-23-1)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA (2016)	2.0×10^{-5}	5.1×10^{-4}	HED_{NOEL}[2]	30	Based on reduced body weight in the offspring of rats exposed by gavage in a two-generation study. NOEL = 0.1 mg/kg/day; LOEL = 0.4 mg/kg/day
MDH (2019)	3.1×10^{-6}	3.1×10^{-4}	HED_{NOEL}[3]	100	Based on immune effects (increased interleukin 4 and decreased sheep red blood cell-specific IgM levels) in male mice exposed for 60 days. NOEL = 0.0167 mg/kg/day; LOEL = 0.083 mg/kg/day.
NJ DEP (2019) Also used by: ◆ NYS DEC (2019) ◆ CA EPA (2019)	1.8×10^{-6}	5.5×10^{-4}	SL_{NOEL}[4]	30	Based on immune effects (decreased plaque forming cell response) in male mice exposed for 60 days. NOEL = 0.0083 mg/kg/day; LOEL = 0.083 mg/kg/day
Health Canada (2018)	6.0×10^{-5}	1.5×10^{-3}	HED_{NOEL}[5]	25	Based on increased liver weights in male rats exposed in the diet for two years. NOEL = 0.021 mg/kg/day; LOEL = 0.098 mg/kg/day.
EFSA (2018)	1.8×10^{-6}	1.8×10^{-6}	$BMSL_{05}$[6]	1	Based on increased total serum cholesterol in epidemiological studies.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]The HED_{NOEL} is the human exposure at which the human internal dose equals the animal internal dose at the animal NOEL. HED_{NOEL} = PFOS serum concentration x PFOS clearance = 6.26 mg/L x 0.000081 L/kg/day = 0.00051

mg/kg/day. PFOS clearance = (ln2/PFOS half-life) x volume of distribution = (0.693/1971 days) x 0.23 L/kg = 0.000081 L/kg-day.

[3]HED_{NOEL} = PFOS serum concentration x PFOS clearance = 2.36 mg/L x 0.00013 L/kg-day = 0.000307 mg/kg-day. PFOS clearance = (ln2/PFOS half-life) x volume of distribution = (0.693/1241 days) x 0.23 L/kg = 0.00013 L/kg-day.

[4]SL_{NOEL} = serum level at the no observed effect level. PFOS serum concentration / uncertainty factors = 0.674 mg/L / 30 = 0.0225 mg/L. Reference dose = PFOS serum concentration x PFOS clearance = 0.0225 mg/L x 0.000081 L/kg-day = 2×10^{-6} mg/kg/day. The PFOS serum concentration of 0.674 mg/L can also be multiplied by the same clearance factor to result in a corresponding human equivalent dose of 5.5×10^{-5} mg/kg/day.

[5]HED_{NOEL} = NOEL / AK_{UF} = 0.021 mg/kg/day /14 = 0.0015 mg/kg/day.

[6]The $BMSL_{05}$ or benchmark serum level, is the 95% lower confidence limit on the serum level corresponding to a 5% increase (relative to controls) in the incidence of an effect.

mg/kg/day: milligrams per kilogram per day; NOEL: no-observed-effect level; LOEL: lowest observed effect level; UF: uncertainty factor; HED = human equivalent dose; SL = serum level; BMSL: benchmark serum level.

2. Recommendation and Rationale

The United States Environmental Protection Agency (US EPA), Minnesota Department of Health (MDH), New Jersey Department of Environmental Protection (NJ DEP), Health Canada, and the European Food Safety Authority Panel on Contaminants in the Food Chain (EFSA CONTAM) all derived reference doses for PFOA.

The European Food Safety Authority Panel on Contaminants in the Food Chain (EFSA CONTAM 2018) tolerable daily intake (TDI) is the only value based on epidemiology studies. EFSA CONTAM's TDI is based on increased total serum cholesterol in human epidemiological studies as part of a scientific opinion on the risks of PFOS in food. In general, cross-sectional studies such as those used by EFSA CONTAM in a weight of evidence approach don't provide sufficient evidence on their own to establish causality. There is also no clear consensus among health agencies about whether the limitations of these cross-sectional studies preclude their use for quantitative risk assessment (NJ DEP 2019; ATSDR 2018). Further, the TDI is based on a risk factor (increased serum cholesterol) rather than an adverse effect. Based on these uncertainties, the EFSA CONTAM TDI is not considered further as the basis for a noncancer PFOS soil cleanup objective.

The US EPA (2016) based its reference dose on reduced body weight in the offspring of rats exposed to PFOS by gavage in a two-generation study (Luebker et al. 2005). The US EPA used a pharmacokinetic model to predict average PFOS serum concentrations from administered doses. The serum concentration at the NOEL was converted to a human equivalent dose using a human one-compartment pharmacokinetic model. Uncertainty factors of 10 for human variation and 3 for phamacodynamic differences between animals and humans were applied to the point of departure to obtain the reference dose of 2×10^{-5} mg/kg/day.

The MDH (2019) derived its reference dose based on immune effects (increased interleukin 4 and decreased sheep red blood cell-specific IgM levels) in adult male mice exposed to PFOS for 60 days (Dong et al. 2011). The measured PFOS serum level at the NOEL was converted to a human equivalent dose using a human one compartment model. The MDH then applied a total uncertainty factor of 100 to the point of departure (10 for human variation, 3 for pharmacodynamic differences between animals and humans, and 3 for database uncertainty) to obtain the reference dose of 3.1×10^{-6} mg/kg/day.

The NJ DEP (NJ DEP 2019) derived a reference dose based on immune effects (decreased plaque forming cell response) in adult male mice exposed to PFOS for 60 days (Dong et al. 2009). A total uncertainty factor of 30 (10 for human variation and 3 for pharmacodynamic differences between humans and animals) was applied to the measured serum concentration at the NOEL to obtain a

reference serum level, which was converted to the reference dose of 2×10^{-6} mg/kg/day using the same one compartment pharmacokinetic model used by the US EPA (2016).

Health Canada (2018) derived a reference dose based on liver toxicity (hepatocellular hypertrophy) in rats exposed in the diet for two years (Butenhoff et al. 2012). The administered dose at the NOEL was adjusted through application of a species and dose range-specific toxicokinetic uncertainty factor of 14 to obtain a human equivalent dose. A total uncertainty factor of 25 (2.5 for toxicodynamic differences and 10 for human variation) was then applied to obtain the reference dose of 6.0×10^{-5} mg/kg/day.

The reference doses derived by the US EPA and Health Canada are based on studies that identify a LOEL at a higher administered dose than the studies used by the MDH and NJ DEP, which suggest a more sensitive toxicological endpoint for the latter derivations. Both the MDH and NJ DEP reference doses are also based on immune effects, which is a well-established and sensitive endpoint for PFOS in animals. In addition, epidemiological studies have reported associations between serum PFOS levels and immunotoxicity (Grandjean et al., 2012; Granum, 2013; Stein et al., 2016), and a recent major report on PFOS immunotoxicity by the National Toxicology Program (2016) concluded that PFOS is presumed to be an immune hazard to humans.

The MDH and NJ DEP are based on separate but similar studies by the same investigators which reported a LOEL at the same administered dose in mice exposed for 60 days (Dong et al. 2009; Dong et al. 2011). The MDH derivation starts with a 3.5-fold higher PFOA serum level at the NOEL (2.36 mg/L compared to 0.674 mg/L), and also employs a 1.6-fold higher human clearance factor calculated with a shorter assumed mean half-life than was used by the NJ DEP (3.4 years [Li et al. 2018] compared to 5.4 years [Olsen et al. 2007]). The Olsen et al. (2007) study is preferred as the basis for estimating the average PFOS half-life because it followed the study participants for a longer period (over 5 years compared to just over 2 years), which better accounts for the possibility that the rate of clearance could change over time. However, the MDH uses an additional uncertainty factor for database deficiencies, resulting in a reference dose that is comparable to that of the NJ DEP value. The slightly lower NJ DEP reference dose (1.8×10^{-6} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for PFOS.

3. Review Dates

Summary table completion: January 2020
Toxicity value recommendation: January 2020

4. References for Summary Table and Recommendation and Rationale

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Butenhoff, J.L., Chang, S.C., Olsen, G.W. et al. 2012. Chronic dietary toxicity and carcinogenicity study with potassium perfluorooctanesulfonate in Sprague Dawley rats. Toxicol 293: 1–15.

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Health Canada. 2018. Guidelines for Canadian Drinking Water Quality: Guideline Technical Document – Perflourooctane Sulfonate (PFOS). Last accessed (9/1/19) at https://www.canada.ca/en/health-canada/services/publications/healthy-living/guidelines-canadian-drinking-water-quality-guideline-technical-document-perfluorooctane-sulfonate/document.html#a11.0.

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5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
European Food Safety Authority
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Perfluorooctanesulfonic Acid (PFOS)
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for PFOS (CAS Number 1763-23-1)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
NYS DEC (2019)	7.8×10^{-8}	12.8	Linearized multistage model with linear extrapolation from $BMSL_{05}$ (2)	Single-compartment human PBPK model [3]	Based on the incidence of hepatocellular adenomas in male rats and the combined incidence of hepatocellular adenomas and carcinomas in female rats exposed to PFOS in the diet for two years. Area under the curve PFOS serum concentrations were modeled to a $BMSL_{05}$ for males and females. The median $BMSL_{05}$ was used for the potency estimate.
NJ DEP (2019)	1.1×10^{-7}	9.0	Gamma dose-response model with linear extrapolation from $BMSL_{10}$ (4)	Single-compartment human PBPK model [5]	Based on the combined incidence of hepatocellular adenomas and carcinomas in female rats in the same study used by NYS DEC. A $BMSL_{10}$ was modeled from measured serum concentrations.
CA EPA (2019)	2.2×10^{-8}	45.5	Linearized multistage model with linear extrapolation from a $BMDL_{05}$ (6)	Single compartment human PBPK model and $BW^{1/8}$ adjustment [7]	Based on the incidence of hepatocellular adenomas in male rats in the same study used by NYS DEC. A $BMDL_{05}$ was modeled based on human equivalent doses.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} cancer potency factor.

[2]The $BMSL_{05}$ is the 95% lower confidence limit on the serum level corresponding to a 5% increase (relative to controls) in the incidence of tumors.

[3]Human equivalent dose = $BMSL_{05}$ x PFOS clearance = 48.1 mg/L x 0.000081 L/kg-day = 3.9×10^{-3} mg/kg/day. One-in-one million dose = 3.9×10^{-3} mg/kg/day / 50,000 = 7.8×10^{-8} mg/kg/day. PFOS clearance = (ln2/PFOS half-life) x volume of distribution = (0.693/1971 days) x 0.23 L/kg = 0.000081 L/kg-day (US EPA 2016).

[4]The $BMSL_{10}$ is the 95% lower confidence limit on the serum level corresponding to a 10% increase (relative to controls) in the incidence of tumors.

[5]Cancer potency based on serum concentration = 0.1 / 136,931 ng/mL = 7.3×10^{-7} per ng/mL. Human cancer potency = [7.3×10^{-7} per ng/mL] x [1 / 0.000081 L/kg-day] x [1L/1000 mL] = 9.0×10^{-6} per ng/kg/day or 9.0 per mg/kg/day.

[6] The $BMDL_{05}$ is the 95% lower confidence limit on the benchmark dose corresponding to a 5% increase (relative to controls) in the incidence of tumors.

[7]Human equivalent doses calculated from each measured serum concentrations using PFOS clearance of 0.000081 L/kg-day (US EPA 2016). Factor for dose adjustment for pharmacodynamic differences is (animal body weight/human body weight)$^{0.125}$. One-in-one million dose = 0.0011 mg/kg/day / 50,000 = 2.2×10^{-8} mg/kg/day.

mg/kg/day: milligrams per kilogram per day; BMSL: lower bound on benchmark serum concentration; PBPK: physiologically-based pharmacokinetic; BMDL: lower bound on benchmark dose; mg/L: milligrams per liter; L/kg-day: liters per kilogram per day; ng/mL: nanograms per milliliter.

2. Recommendation and Rationale

New York State Department of Environmental Conservation (NYS DEC), the New Jersey Department of Environmental Protection (NJ DEP) and the California Environmental Protection Agency (CA EPA) all derived cancer potency factors for PFOS based on the same two-year dietary study in rats (Butenhoff et al., 2012; OECD, 2002). All of the derivations use a one compartment pharmacokinetic model to obtain their estimates of human equivalent doses. The CA EPA derivation applies an additional pharmacodynamic adjustment factor to the human equivalent dose, which suggests a greater sensitivity of humans to the carcinogenic effects of PFOS compared to rats. However, the technical documentation for the CA EPA derivation provides no detailed justification for this assumption, and therefore this potency estimate is not considered further. The potency estimates of the NYS DEC and the NJ DEP derivations are comparable. The NJ DEP based its potency estimate on hepatocellular tumors in the female rats and included the tumor incidence from a high dose recovery group in its dose response modeling. The recovery group was exposed for the first year of the study and then fed a control diet for the remainder, and thus the dose response modeling included animals exposed to PFOS for disparate lengths of time. The NYS DEC derivation used only tumor incidence data for animals exposed for equal periods of time (i.e., for the entire length of the study). The NYS DEC derivation also used a median $BMSL_{05}$ calculated from separate values for males and females in the absence of evidence that one sex is a better surrogate for humans, and that the $BMSL_{05}$ estimates for males and females differed by only about 2-fold. Based on these considerations, the NYS DEC cancer potency factor (12.8 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for PFOS. The PFOS risk specific dose calculated from this toxicity value is 7.8×10^{-8} mg/kg/day.

3. Review Dates

Summary table completion: January 2020
Toxicity value recommendation: January 2020

4. References for Summary Table and Recommendation and Rationale

Butenhoff JL, SC Chang, GW Olsen. 2012. Chronic dietary toxicity and carcinogenicity study with potassium perfluorooctanesulfonate in Sprague Dawley rats. Toxicology 293(1-3): 1-15.

CA EPA (California Environmental Protection Agency). 2019. Perflurooctanoic Acid and Perfluorooctane Sulfonate in Drinking Water. Last accessed (9/15/2019) at https://oehha.ca.gov/media/downloads/water/chemicals/nl/final-pfoa-pfosnl082119.pdf

NYS DEC (New York State Department of Environmental Conservation). 2019. Draft Human Health Fact Sheet. Ambient Water Quality Value for Protection of Human Health and Sources of Potable Water. Perfluorooctane Sulfonic Acid. Albany, NY: Division of Water.

NJ DEP (New Jersey Department of Environmental Protection). 2019. Technical Support Document: Interim Specific Ground Water Criterion for Perfluorooctane Sulfonate (PFOS) (CAS #: 1763-23-1; Chemical Formula: C8HF17O3S). Division of Science and Research. Last accessed (04/09/19) at https://www.nj.gov/dep/dsr/supportdocs/NewSupportDocuments.html.

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5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Perfluorooctanesulfonic Acid (PFOS)
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for PFOS (CAS Number 1763-23-1)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	A reference concentration for PFOS is not available from the authoritative bodies listed in item 5 (below).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

PFOS is a toxicant that is expected to be absorbed into the body and cause systemic non-cancer effects following oral or inhalation exposure. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the recommended reference dose based on systemic effects (1.8×10^{-6} mg/kg/day; see Oral Non-Cancer Toxicity Value Documentation). Therefore, a reference concentration of 6.3×10^{-3} mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for PFOS.

3. Review Dates

Summary table completion: January 2020
Toxicity value recommendation: January 2020

4. References for Summary Table and Recommendation and Rationale

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
Integrated Risk Information System

Office of Drinking Water
Office of Pesticide Programs
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Health Effects Assessment Summary Tables
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Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Perfluorooctanesulfonic Acid (PFOS)
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for PFOS (CAS Number 1763-23-1)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
---	---	---	---	---	A unit risk for PFOS is not available from the authoritative bodies listed in item 5 (below).

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} concentration), where 1×10^{-6} air concentration = 1×10^{-6} /unit risk.

2. Recommendation and Rationale

PFOS is a toxicant that is expected to be absorbed into the body and cause systemic cancer effects after oral or inhalation exposure. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day was used to derive a unit risk from the recommended cancer potency factor. The recommended oral cancer potency factor for PFOS is 12.8 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for PFOS). Therefore, a unit risk of 3.6×10^{-3} per mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for PFOS. The risk specific air concentration calculated from this toxicity value is 2.7×10^{-4} mcg/m^3.
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3. Review Dates

Summary table completion: January 2020
Toxicity value recommendation: January 2020

4. References for Summary Table and Recommendation and Rationale

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health

United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Phenanthrene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Phenanthrene (CAS Number 85-01-8)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
RIVM (2001)	0.04	--	--	--	Based on RIVM's evaluation of total petroleum hydrocarbons and its designation of phenanthrene as a non-carcinogenic aromatic hydrocarbon with an equivalent carbon number[2] >8 to 16.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]Equivalent carbon (EC) number is an index based on the boiling point of a chemical normalized to the boiling point of n-alkanes or its retention time in a boiling point gas chromatographic column (GC). In other words, the EC number of compound X represents the number of carbon atoms that an imaginary n-alkane should have in order to present exactly the same boiling point as compound X.

2. Recommendation and Rationale

Chemical-specific reference doses for phenanthrene have not been derived by the authoritative bodies listed in item 5 (see below). Phenanthrene is an aromatic hydrocarbon and can be placed in a specific fraction of total petroleum hydrocarbons (i.e., non-carcinogenic aromatic hydrocarbon with an equivalent carbon (EC) number in the $>EC_8$ to EC_{16} range). The RIVM reference dose for this fraction of total petroleum hydrocarbons is 0.04 mg/kg/day, and thus this value became the reference dose for phenanthrene. The reference dose for the $>EC_8$ to EC_{16} fraction was a composite value based on the reference doses for eight chemicals (isopropylbenzene, acenaphthene, biphenyl, fluorene, anthracene, fluoranthene, naphthalene, and pyrene) and a mixture of two chemicals (naphthalene and methylnaphthalene) within this fraction. These reference doses ranged from 0.03 to 0.3 mg/kg/day, and four of the reference doses were 0.04 mg/kg/day.

Phenanthrene also is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). However, four of the chemicals (isopropylbenzene, biphenyl, naphthalene, and methylnaphthalene) used to obtain the composite RIVM reference dose are not polycyclic aromatic hydrocarbons, which weakens confidence in using them as chemical surrogates for phenanthrene.

Reference doses derived from chemical-specific toxicity data are available for six polycyclic aromatic hydrocarbons identified as priority contaminants in the Brownfield Cleanup Program (acenaphthene, anthracene, benzo[a]pyrene, fluoranthene, fluorene, and pyrene, see NYS [2006]). Phenanthrene is chemically similar to each of these six listed polycyclic aromatic hydrocarbons. Each of these six priority contaminants could be used to represent the noncancer toxicity of phenanthrene. Similarity of

chemical structure cannot be used as a basis of choosing a chemical surrogate for phenanthrene because toxicity data are insufficient to accurately describe the relationship between the chemical structure and non-cancer toxicity of polycyclic aromatic hydrocarbons. The recommended reference dose for benzo[a]pyrene is lower than that of the other five polycyclic aromatic hydrocarbons, and is also lower than the RIVM reference dose for the $>EC_8$ to EC_{16} fraction of total petroleum hydrocarbons. Without data on which of these six polycyclic aromatic hydrocarbons or the $>EC_8$ to EC_{16} fraction of total petroleum hydrocarbons would be the best surrogate for phenanthrene, the recommended reference dose for benzo[a]pyrene (3×10^{-4} mg/kg/day, see Oral Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for phenanthrene.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/14/2018) at http://www.dec.ny.gov/chemical/34189.html.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/14/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Phenanthrene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Phenanthrene (CAS Number 85-01-8)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1995)	--	--	--	--	Human data are not available. Data from a single gavage study in rats are inadequate. Convincing evidence of carcinogenicity was not observed in skin painting and injection studies in mice.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for phenanthrene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. Toxicological Profile for Polycyclic Aromatic Hydrocarbons. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Phenanthrene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Phenanthrene (CAS Number 85-01-8)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

Phenanthrene is a polycyclic aromatic hydrocarbon (i.e., a chemical with three or more fused aromatic rings containing only carbon and hydrogen atoms). A reference concentration based on chemical-specific inhalation toxicity data for phenanthrene is not available from the authoritative bodies listed in item 5 (below).

Benzo[a]pyrene is the only polycyclic aromatic hydrocarbon identified as a priority contaminant in the Brownfield Cleanup Program for which a reference concentration is available. Benzo[a]pyrene is chemically similar to phenanthrene and can be used to represent the noncancer inhalation toxicity of phenanthrene (see Inhalation Non-Cancer Toxicity Value Documentation for Benzo[a]pyrene). Therefore, based on using benzo[a]pyrene as a chemical surrogate, a reference concentration of 2×10^{-3} mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for phenanthrene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table

NYS (New York State). 2006. New York State Brownfield Cleanup Program. Development of Soil Cleanup Objectives. Technical Support Document. Last accessed (01/13/2018) at http://www.dec.ny.gov/chemical/34189.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada

National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Phenanthrene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Phenanthrene (CAS Number 85-01-8)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for phenanthrene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Phenol
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

6. Summary of Available Oral Reference Doses for Phenol (CAS Number 108-95-2)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA RSL	0.3	93	$BMDL_{1sd}$	300	Based on decreases in body weight gain in pregnant rats exposed by gavage on gestation days 6 through 15. Study NOEL = 60 mg/kg/day. Study LOEL = 120 mg/kg/day.
US EPA OPP*	0.6	60	NOEL	100	Based on the same study and effects as used by US EPA IRIS.
HC PSAP	0.12	12	NOEL	100	Based on histopathological changes in the kidneys of female rats in 14-day gavage study. Study LOEL = 40 mg/kg/day.
RIVM (2001)	0.04	40	NOEL	1000	Based on decrease in number of live pups born to pregnant rats exposed by gavage on gestation days 6 through 19. Study LOEL = 53 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.

$BMDL_{1sd}$: 95% lower confidence limit on dose corresponding to a one standard deviation change from background; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The available oral reference dose values from authoritative bodies listed in section 5 (below) are based on effects observed in developmental studies where pregnant animals were exposed during gestation, or (in one case) a relatively short (14 day) sub-chronic study reporting kidney toxicity. The increase in the incidence of histopathological kidney changes in the study used by Health Canada to derive its reference dose (0.12 mg/kg/day) was not statistically significant. Thus, the exposure level of 40 mg/kg/day,

designated by Health Canada as a LOEL, may in fact be a NOEL. The uncertainty factor of 100 also does not appear sufficient for a subchronic study in animals. The effects observed in the study used by RIVM to derive its reference dose (0.04 mg/kg/day) were accompanied by maternal toxicity, which has not been observed in other studies at similarly low dose levels. This raises questions about the reliability of the LOEL of 53 mg/kg/day. RIVM also used a subchronic to chronic uncertainty factor for a study showing adverse effects on development in offspring of animals exposed during gestation. This is not consistent with typical risk assessment practices used by health agencies in the United States, which recognize the developmental period as a susceptible lifestage where exposure during gestation is more relevant to the induction of developmental effects than lifetime exposure. US EPA OPP and US EPA IRIS both based their reference dose on maternal effects observed at a lower exposure level than were effects on the developing fetuses. The US EPA IRIS assessment used benchmark modeling to identify the point of departure, and applied 10-fold uncertainty factors to account for human and animal-to-human variability. An additional uncertainty factor of 3 was used to account for uncertainties regarding immune system and hematological toxicity. The US EPA OPP assessment applied a default total uncertainty of 100 to a NOEL point of departure from the same study. The US EPA IRIS assessment is more consistent with generally-accepted risk assessment practices. Therefore, the US EPA reference dose (0.3 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer soil cleanup objective for phenol.

3. Review Dates

Summary table completion: March, 2004; revised January, 2018
Toxicity value recommendation: March, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/19/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/19/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/19/2018) at http://www.epa.gov/iris/.

US EPA OPP (United States Environmental Protection Agency, Office of Pesticide Programs). Pesticide Reregistration Status. Last accessed (01/19/2018) at http://www.epa.gov/opp00001/reregistration/status.htm.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/19/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada

National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Phenol
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Phenol (CAS Number 108-95-2)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATDSR (1998)	--	--	--	--	Human data consist of limited and inadequate epidemiological studies. Available animal studies provide no convincing evidence of carcinogenicity. Limited positive carcinogenic responses in one animal study were not observed across species or sexes, and were not dose-related.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for phenol is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: March, 2004; no revision January, 2018
Toxicity value recommendation: March, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1998. Toxicological Profile for Polycyclic Aromatic Hydrocarbons. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Phenol
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Phenol (CAS Number 108-95-2)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
Cal EPA (2003)	200	2×10^4	NOEL	100	Based on the absence of effects in a 90-day inhalation study in rats, mice and monkeys exposed continuously via inhalation. A LOEL of 1×10^5 mcg/m^3 is based on neurological impairment and liver toxicity in rats exposed continuously by inhalation for 15 days in a separate study.
RIVM (2001)	20	2×10^4	NOEL	1000	Based on the same study used by Cal EPA (2003).

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The two reference concentrations for phenol derived by authoritative bodies from the list in item 5 (below) are based on the same single dose study showing an absence of effects in rats, mice and monkeys exposed continuously via inhalation. RIVM applied a total uncertainty factor of 1000 including 10-fold to account for interspecies variability, 10-fold to account for intraspecies variability, and 10-fold to account for the use of a subchronic study. Cal EPA applied a total uncertainty factor of 100 including 3-fold to account for interspecies variability, 10-fold to account for intraspecies variability, and 3-fold to account for the use of a subchronic study. Cal EPA used a default pharmacokinetic adjustment (equal to one) for a systemic gas in their derivation, which is the basis for the 3-fold uncertainty factor for interspecies variability. While this approach is more consistent with currently accepted risk assessment practice, Cal EPA did not adequately justify departure from the

default uncertainty factor of 10 for use of a subchronic study, particularly for the short term, single dose study used to estimate their LOEL. A full 10-fold uncertainty factor for use of a subchronic study is supported given the uncertainties in the critical study's dose-response and the point of departure estimate. Therefore, the RIVM reference concentration (20 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for phenol.

3. Review Dates

Summary table completion: November, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2004. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Phenol. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. Last accessed (01/17/2018) at http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Available at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Phenol
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Phenol (CAS Number 108-95-2)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA (2004)	--	--	--	--	Limited human data are either inadequate or provide no evidence of carcinogenicity. Chronic cancer bioassays by the inhalation route in animals are not available.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2.Recommendation and Rationale

An inhalation unit risk for phenol is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3.Review Dates

Summary table completion: November, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency

- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: *n*-Propylbenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for *n*-Propylbenzene (CAS Number 103-65-1)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA OSRTI Also used by: ♦ US EPA RSL	0.1	--	--	--	Based on toxicity data for ethylbenzene.
CA EPA NL	0.037	--	--	--	Based on toxicity data for cumene (isopropylbenzene).

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake and chronic minimal risk level.

UF: uncertainty factor.

2. Recommendation and Rationale

An oral reference dose for *n*-propylbenzene is not available. The US EPA and the CA EPA each developed a reference dose for *n*-propylbenzene based on a surrogate chemical.

The US EPA OSRTI value for *n*-propylbenzene is the US EPA IRIS oral reference dose for ethylbenzene, which was used as a surrogate chemical for *n*-propylbenzene based on similar patterns of absorption, metabolism, and similar endpoints for acute toxicity. Ethylbenzene and *n*-propylbenzene were considered to be structurally similar in that they both contain a single straight chain alkyl substituent, with ethylbenzene having one less carbon than *n*-propylbenzene, and therefore other similar chemicals with branched alkyl substituents were not used. Finally, based on the greater acute and ototoxicity of ethylbenzene compared to *n*-propylbenzene, the US EPA concluded that a value based on ethylbenzene would likely be health protective. The US EPA IRIS reference dose for ethylbenzene is based on histopathologic and organ weight changes in the liver and kidneys of rats exposed for 182 days by gavage. A total uncertainty factor of 1000 (10 each to account for animal-to-human extrapolation, human variation and the use of a subchronic study) was applied to the adjusted NOEL of 97 mg/kg/day to obtain a reference dose of 0.1 mg/kg/day.

The CA EPA NL value for *n*-propylbenzene uses cumene (isopropylbenzene) as a surrogate chemical. The oral reference dose for cumene is based on increased average kidney weights in female rats exposed by gavage 139 times over a 194-day period. A total uncertainty factor of 3000 (10 each to account for animal-to-human extrapolation and human variation, 3 for the use of a subchronic study and an additional 10 for database deficiencies) was applied to the adjusted NOEL of 110 mg/kg/day to obtain a reference dose of 0.037 mg/kg/day. A proposed CA EPA NL value was originally based on the non-cancer effects of ethylbenzene as a surrogate for *n*-propylbenzene. When ethylbenzene was shown to

have carcinogenic potential in a chronic NTP study, CA EPA changed the surrogate to cumene based on uncertainties about whether *n*-propylbenzene would have similar carcinogenic effects as ethylbenzene. However, a clear justification for choosing cumene as a surrogate instead of ethylbenzene was not presented.

The available information on the toxicity and chemical/physical properties of *n*-propylbenzene, cumene and ethylbenzene does not allow for a definitive conclusion about the best choice of a chemical surrogate for *n*-propylbenzene. Furthermore, both cumene and ethylbenzene have chemical structures similar to *n*-propylbenzene with respect to the alkyl group attached to their benzene rings. Cumene has the same number of carbons (three) in the alkyl group but is a branched structure rather than a straight-chained structure. Ethylbenzene contains a straight-chained alkyl group, but having only two, not three carbons. Thus, a definitive choice for a surrogate based on chemical structure is difficult. However, the toxicological database for ethylbenzene is more complete than that of cumene, and consists of a chronic inhalation cancer study, oral subchronic studies evaluating systemic toxicity and several inhalation studies that evaluate reproductive/developmental toxicity. The more complete toxicological database, the similarity in chemical structure and properties, and the greater acute and ototoxicity of ethylbenzene compared to *n*-propylbenzene support the use of ethylbenzene as a surrogate for *n*-propylbenzene. Therefore, the US EPA IRIS reference dose for ethylbenzene (0.1 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *n*-propylbenzene.

3. Review Dates

Summary table completion: April, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table and Text

CA EPA NL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Notification Levels for Chemicals in Drinking Water. Last accessed (01/14/2018) at http://oehha.ca.gov/water/pals/index.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/14/2018) at http://www.epa.gov/iris/.

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund . Last accessed (01/14/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/14/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health

United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *n*-Propylbenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for *n*-Propylbenzene (CAS Number 103-65-1)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	No information available.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for *n*-propylbenzene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: April, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization

Chemical Name: *n*-Propylbenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for *n*-Propylbenzene (CAS Number 103-65-1)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA OSRTI Also used by: ♦ US EPA RSL	1000	--	--	--	Based on toxicity data for ethylbenzene.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

The US EPA OSRTI value is the only available reference concentration for *n*-propylbenzene from an authoritative body listed in item 5 (below). Ethylbenzene is structurally and chemically similar to *n*-propylbenzene and the similarity between the two chemicals provides a basis for using toxicity data for ethylbenzene to represent *n*-propylbenzene. However, the US EPA OSRTI value is not the reference concentration that was recommended as the inhalation non-cancer toxicity value for ethylbenzene. The recommended inhalation reference concentration for ethylbenzene is 260 mcg/m^3 (ATSDR), and is therefore the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *n*-propylbenzene.

3. Review Dates

Summary table completion: February, 2005; revised January, 2018
Toxicity value recommendation: February, 2005; revised January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/19/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund . Last accessed (01/19/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/19/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: *n*-Propylbenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for *n*-Propylbenzene (CAS Number 103-65-1)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for *n*-propylbenzene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Pyrene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Pyrene (CAS Number 129-00-0)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA OSRTI Also used by: • US EPA RSL • US EPA ODW (2012)	0.03	75	NOEL	3000	Based on kidney toxicity in a 13-week gavage study in mice. Study LOEL = 125 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The US EPA value is the only available reference dose for pyrene from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the US EPA reference dose (0.03 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for pyrene.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2012 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/13/2018) at https://www.epa.gov/sites/production/files/2015-09/documents/dwstandards2012.pdf

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/13/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Division of Drinking Water and Environmental Management

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Pyrene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Pyrene (CAS Number 129-00-0)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1995)	--	--	--	--	Human data are not available. Data from intraperitoneal injection, subcutaneous injection and skin painting studies in mice do not provide convincing evidence for carcinogenicity.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for pyrene is not available. *

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. Toxicological Profile for Polycyclic Aromatic Hydrocarbons. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Pyrene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Pyrene (CAS Number 129-00-0)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for pyrene is not available from the authoritative bodies listed in item number 5 (below). Pyrene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for pyrene is 0.03 mg/kg/day. Therefore, a reference concentration of 100 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for pyrene.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Pyrene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Pyrene (CAS Number 129-00-0)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for pyrene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Selenium
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Inorganic Selenium

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW ♦ US EPA HEAST (1997)	5×10^{-3}	0.015	NOEL	3	Based on the incidence of clinical selenosis (nail disease) in a human epidemiological study of a population of approximately 400 individuals living in an area of China with unusually high environmental concentrations of selenium. Study LOEL = 0.023 mg/kg/day.
CA EPA PHG*	5×10^{-3}	0.015	NOEL	3	Based on a same study population used by US EPA IRIS.
ATSDR	5×10^{-3}	0.015	NOEL	3	Based on a sub-sample of the same study population used by US EPA IRIS.
IOM (2000)*	5.5×10^{-3} [2]	0.011[2]	NOEL	2	Based on a sub-sample of the same study population used by US EPA IRIS.
WHO*	5.5×10^{-3} [2]	-	-	-	Adopted IOM (2000) derivation

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]A NOEL expressed in mg/kg/day was not derived, rather it was expressed as 0.8 mg/person/day, which was converted to a NOEL of 1.1×10^{-2} mg/kg/day assuming a 70-kg adult. A reference dose expressed in mg/kg/day was not derived, rather it was expressed as 0.4 mg/person/day, which was converted to a reference dose of 0.0057 mg/kg/day assuming a 70-kg adult.

NOEL: no-observed-effect level; LOEL: lowest- observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for all the selenium reference doses is essentially identical with respect to choice of study population, species, adverse effect and identification of the point of departure (0.011 or 0.015 mg/kg/day). The derivations are based on the same human epidemiological data, but US EPA, CA EPA, and ATSDR used a total uncertainty factor of 3 to account for human variation, whereas IOM (2000)

and WHO used a total uncertainty factor of 2 to account for human variation. Other human population-based studies found similar NOELs associated with lifetime consumption above the recommended daily allowance suggesting that the use of a factor less than 10 is reasonable. The use a 3-fold uncertainty factor is more consistent with generally accepted risk assessment practice than the use of 2 when a full 10-fold uncertainty factor appears unnecessary. The US EPA reference dose is based on a larger population than the reference doses of CA EPA and ATSDR. Therefore, the US EPA reference dose (5×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for selenium.

3. Review Dates

Summary table completion: August, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/12/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/12/2018) at https://oehha.ca.gov/water/public-health-goals-phgs
.
IOM (Institute of Medicine). 2000. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids. Washington DC: National Academy Press.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/12/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/12/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/12/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/12/2018) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/12/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment

Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
    Integrated Risk Information System
    Office of Drinking Water
    Office of Pesticide Programs
    Office of Superfund Remediation and Technology Innovation
        Health Effects Assessment Summary Tables
        Provisional Peer Reviewed Toxicity Values
    Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Selenium
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Selenium

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Inadequate human data and inadequate evidence of carcinogenicity in animals.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for selenium is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: August, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency

- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Selenium
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Inorganic Selenium

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for selenium is not available from the authoritative bodies listed in item number 5 (below). Selenium is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for selenium is 5 $x10^{-3}$ mg/kg/day. Therefore, a reference concentration of 18 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for selenium.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Selenium
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Selenium

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for selenium is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Silver
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Inorganic Silver

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2004) • US EPA ODW (2004) • US EPA HEAST (1997)	5×10^{-3}	0.014	LOEL	3	Based on the incidence of argyria (a medically benign but permanent bluish-gray discoloration of the skin) in 10 human males and two females who were administered 31 to100 intravenous injections of silver arsphenamine (total dose was 4 to 20 grams or 1 to 5 grams as silver) over a 2 to 9.75-year period.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The US EPA value is the only available reference dose for silver from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore the US EPA reference dose (5×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for silver.

3. Review Dates

Summary table completion: August, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2004. 2004 Edition of the Drinking Water Standards and Health Advisories. EPA 822-R-04-005. Office of Water. Washington, DC. http://www.epa.gov/waterscience/drinking/

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Silver
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Silver

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	No evidence of cancer in humans has been reported despite frequent therapeutic use of the compound over the years.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for silver is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: August, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency

- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Silver
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Inorganic Silver

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for silver is not available from the authoritative bodies listed in item number 5 (below). Silver is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for silver is 5×10^{-3} mg/kg/day. Therefore, a reference concentration of 18 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for silver.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides

Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Silver
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Silver

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for silver is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Tetrachloroethene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Tetrachloroethene (CAS Number 127-18-4)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL	0.006 (2)	9.7	LOEL	1000	Based on neurotoxicity (reaction time, cognitive effects) in occupationally exposed adults. The point of departure (oral dose) was derived using a human PBPK model-based $route_{Inhalation}$-to-$route_{Oral}$ extrapolation from workplace inhalation exposures.
		2.6	LOEL	1000	Based on neurotoxicity (color vision) in occupationally exposed adults. The point of departure (oral dose) was derived using a human PBPK model-based $route_{Inhalation}$-to-$route_{Oral}$ extrapolation from workplace inhalation exposures.
US EPA ODW	0.01 (3)	14	NOEL	1000	Based on liver toxicity in mice exposed via gavage 5 days/week in a 6-week study and reduced weight gain in rats exposed via drinking water in a 90-day study. Study LOEL (mice) = 71 mg/kg/day, study LOEL (rats) = 400 mg/kg/day.
US EPA HEAST (1997)	0.1	14	NOEL	100	Based on liver toxicity in mice exposed via gavage 5 days/week in a 6-week study. Study LOEL = 71 mg/kg/day.

CA EPA PHG*	0.032 [4]	0.29 4.15 8.48	LOEL	30 100 100	Based on neurobehavioral endpoints (delayed reaction times) observed in epidemiological studies of humans with occupational or residential exposures. The point of departure (oral doses) were calculated from residential or workplace inhalation exposures using a default $route_{Inhalation}$-to-$route_{Oral}$ extrapolation assuming a 65 kg adult continuously exposed and breathing 20 m^3 of air/day for residential exposures, or assuming a 65 kg adult or a 60 kg woman occupationally exposed and breathing 10 m^3 of air/workday, and working 5 days/week. In both cases, an inhalation absorption factor of 0.7 was used to account for the incomplete uptake of tetrachloroethene by the respiratory system.

HC PSAP	0.034	170	LOEL	5000	Based on reduced survival, hepatotoxic effects (males), lung congestion and nephrotoxic effects (males and females) in mice exposed via inhalation 6 hours/day, 5 days/week in a 103-week study. A study NOEL was not identified.
HC DWG	0.014	14	NOEL	1000	Based on reduced weight gain and altered liver or kidney to body weight ratios in rats exposed via drinking water in a 90-day study. Study LOEL = 400 mg/kg/day.
RIVM (2001)	0.016	16	NOEL	1000	Based on liver toxicity in rats exposed via gavage in a 4-week study. Study LOEL = 81 mg/kg/day.
WHO (2011)	0.014	14	NOEL	1000	Based on liver toxicity in mice exposed via gavage 5 days/week in a 6-week study and rats exposed via drinking water in a 90-day study. Study LOEL (mice) = 71 mg/kg/day, study LOEL (rats) = 400 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.
[2]The reference dose is the midpoint (i.e., median, rounded to one significant figure) of the range of the two candidate reference doses (i.e., points of departure/uncertainty factors).
[3]The US EPA ODW adopted the then current US EPA IRIS reference dose, which was replaced by a new reference dose in 2012.
[4]The reference dose is the geometric mean of the three candidate reference doses (i.e., points of departure/uncertainty factors).

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor; PBPK: physiologically based pharmacokinetic.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

Data from epidemiologic studies of good quality are generally preferred over animal studies for evaluating the noncarcinogenic risk of chemical exposures (US EPA, 1994). The US EPA IRIS and the CA EPA PHG programs are the only authoritative bodies listed in item 5 that derived a reference dose based on human studies. More importantly, the estimates were based on epidemiologic studies that provide evidence of a causal association between tetrachloroethene exposure and nervous system effects, which were identified by the use of standardized test methodology to evaluate neurobehavioral or visual function. Both derivations are consistent with generally accepted risk assessment practices, including the appropriate use of uncertainty factors. The US EPA IRIS reference dose is preferred over the CA EPA reference dose because it is based on a more scientifically defensible route$_{Inhalation}$-to-route$_{Oral}$ extrapolation (i.e., a tetrachloroethene-specific PBPK model in humans) rather than on a default method based on body weight and daily inhalation rate. Therefore, the US EPA IRIS reference dose (0.006 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for tetrachloroethene.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/14/2018) at https://oehha.ca.gov/water/public-health-goals-phgs.

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/14/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/14/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/14/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA (United States Environmental Protection Agency). 1994. Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry. EPA 600/8-90/066F. Last accessed (01/14/2018) at http://www.epa.gov/iris/backgrd.html#other.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/14/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/14/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2012 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/14/2018) at http://water.epa.gov/action/advisories/drinking/upload/dwstandards2012.pdf.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/14/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/14/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Tetrachloroethene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Tetrachloroethene (CAS Number 127-18-4)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS* Also used by: ◆ US EPA RSL	4.8×10^{-4}	2.1×10^{-3}	linearized multistage model, linear extrapolation from the $BMDL_{10}$ [(2)]	PBPK models, and $BW^{¾}$ [(3)] scaling of metabolized dose	Based on hepatocellular carcinomas and adenomas in male Crj:BDF1 mice exposed via inhalation 6 hours/day, 5 days/week in a 104-week study.
CA EPA PHG	2.4×10^{-6}	0.43 [(4)]	multistage in dose, Weibull in time model, linear extrapolation from LED_{10} [(5)]	PBPK models, and $BW^{¾}$ [(3)] scaling of metabolized dose	Based on hepatocellular carcinomas in both sexes of $B6C3F_1$ mice exposed via gavage 5 days/week for 78 weeks, and observed for 90 weeks.
Clewell et al. (2005)	3.4×10^{-4}	2.9×10^{-3}	time to tumor model, linear extrapolation from LED_{10} [(5)]	PBPK models, and 1 [(6)]	Based on hepatocellular carcinomas in both sexes of $B6C3F_1$ mice exposed by inhalation for 6 hours/day, 5 days/week for 104 weeks.

[1] The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2] $BMDL_{10}$: The lower 95% confidence limit on the benchmark air dose associated with a 10% increase (relative to controls) in the incidence of tumors.

[3] Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.

[4] The CA EPA PHG recommended oral cancer potency factor was 0.54 per mg-metabolized/kg/day. The metabolized tetrachloroethene dose associated with an excess risk of 1×10^{-6} = $1 \times 10^{-6}/0.54$ per mg-metabolized/kg/day = 1.8×10^{-6} mg-metabolized/kg/day. However, CA EPA assumed humans metabolize only 0.79 of ingested tetrachloroethene, so it requires an ingestion rate of 2.3×10^{-6} mg tetrachloroethene/kg/day to produce 1.8×10^{-6} mg of metabolized tetrachloroethene/kg/day. The cancer potency factor (tetrachloroethene dose) =$1 \times 10^{-6}/2.3 \times 10^{-6}$ mg tetrachloroethene/kg/day or 0.43 per mg tetrachloroethene/kg/day.

[5] LED_{10}: The lower bound on the benchmark dose associated with a 10% increase (relative to controls) in the incidence of tumors (equivalent to the $BMDL_{10}$).

[6] Factor for dose adjustment from animals to humans is 1 (equal risk at equal metabolized dose).

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA IRIS, CA EPA, and Clewell et al. (2005) all used interspecies extrapolations based on animal and human PBPK models and metabolized doses in their derivations of a cancer potency factor for tetrachloroethene. In addition, the US EPA IRIS and Clewell et al. (2005) used $route_{Inhalation}$-to-$route_{Oral}$ extrapolations based on PBPK models and metabolized doses. The CA EPA derivation used an oral study. Typically, an oral study would be preferred to an inhalation study as the basis of an oral cancer potency factor when other factors are similar. However, US EPA (2012) identified several limitations (including significantly higher early noncancer morbidity and mortality in treated groups, a variable dosing schedule, and short study duration) of the oral study used by CA EPA and concluded that the results were less useful for quantitative risk assessment than the inhalation studies, even for evaluating oral exposures. The oral study used relatively large bolus (gavage) doses, which are unlikely to resemble human exposures associated with soil contamination at Brownfield sites. This is important because large bolus doses are likely associated with saturable metabolism processes, and the pharmacokinetics (and toxicity) at high doses are likely to be different from pharmacokinetics (and toxicity) prevalent at low environmental exposure levels. Thus, the CA EPA derivation was not considered further as the basis of the oral cancer-based soil cleanup objective for tetrachloroethene.

The US EPA IRIS derivation used the most recent and complete PBPK models for tetrachloroethene in mice and humans, and is an improvement (see Chiu and Ginsberg, 2011) over the models used by Clewell et al. (2005). Moreover, the inhalation study used by US EPA IRIS provides a better basis for a quantitative risk assessment than the inhalation study used by Clewell et al. (2005) because it had lower exposure levels and one more exposed group than the study used by Clewell et al. (2005). Thus, the US EPA cancer potency factor (2.1×10^{-3} per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for tetrachloroethene. The tetrachloroethene risk specific dose calculated from this toxicity value is 4.8×10^{-4} mg/kg/day.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: August, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/15/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

Chiu WA, Ginsberg GL. 2011. Development and Evaluation of a Harmonized Physiologically Based Pharmacokinetic (PBPK) Model for Perchloroethylene Toxicokinetics in Mice, Rats, and Humans. Toxicol Appl Pharmacol. 253(3):203-234.

Clewell HJ, et al. 2005. Evaluation of Physiologically Based Pharmacokinetic Models in Risk Assessment: An Example with Perchloroethylene. Crit Rev Toxicol 35(5): 413-433.

US EPA (United States Environmental Protection Agency). 2012. Toxicological Review of Tetrachloroethylene (Perchloroethylene) (CAS No. 127-18-4) In Support of Summary Information on the Integrated Risk Information System (IRIS). EPA/635/R-08/011F. Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Tetrachloroethene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Tetrachloroethene (CAS Number 127-18-4)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
General Population					
US EPA IRIS* Also used by: ◆ US EPA RSL*	40 (2)	56,000	$LOEL_{ADJ}$ [3]	1000	Based on neurotoxicity (reaction time, cognitive effects) in workers chronically exposed in dry cleaning facilities. Study $LOEL_{OCCUP}$ [4] = 156 mg/m^3.
		15,000	$LOEL_{ADJ}$ [3]	1000	Based on neurotoxicity (color vision) in workers chronically exposed in dry cleaning facilities. Study $LOEL_{OCCUP}$ = 42 mg/m^3.
ATSDR	270 (0.04 ppm)	2.4×10^4 (3.6 ppm)	$LOEL_{ADJ}$ [4]	100	Based on neurobehavioral effects in 60 women chronically exposed in dry cleaning facilities. Study $LOEL_{OCCUP}$ = 103 mg/m^3 (15 ppm).
NYS DOH (2013)*	30 (5)	56,000	$LOEL_{ADJ}$ [3]	1000	Based on the same studies, toxicity endpoints, points of departure and uncertainty factors used by US EPA IRIS.
		15,000	$LOEL_{ADJ}$ [3]	1000	
WHO (2000)	250	2.4×10^4	$LOEL_{ADJ}$ [4]	100	Based on renal toxicity in 50 workers chronically exposed in dry cleaning facilities. Study $LOEL_{OCCUP}$ = 102 mg/m^3.
RIVM (2001)	250	2.4×10^4	--	--	RIVM (2001) adopted the derivation and reference concentration of WHO (2000).
HC PSAP (1996); TERA	360	3.6×10^5	$LOEL_{ADJ}$ [6]	1000	Based on reduced survival and liver toxicity in male mice, and lung congestion and kidney toxicity in male and female mice exposed via inhalation for 6 hours/day, 5 days/week in a 103-week study. Study $LOEL_{EXP}$ = 678 mg/m^3; a study $NOEL_{EXP}$ was not identified.

CA EPA REL	35	--	--	--	Based on kidney and liver effects in mice; further details are unavailable.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

[2]The reference concentration is the midpoint (i.e., median, rounded to one significant figure) of the range of the two candidate reference concentrations (i.e., points of departure/uncertainty factors).

[3]$LOEL_{ADJ}$ = $LOEL_{OCCUP}$ x 10 m^3/20 m^3 x 5 days/7 days.

[4]$LOEL_{ADJ}$ = $LOEL_{OCCUP}$ x 8 hours/24 hours x 5 days/7 days.

[5]The USEPA RfC of 35.5 mcg/m^3 was rounded down to 30 mcg/m^3 based on a study suggesting potential effects of tetrachloroethene on vision in children residentially exposed to about 300 mcg/m^3 (Storm et al., 2011).

[6]$LOEL_{ADJ}$ = [$LOEL_{EXP}$ x 6 hours/24 hours x 5 days/7 day] x [0.04 m^3/day/0.03 kg]/[12 m^3/day/27 kg], which accounts for the ratio of the inhalation volume/body weight of mice to humans aged 5 to 11 years.

NOEL: no-observed-effect level; $NOEL_{EXP}$: NOEL based on experimental exposure; LOEL: lowest-observed-effect level; $LOEL_{EXP}$: LOEL based on experimental exposure; $LOEL_{OCCUP}$: LOEL based on occupational exposures; $LOEL_{ADJ}$: LOEL adjusted for continuous exposure; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The available reference concentrations for tetrachloroethene derived by authoritative bodies from the list in item 5 (below) are based primarily on central nervous system, kidney, and liver effects observed in human occupational studies or liver, kidney and lung effects in mice exposed via inhalation. The US EPA IRIS, ATSDR, WHO and NYS DOH reference concentrations are all based on good quality human studies showing associations between workplace air exposure to tetrachloroethene and effects on the central nervous system, kidney, or liver. Moreover, the collective data support a causal relationship, particularly for central nervous system effects. The HC PSAP reference concentration is based on an animal study. The CA EPA REL reference concentration is also based on an animal study, and additional details of the derivation are not provided in the available documentation. Therefore, the HC PSAP and CA EPA reference concentrations are not further considered as potential toxicity values for use in the derivation of an inhalation non-cancer-based soil cleanup objective for tetrachloroethene.

The recommended reference concentrations of the US EPA IRIS, ATSDR, NYS DOH, and WHO are based on effects observed in studies of dry cleaning workers exposed via inhalation. Each agency used a total uncertainty factor of 100 to compensate for human variation (10) and the use of a LOEL (10). In addition, the US EPA IRIS program used an additional uncertainty factor of 10 to compensate for data gaps. Specifically, an uncertainty factor of 10 was used to address the lack of data to characterize adequately the hazard and dose response in the human population (i.e., uncertainties associated with database deficiencies on neurological, developmental, and immunological effects).

The US EPA reference concentration is based on human studies, including studies of residential exposures that were not available when the other authoritative bodies derived their reference concentrations. Although the earlier studies used by the other authoritative bodies were considered by the US EPA (2012) to be too limited to be the basis of a reference concentration, they raise concerns about data gaps because the points of departure of these studies were lower than those identified in the occupational studies used to derived the reference concentration (US EPA, 2012). Moreover, a committee of the National Research Council of the US National Academy of Sciences reviewed the draft US EPA IRIS document and noted "…that a factor of 3 may be inadequate to account for database

deficiencies." Consequently, US EPA (2012) increased the uncertainty factor for database deficiencies from a draft value of 3 to the final value of 10.

The NYS DOH used the US EPA's reference concentration derivation with respect to studies, points of departure and uncertainty factors, but rounded the midpoint of the US EPA's two candidate reference concentrations (35.5 mcg/m^3) downward rather than upward based on a study that suggested potential effects of tetrachloroethene (reduced visual contrast sensitivity) in children residentially exposed to about 300 mcg/m^3 (Storm et al., 2011). This rounding increased the margin of exposure for visual contrast sensitivity from 7.5 to 10, and increased the margin of exposure for color vision effects from 375 to 500. Therefore, the NYS DOH reference concentration (30 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for tetrachloroethene.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004, revised January, 2018

4. References for Summary Table and Recommendation and Rationale

(Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/15/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/15/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

HC PSAP (Health Canada). 1996. Priority Substances Assessment Program. Health-Based Tolerable Daily Intakes/Concentrations and Tumorigenic Doses/ Concentrations for Priority Substances. Cat. H46-2/96-194E. Last accessed (01/15/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

NYS DOH (New York State Department of Health). 2013. Reduction of the Tetrachloroethene Ambient Air Guideline and Immediate Action Level. Memo from Daniel Luttinger to A. Kevin Gleason. March 7, 2013.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/15/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

Storm JE, Mazor KA, Aldous KM, Blount BC, Brodie SE, Serle JB. 2011. Visual contrast sensitivity in children exposed to tetrachloroethylene. Arch Environ Occup Health. 66(3):166-177. Erratum in: Arch Environ Occup Health. 2011 Oct; 66(4):250.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/15/2018) at https://www.tera.org/iter/

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA (United States Environmental Protection Agency. 2012. Toxicological Review of Tetrachloroethylene (Perchloroethylene) (CAS No. 127-18-4) In Support of Summary Information on the Integrated Risk Information System (IRIS). EPA/635/R-08/011F. Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2000. Air Quality Guidelines for Europe. Last accessed (01/15/2018) at http://www.euro.who.int/en/what-we-publish/abstracts/air-quality-guidelines-for-europe.

6. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Tetrachloroethene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for Tetrachloroethene (CAS Number 127-18-4)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS ◆ Also used by: US EPA RSL	3.8	2.6×10^{-7}	multistage model, linear extrapolation from the $BMDL_{10}$ (2)	PBPK[3] models, and $BW^{¾}$ (4) scaling of metabolized dose	Value based on one cancer site in male mice exposed via inhalation 6 hours/day, 5 days/week in a 104-week study.
CA EPA CPF (2016)	0.16	6.1×10^{-6}	multistage model, linear extrapolation from the $BMDL_{05}$ (2)	PBPK[3] models, and $BW^{¾}$ (4) scaling of metabolized dose	Geometric mean of four values each based on one or more cancer sites/types in male rats or mice exposed via inhalation 6 hours/day, 5 days/week in 103 or 104-week studies.
CA EPA PHG	0.029	3.4×10^{-5} (5)	multistage in dose, Weibull in time model, linear extrapolation from LED_{10} (6)	PBPK[3] models, and $BW^{¾}$ (4) scaling of metabolized dose	Geometric mean of four values each based on one cancer site in male or female mice, or one cancer type in male or female rats exposed via inhalation 6 hours/day, 5 days/week in 103-week studies.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million, where 1×10^{-6} air concentration = 1×10^{-6}/ unit risk.

[2]$BMDL_{05}$ and $BMDL_{10}$: The lower 95% confidence limit on the benchmark air dose associated with a 5 or a 10% increase (relative to controls) in the incidence of tumors.

[3]PBPK: Physiologically based pharmacokinetic

[4]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.

[5]The CA EPA PHG recommended inhalation cancer potency factor was 0.15 per mg-metabolized/kg/day. The metabolized dose associated with an excess risk of 1×10^{-6} = 1×10^{-6}/0.15 per mg-metabolized/kg/day = 6.7×10^{-6} mg-metabolized/kg/day. However, CA EPA assumed humans metabolize only 0.79 of ingested tetrachloroethene, so it requires an ingestion rate of 8.5×10^{-6} mg tetrachloroethene/kg/day to produce 6.7×10^{-6} mg of metabolized tetrachloroethene/kg/day. The inhalation cancer potency factor (inhaled dose) =1×10^{-6}/8.5×10^{-6} mg tetrachloroethene/kg/day or 0.12 per mg tetrachloroethene/kg/day, and the unit risk = 3.4×10^{-5} per mcg/m^3 [(0.12 per mg/kg/day x 20 m^3/person/day)/(70 kg person x 1000 mcg/mg)].

[6]LED_{10}: The lower bound on the benchmark dose associated with a 10% increase (relative to controls) in the incidence of tumors (equivalent to the $BMDL_{10}$).

2. Recommendation and Rationale

The inhalation unit risks for tetrachloroethene derived by the US EPA IRIS, CA EPA CPF, and CA EPA PHG are all based on chronic inhalation bioassays in rodents. The derivations differ in the tumor sites, dose-response models, internal dose metrics and methods used to obtain each agency's recommended unit risk.

The US EPA IRIS based its unit risk on hepatocellular adenomas or carcinomas in male mice in a single two-year inhalation study (US EPA 2012). They used an animal PBPK model to convert the administered tetrachloroethene air concentrations to corresponding measures of internal dose (i.e., tetrachloroethene oxidation-only liver metabolism), and then modelled the dose-response data using a multistage model to obtain a $BMDL_{10}$. The US EPA IRIS then calculated an animal slope factor (expressed in units of risk/lifetime average daily metabolized dose) from the $BMDL_{10}$, which was then converted to a human slope factor (expressed as risk/human equivalent lifetime daily metabolized dose) using body weight scaling. Finally, The US EPA IRIS calculated the human unit risk (expressed as risk/human equivalent lifetime continuous air concentration) using a human PBPK model.

The CA EPA CPF (2016) used similar methods as the US EPA IRIS to derive its unit risk, except that 1) they used a different measure of internal dose (i.e., total metabolized dose, consisting of tetrachloroethene oxidation plus conjugation) than did the US EPA IRIS, and 2) the final unit risk was the geometric mean of four unit risks from two chronic rodent bioassays and multiple tumor sites, including a) combined hepatocellular adenomas or carcinomas, Harderian gland tumors, hemangiomas or hemangiosarcomas in male mice, b) mononuclear cell leukemia in male rats, c) combined mononuclear cell leukemia, testicular interstitial cell carcinomas, renal adenomas or carcinomas, and brain gliomas in male rats, and d) combined hepatocellular adenomas or carcinomas in male mice.

In 2009, the CA EPA PHG derived a tetrachloroethene unit risk using total metabolized dose as the internal dose metric. It was the geometric mean of four unit risks derived from one of the two chronic bioassays also used by the CA EPA CPF in 2016. However, the CA EPA PHG used a different set of tumor sites (liver carcinomas or adenomas in male and female mice, and mononuclear cell leukemias in male and female rats) than the CA EPA CPF. More importantly, the CA EPA PHG used a PBPK model, which although useful at the time, has been replaced by a newer PBPK model [Chiu and Ginsberg (2011)] that better describes important pathways of the pharmacokinetics of tetrachloroethene metabolism in mice, rats, and humans. Thus, the CA EPA PHG unit risk is not considered further given the use of the new PBPK model by the US EPA IRIS and the CA EPA CPF to derive their recommended unit risks.

The derivations of the US EPA IRIS and the CA EPA CPF both represent scientifically valid derivations of a tetrachloroethene unit risk. There remains some uncertainty regarding two aspects of tetrachloroethene carcinogenicity that make it difficult to determine which unit risk to recommend for the derivation of an inhalation cancer-based soil cleanup objective for tetrachloroethene. First, the mode of action for the various cancers induced by tetrachloroethene is still uncertain, although the mode(s) of action most likely involves the oxidative and conjugative metabolites of tetrachloroethene. Secondly, tetrachloroethene induces tumors at several sites in mice and rats, and the data are insufficient to rank the tetrachloroethene related cancers (for example, liver, kidney, and mononuclear leukemia) as to their relevance to evaluating the human cancer risk from tetrachloroethene. The cancer most strongly associated with tetrachloroethene exposure in humans is bladder cancer (Laanderen et al., 2014), which is not a known tetrachloroethene-related cancer in rodents.

Given the likelihood of the importance of metabolites in the carcinogenicity of tetrachloroethene, and the uncertainties regarding the human relevance of cancers observed/not observed in rodents, the unit risk (i.e., the CA EPA CPF value) that uses a more inclusive measure of metabolism (total metabolism instead of only oxidative liver metabolism) and a broad range of dose-response data (multiple cancer sites in mice and rats instead of only liver tumors in mice) provides the most robust foundation for an animal-based estimate of the potency of tetrachloroethene to cause cancer in humans. Thus, the CA EPA CPF unit risk (6.1×10^{-6} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for tetrachloroethene. The tetrachloroethene risk specific air concentration calculated from this toxicity value is 0.16 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: September, 2004, revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2016. Air Toxics Hot Spots Program: Perchloroethylene Inhalation Cancer Potency Factor. Technical Support Document for Cancer Potency Factors. Appendix B. September, 2016. Last accessed (01/17/2018) at https://oehha.ca.gov/media/downloads/crnr/pceurf090816.pdf.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/17/2018) at http://www.oehha.ca.gov/water/phg/allphgs.html.

Chiu WA, Ginsberg GL. 2011. Development and Evaluation of a Harmonized Physiologically Based Pharmacokinetic (PBPK) Model for Perchloroethylene Toxicokinetics in Mice, Rats, and Humans. Toxicol Appl Pharmacol. 253(3):203-234.

Laanderen J, Straif K, Ruder A, et al. 2014. Tetrachloroethylene exposure and bladder cancer risk: a meta-analysis of dry-cleaning-worker studies. Environ Health Perspect. 122(7):661-666.

US EPA (United States Environmental Protection Agency). 2012. Toxicological Review of Tetrachloroethylene (Perchloroethylene) (CAS No. 127-18-4) In Support of Summary Information on the Integrated Risk Information System (IRIS). EPA/635/R-08/011F. Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)

New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Toluene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Toluene (CAS Number 108-88-3)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS* Also used by: • US EPA RSL • US EPA ODW	0.08	238	$BMDL_{1SD}$	3000	Based on liver and kidney weight and histopathologic changes in rats exposed for 13 weeks by corn oil gavage. Study LOEL = 446 mg/kg/day. A benchmark dose model was fit to absolute kidney weight from male rats. The BMR was a 1 standard deviation increase above the control mean.
WHO (2011)	0.22	223	LOEL	1000	Based on increased liver weight in mice exposed by corn oil gavage for 13 weeks.
HC $PSAP_1$ (supported by TERA documentation)	0.22	223	NOEL	1000	Based on increased liver weight in mice exposed by corn oil gavage for 13 weeks.
RIVM (2001)	0.223	223	LOEL	1000	Based on increased liver weight in mice exposed by corn oil gavage for 13 weeks.
HC $PSAP_2$	1.25	125	NOEL	100	Based on unspecified chronic inhalation study in animals exposed 6.5 hours per day, 5 days per week.
HC $PSAP_3$	1.07	10.7	NOEL	10	Based on respiratory tract irritation and decreased scores on neurological function tests in humans in 6-hour inhalation exposures.
CA EPA PHG*	0.022	22	NOEL	1000	Based on liver and thymus weight changes and markers of decreased immune function in mice exposed via drinking water for 28 days. Study LOEL = 105 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.

$BMDL_{1sd}$: 95% lower confidence limit on the benchmark dose associated with a 1 standard deviation increase above the mean background response; BMR: benchmark response; NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The bases for five of the derived reference doses for toluene include adverse effects in rats and mice exposed via oral gavage at the same doses in two 13-week studies and effects in mice exposed via drinking water for 28 days. Two other reference doses (HC $PSAP_2$ and HC $PSAP_3$) are based on inhalation studies. These are not considered further because good quality oral data (the preferred basis for oral reference dose) are available, the documentation of the HC $PSAP_2$ value based on an inhalation study in animals is limited, and the HC $PSAP_3$ value was derived from a six-hour human inhalation exposure, which is too short for deriving a chronic reference dose.

The values derived by WHO, RIVM and HC $PSAP_1$ are all based on the same 13-week gavage study in mice. WHO, RIVM and HC $PSAP_1$ selected the same dose (223 mg/kg/day) as the point of departure of the study. The HC $PSAP_1$ considered the liver weight changes to be of insignificant toxicological importance and identified this dose as a NOEL, whereas WHO (and RIVM based on the WHO analysis) considered the dose a minimal LOEL due to changes in relative liver weight unaccompanied by any histological changes. However, all three agencies used the same total uncertainty factor (1000) to derive its reference dose, thus, the identification of the point of departure as a NOEL or LOEL is moot. WHO and RIVM divided its uncertainty factors into a 10-fold factor for animal-to-human extrapolation, a 10-fold factor for human variation, and 10-fold factor for the use of a LOEL from a subchronic study. HC $PSAP_1$ used a 10-fold factor for animal-to-human extrapolation, a 10-fold factor for human variation, and a 10-fold factor for the use of a subchronic NOEL.

CA EPA PHG derived a value based on immune-system effects and organ weight changes observed in mice exposed via drinking water for 28 consecutive days. This study identified a lower LOEL (105 mg/kg/day) than the NOEL obtained from the 13-week gavage studies (223 mg/kg/day). However, US EPA IRIS noted that other studies of similar quality did not detect immunological effects in several immune assays, including some of the same assays used in the study CA EPA. US EPA IRIS, therefore, concluded that immunotoxicity data from this study are insufficient to determine whether immune effects are more sensitive than kidney effects, which were used by US EPA IRIS to derive its reference dose. In addition, we are concerned that the CA EPA PHG did not review these other studies, even though they were published prior to the adoption of the CA EPA PHG for toluene.

US EPA IRIS used a benchmark dose model to estimate a $BMDL_{1SD}$ point of departure of 238 mg/kg/day for the absolute kidney weight changes in male rats exposed via gavage for 13 weeks, which is similar to the NOEL/minimal LOEL point of departure in mice used by the other agencies. US EPA IRIS applied a 3000 total uncertainty factor to this point of departure (a 10-fold factor each for animal-to-human extrapolation and human variability, a 10-fold factor for use of a subchronic study, and a 3-fold factor for database uncertainties). US EPA IRIS cited database limitations, including lack of adequate data on oral neurotoxicity and immunotoxicity and lack of an oral two-generation reproductive study, as the basis for the database uncertainty factor.

The US EPA IRIS derivation is more consistent with generally-accepted risk assessment practices than the other derivations, and the immune system effects used by CA EPA PHG in its assessment are of questionable reproducibility. Therefore, the US EPA IRIS reference dose (0.08 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for toluene.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/15/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/15/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/15/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/15/2018) at https://www.tera.org/iter/

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2012 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/15/2018) at http://water.epa.gov/drink/standards/hascience.cfm.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/15/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies (see Table __for Internet Websites)

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)

New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Toluene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Toluene (CAS Number 108-88-3)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (2000)	--	--	--	--	Studies evaluating the carcinogenicity of toluene following oral exposure in humans are not available. One long-term oral study showed an increase in tumors that was not dose-related. The limited data and the limitations of the available study preclude a definitive conclusion regarding the carcinogenicity of toluene following oral exposure.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for toluene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2000. Toxicological Profile for Toluene. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Toluene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Toluene (CAS Number 108-88-3)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL	5000	4.6×10^4	NOEL	10	Based on neurological effects in workers chronically exposed by inhalation. A mean NOEL was obtained from 4 of the 10 occupational studies evaluated. The average NOEL was adjusted to a continuous exposure level accounting for exposure 5 days per week and allocating 50% of daily inhalation volume to an 8-hour workday.
RIVM (2001)	400	1.19×10^5	LOEL	300	Based on neurobehavioral changes from chronic exposure to toluene in an occupational study of female workers employed at an electronic assembly plant.
ATSDR	300**	3×10^4	LOEL	100	Based on alcohol- and age-adjusted color vision impairment in three groups of Croatian workers.
CA EPA REL	300	2.6×10^4	NOEL	100	Based on decreased brain weight and altered dopamine receptor binding in male rats in a 4-week inhalation study. Study LOEL = 5.2×10^4 mcg/m^3.
HC PSAP	3.75×10^3	3.75×10^4	NOEL	10	Based on neurological effects and respiratory irritation in a clinical study with human volunteers. Study LOEL = 9.4×10^4 mcg/m^3.

WHO (2000)	260	7.9×10^4	LOEL	300	Based on central nervous system effects observed with chronic occupational exposure.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.
**The ATSDR value is reported as 0.08 parts per million (ppm). For toluene, 1 ppm = 3.77 mg/m^3.

2. Recommendation and Rationale

The reference concentrations for toluene derived by authoritative bodies from the list in item 5 (below) are all based on central nervous system effects, mostly observed in human workers or volunteers exposed via inhalation or, in one case, observed in rats in a subchronic inhalation study. The five derivations based on human data (US EPA IRIS, ATSDR, Health Canada, RIVM and WHO) all estimate the human equivalent concentration based on an adjustment from non-continuous to continuous exposure. Of those five, three are LOEL points of departure from occupational studies, one (HC PSAP) is a NOEL from a volunteer clinical chamber study and one (US EPA IRIS) is a mean of NOELs identified among a selection of 10 occupational studies. The chamber study NOEL is higher than ATSDR's observed occupational LOEL, and HC PSAP chose to apply only a 10-fold uncertainty factor to account for human variability, without any additional uncertainty factor accounting for the short exposure duration (4 days). The ATSDR applied a total uncertainty factor of 100, including 10-fold to account for human variability and 10-fold for use of a minimal LOEL. The WHO's application of uncertainty factors was similar, with the same 10-fold factors for human variability and use of a LOEL and an additional 3-fold factor to account for potential effects on the developing central nervous system. US EPA IRIS applied a 10-fold uncertainty factor to account for human variability to their mean NOEL point of departure. The CA EPA based their derivation on a rat NOEL in a 4 week inhalation study where decreased brain weight and altered brain dopamine receptor binding were observed. They adjusted for continuous exposure and used a default pharmacokinetic adjustment (equal to 1) based on the assumption that the blood:air partitioning coefficients in rats and humans were equal. The CA EPA applied a total uncertainty factor of 100, including 10-fold to account for human variability and 10-fold to account for the use of a subchronic NOEL. The CA EPA chose not to include the default 3-fold factor for animal-to-human variability after applying a pharmacokinetic adjustment based on their conclusion that a number of human occupational studies, and studies in laboratory animals all indicated very similar effect levels for neurotoxicity associated with inhalation exposure when expressed on a equivalent time-weighted average basis. All of the derivations are similarly consistent with generally-accepted risk assessment practices. The US EPA IRIS assessment reflects the most robust evaluation of human occupational data (10 studies, four or which identified NOELs) and the lowest LOELs among the studies selected for the US EPA IRIS assessment include the LOELs identified by ATSDR and WHO. The US EPA IRIS assessment reflects newer human data than the other assessments and the identified NOELs are generally lower than the previously identified LOELs, justifying the reduced uncertainty factor applied by US EPA. Therefore, the US EPA IRIS reference concentration (5000 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for toluene.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/17/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/17/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

WHO (World Health Organization). 2000. Air Quality Guidelines for Europe. Last accessed (01/17/2018) at http://www.euro.who.int/en/what-we-publish/abstracts/air-quality-guidelines-for-europe.

5. Authoritative Bodies

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- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Toluene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Toluene (CAS Number 108-88-3)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	No human data and inadequate animal data. Toluene did not produce positive results in the majority of genotoxic assays.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for toluene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical: 1,1,1-Trichloroethane
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for 1,1,1-Trichloroethane (CAS Number 71-55-6)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL* ♦ US EPA ODW*	2	2155	$BMDL_{10}$ [2]	1000	Based on reduced body weight observed in female mice exposed via the diet (microcapsules containing 1,1,1-trichloroethane) in a 13-week study. Study NOEL = 1340 mg/kg/day. Study LOEL = 2820 mg/kg/day.
CA EPA PHG*	0.076	76 [3]	NOEL	1000	Based on central nervous system effects (increased glial fibrillary acidic protein in brain, which is indicative of astrocytic injury) in Mongolian gerbils exposed continuously via inhalation for 90 days. Study NOEL = 70 ppm (380 mg/m^3)**, equivalent to daily absorbed dose of 76 mg/kg/day. Study LOEL = 210 ppm (1149 mg/m^3)**, equivalent to a daily absorbed dose of 230 mg/kg/day.[3]
WHO (2011)*	0.60	600	NOEL	1000	Based on renal lesions in male rats exposed via diet (microcapsules containing 1,1,1-trichloroethane) in a 13-week study. Study LOEL = 1200 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]$BMDL_{10}$: The lower 95% confidence limit on the benchmark dose (BMD) associated with a 10% change (relative to the control mean).

[3]The inhaled dose NOEL (76 mg/kg/day) was estimated from the air concentrations NOEL (378 mg/m^3) assuming a gerbil breathing rate of 0.032 m^3/day, a body weight of 0.048 kg, and an absorption rate of 30% for inhaled 1,1,1-trichloroethane. The same values were used to estimate the daily absorbed dose at the LOEL of 1134 mg/m^3.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

**Conversion factor is 1 ppm = 5.46 mg/m^3.

2. Recommendation and Rationale

The US EPA IRIS reference dose for 1,1,1-trichloroethane is based on the reduced body weights observed in mice exposed via the diet in 13-week studies. The WHO reference dose is based on the kidney toxicity observed only in male rats exposed via the diet in 13-week studies. Both agencies used the same total uncertainty factor of 1000. Both used uncertainty factors of 10 each to compensate for animal-to-human extrapolation and human variation. US EPA used an uncertainty factor of 3 each to compensate for the use of a subchronic study and deficiencies in the toxicity database. The WHO used an uncertainty factor of 10 for the use of a subchronic study. The CA EPA reference dose is based on an inhalation study in gerbils and $route_{Inhalation}$-to-$route_{Oral}$ extrapolation. The dietary studies in rats and mice were well designed and conducted, and were peer-reviewed. The selection of good quality oral studies over an inhalation study to derive an oral reference dose is consistent with generally accepted risk assessment practices.

The US EPA and WHO had differing opinions about the numerical value of the NOEL in the rat 13-week study. The US EPA (2007) noted (as did the authors of the NTP (2000) study) that the renal lesions in male rats at $\geq$ 1200 mg/kg/day were consistent with alpha-2-microglobulin nephropathy, as indicated by significant, dose-related increases in incidence and/or severity of renal tubule hyaline degeneration, cast formation, and regeneration and chronic interstitial inflammation of the kidney. Moreover, the US EPA (2007) observed that 1,1,1-trichloroethane related lesions were not observed in other tissues the male rats, nor were any 1,1,1-trichloroethane related lesions observed in female rats. The US EPA (2007) noted that "Renal changes associated with alpha-2-microglobulin in male rats are specific to this sex and species and are not considered to be predictive for effects in humans (U.S. EPA, 1991)." The US EPA (2007) identified the NOELs for the rat study to be 2400 mg/kg/day for male rats (sperm effects) and 2500 mg/kg/day for female rats (liver effects), which are much higher than the WHO NOEL of 600 mg/kg/day in male rats and the US EPA (2007) LOEL and NOEL for reduced body weights in the male mice (850 mg/kg/day) and female mice (1340 mg/kg/day), respectively.

The selection of a point-of-departure based on benchmark dose modeling rather than a NOEL also is consistent with generally accepted risk assessment practices. The US EPA selected the female mouse data set rather than the male mouse data set because it provided a better relationship of dose and response than does the male data set. Therefore, the US EPA reference dose (2 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,1,1-trichloroethane.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/15/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

NTP (National Toxicology Program). 2000. NTP Technical Report on the Toxicity Studies of 1,1,1-Trichlorethane (CAS No. 76-55-6) Administered in Microcapsules in Feed to F344/N Rats and B6C3F1 Mice. Toxicity Report Series Number 41. Last accessed (01/15/2018) at http://ntp.niehs.nih.gov/index.cfm?objectid=0847F677-A230-6EFD-383FBF29E52E38C8.

US EPA (United States Environmental Protection Agency). 2007. Toxicological Review of 1,1,1-Trichloroethane (CAS No. 71-55-6) In Support of Summary Information on the Integrated Risk Information System (IRIS). EPA/635/R-03/013. Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/15/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/15/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,1,1-Trichloroethane
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 1,1,1-Trichloroethane (CAS Number 71-55-6)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1995)	--	--	--	--	Human data are not available and no convincing evidence of carcinogenic effects was observed in two studies in laboratory animals.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for 1,1,1-trichloroethane is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. Toxicological Profile for 1,1,1-Trichloroethane. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,1,1-Trichloroethane
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for 1,1,1-Trichloroethane (CAS Number 71-55-6)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL*	5000 [2]	1.6×10^6	$NOEL_{HEC}$[3]	100	Based on adaptive physiologic response (very slight microscopic hepatic changes [such as altered cytoplasmic staining in the cells surrounding the central vein]) observed in the liver of rats exposed via inhalation 6 hours/day, 5 days/week in a 2-year study ($NOEL_{EXP}$ = 8190 mg/m^3, highest exposure level tested, with $NOEL_{ADJ}$ = 1460 mg/m^3) and on occasional mild liver ultrastructural variations in mice exposed via inhalation continuously for up to 14 weeks (NOEL = 1370 mg/m^3 and LOEL = 5460 mg/m^3).
CA EPA REL	1000	380,000	NOEL	300	Based on central nervous system effects (increased glial fibrillary acidic protein in the brain, which is indicative of astrocytic injury) in Mongolian gerbils exposed continuously via inhalation for 90 days. Study LOEL = 1149 mg/m^3.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

[2]Because the chronic reference concentration of 16,000 mcg/m^3 (obtained by dividing the point of departure [1.6×10^6 mcg/m^3] by a UF of 100) based on adaptive liver changes in rats was higher than the reference concentration (5000 mcg/m^3) for short-term exposures (more than 24 hours, up to 30 days) based on nervous system effects in humans (US EPA IRIS), the chronic reference concentration was set at 5000 mcg/m^3 so as not to exceed the limiting reference concentration derived for short-term exposure.

[3]The $NOEL_{HEC}$ was estimated from the rat $NOEL_{ADJ}$ of 1460 mg/m^3 ($NOEL_{ADJ}$ = $NOEL_{EXP}$ (8190 mg/m^3) x 6 hours/day x 5 days/week) using PBPK models for rats and humans.

NOEL: no-observed-effect level; $NOEL_{EXP}$: experimental NOEL; $NOEL_{ADJ}$: $NOEL_{EXP}$ adjusted to continuous exposure; LOEL: lowest-observed-effect level; HEC: human equivalent concentration; PBPK: physiologically based pharmacokinetic.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The US EPA chronic reference concentration for 1,1,1-trichloroethane is based on mild effects in the livers of rats exposed via inhalation for 2 years, with supporting evidence from a study in mice exposed via inhalation for up to 14 weeks. The $NOEL_{HEC}$ was estimated from the rat $NOEL_{ADJ}$ (1460 mg/m^3), which was derived from the $NOAEL_{EXP}$ (8190 mg/m^3) and the use of PBPK models for dosimetric adjustments between animals and humans. This compensates for animal-human differences in the pharmacokinetics of inhaled 1,1,1-trichloroethane. The US EPA applied a 100-fold uncertainty factor to compensate for animal and human differences in sensitivity (3), human variation (10) and database deficiencies (3) given some uncertainty related to the potential neurotoxicity of 1,1,1-trichloroethane following repeated exposure. However, the derived chronic reference concentration (16,000 mcg/m^3) based on mild liver effects in rats was higher than the US EPA short-term reference concentration (5000 mcg/m^3) based on nervous system effects in humans. Thus, the US EPA set the chronic reference concentration at 5000 mcg/m^3 so as not to exceed the limiting reference value derived for short-term exposure. The US EPA (2007) provided a scientifically justified rationale for the decision, which was supported by peer-review. There are several reasons why the effect levels for short-term and chronic inhalation exposures might not necessarily be expected to follow a continuum from higher to lower (i.e., the inconsistency is not necessarily an artifact).

(1) The target organ for short-term exposure (central nervous system [CNS] effects in humans) differs from that for chronic exposures (liver effects in rats and mice).

(2) Although the modes of action for the CNS and liver effects have not been established, it is likely that the modes of action at the two sites of toxicity are different.

(3) Human test batteries proved to be more sensitive than animal models of acute neurobehavioral toxicity, and sensitive testing for neurobehavioral effects in either humans or animals is unavailable following repeated exposure.

(4) The short-term reference concentration is based on analysis of peak exposure, whereas chronic reference concentration is based on area-under-the-curve exposure.

The US EPA considered the scientific quality of the study used by the CA EPA to derive their reference concentration for 1,1,1-trichloroethane and specifically asked peer-reviewers to comment on the scientific quality of the study. The US EPA (2007) raised concerns about the strength and consistency of evidence on the dose-response relationship between exposure and neurochemical parameters, the quality control/assurances of the brain dissection methods and subsequent effects on brain measurement of neurochemical parameters, and lack of supporting pathological, physiological, or neurochemical findings from other studies. During peer-review, four of five reviewers supported the US EPA conclusion that the study was unreliable as the basis for the reference concentration. One reviewer raised additional concerns regarding statistical analysis of the neurochemistry data. Another reviewer observed that more information is needed to link the protein changes in the brain with pathology of the brain and alterations in behavior, combined with a hypothesis about mode of action. Consequently, the US EPA did not consider the study to be adequate to establish a critical effect for chronic exposure to 1,1,1-trichloroethane. Therefore, the US EPA reference concentration (5000 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,1,1-trichloroethane.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/18/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

US EPA (United States Environmental Protection Agency). 2007. Toxicological Review of 1,1,1-Trichloroethane (CAS No. 71-55-6) In Support of Summary Information on the Integrated Risk Information System (IRIS). Last accessed (01/18/2018) at http://www.epa.gov/iris/.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/18/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/18/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,1,1-Trichloroethane
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 1,1,1-Trichloroethane (CAS Number 71-55-6)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	There are no reported human data, and one intermediate-term inhalation animal study did not demonstrate carcinogenicity.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} air concentration), where 1×10^{-6} concentration = 1×10^{-6} / inhalation unit risk.

2. Recommendation and Rationale

An inhalation unit risk for 1,1,1-trichloroethane is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: July, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Trichloroethene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Trichloroethene (CAS Number 79-01-6)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL* ♦ ATSDR*	5×10^{-4} **	0.048	$HED_{99,LOAEL}$ [2]	100	Based on decreased thymus weight in female mice exposed via drinking water each day for 30 weeks. High-to-low dose and animal-to-human extrapolations were based on internal dose estimates from PBPK models.
		0.37	LOEL	1000	Based on decreased plaque-forming cell (PFC) response, increased delayed-type hypersensitivity in mice exposed via drinking water exposure from gestation day 0 to 3 or 8 weeks of age.
		0.0051	$HED_{99,BMDL01}$ [3,4]	10	Based on increased fetal heart malformations in offspring of rat dams exposed via drinking water on gestation days 1 to 22. High-to-low dose and animal-to-human extrapolations were based on internal dose estimates from PBPK models.
US EPA ODW	7×10^{-3}	--	--	--	Information on derivation not available.
HC DWQ	1.46×10^{-3}	0.146	$BMDL_{10}$ [4]	100	Based on increased incidence of heart malformations in rats pups born to females exposed via drinking water prior to and during gestation days 1 to 22.
WHO (2011)*	1.46×10^{-3}	0.146	$BMDL_{10}$ [4]	100	Based on HC DWQ derivation.
CA EPA PHG*	0.50	50	BMD_{10} [5]	100	Based on kidney nephropathy in male rats exposed via gavage 5 days/week for 103 weeks (incorrectly identified as a 52-week exposure in CA EPA PHG).
RIVM (2001)	0.05	50	NOEL	1000	Based on kidney toxicity in male rats exposed via gavage 5 days/week for 52 weeks. Study LOEL = 250

					mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.

[2]$HED_{99,LOAEL}$: 99^{th} percentile of human equivalent dose (HED) at which the human internal dose equals the mouse internal dose at the mouse LOEL. It can be interpreted as being the dose at which there is 99% likelihood that a randomly selected individual will have an internal dose less than or equal to the internal dose of the rodent at the LOEL.

[3]$HED_{99,BMDL01}$: the 99^{th} percentile of HED at which the human internal dose equals the rat internal dose at the $BMDL_{01}$. It can be interpreted as being the dose at which there is 99% likelihood that a randomly selected individual will have an internal dose less than or equal to the internal dose of the rodent at the $BMDL_{01}$.

[4]$BMDL_{01\ or\ 10}$: 95% lower confidence limit on the benchmark dose associated with a 1% or 10% increase (relative to controls) in the incidence of an adverse effect;

[5]BMD_{10}: benchmark dose associated with a 10% increase (relative to controls) in the incidence of an adverse effect.

NOEL: no-observed-effect level; LOEL: lowest-observed-effect level; UF: uncertainty factor; PBPK: physiologically based pharmacokinetic.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

**The three candidate reference doses (point of departure/UF) support a reference dose of 5×10^{-4} mg/kg/day.

2. Recommendation and Rationale

The studies used as the partial basis (US EPA IRIS) or sole basis (WHO, HC) for an agency's reference dose for trichloroethene were limited by many methodological limitations, including the reliability of the technique to identify heart malformations, the lack of a clearly defined dose-response relationship, and apparent deficiencies in the conduct and reporting of the study (NYS DOH, 2006). Additional concerns are raised by the failures of other more recent studies to detect trichloroethene-induced fetal heart malformations in rats, even though the studies used sufficiently high exposure levels and adequate heart dissection techniques (NYS DOH, 2006). Collectively, these uncertainties weaken confidence in the usefulness of the study results for use in dose-response assessment. Consequently, CA EPA (2009) and NYS DOH (2006) declined to use the study in the derivation of a reference dose and concentration, respectively.

The basis for the CA EPA reference dose for trichloroethene is a gavage study, which is not a preferred mode of administration for solvents such as trichloroethene, where the pharmacokinetics, and thus toxicity, of a large single daily dose are likely to be substantially different that the pharmacokinetics of the same daily dose delivered via contaminated soil, as would be expected at Brownfield sites. Moreover, the study had serious methodological limitations, including excessive chemically induced toxicity (i.e., kidney toxicity and central nervous system toxicity characterized by sedation, loss of consciousness, tremors and convulsions), substantially early mortality, and deficiencies in the conduct of the studies (NTP, 1988). CA EPA applied a total uncertainty factor of 100 to the NOEL to compensate for animal to human extrapolation (10) and human variation (10).

The basis for the RIVM reference dose for trichloroethene is histological changes in the kidney of male rats exposed via gavage 5 days/week for 52 weeks. The study has methodological limitations including failure to report the survival rate during the study and lack of good laboratory practices. Moreover, a gavage study is not the preferred basis for a toxicity value for use in the Brownfield Cleanup Program. RIVM applied a total uncertainty factor of 1000 to the NOEL to compensate for animal to human extrapolation (10), human variation (10), and database limitations (10).

The US EPA IRIS reference dose for trichloroethene is based on the results of three studies and uses points of departure based on adult and fetal immunotoxicity in mice and fetal heart malformations in rats. The importance of the candidate reference dose (5.1×10^{-4}) based on the study on fetal heart malformations (with its methodological limitation) is reduced because the immunotoxicity endpoints, although based on different life stages, measures of immune response, and points of departure, yield (with appropriate use of uncertainty factors) candidate reference doses (4.8×10^{-4} and 3.7×10^{-4} mg/kg/day) that support the reference dose of 5×10^{-4} mg/kg/day.

The US EPA IRIS used different uncertainty factor with each point of departure.

- An uncertainty factor of 100 was applied to the $HED_{99,LOAEL}$ for decreased thymus weight in mice to compensate for animal-to-human extrapolation in sensitivity (3), use of a LOEL (10), and human variation in pharmacodynamics (i.e., sensitivity) (3). An uncertainty factor of 3 (rather than 10) was used for animal-to-human extrapolation because PBPK models were used to compensate for pharmacokinetic (but not pharmacodynamic)) differences between animals and humans. An uncertainty factor of 3 (rather than 10) was used for human variation because a probabilistic human PBPK model and the use of $HED_{99,LOAEL}$ as the point of departure compensated for pharmacokinetic (but not for pharmacodynamic) variation among humans.

- An uncertainty factor of 1000 was applied to the mouse LOEL for decreased plaque-forming cell response mice to compensate for animal-to-human extrapolation (10), use of LOEL (10), and human variation (10).

- An uncertainty factor of 10 was applied to the $HED_{99,BMDL01}$ for increased incidence of fetal heart malformations in rats to compensate for animal-to-human extrapolation in sensitivity (3) and human variation (3). The rationales for the use of 3 for these factors (rather than 10) were the same as used for the thymus data.

The US EPA IRIS derivation was peer-reviewed by national experts and is well documented. It is consistent with generally accepted risk assessment practices for high-to-low dose and animal-to-human extrapolations, including the use of benchmark dose models when possible, animal-to-human extrapolations based on PBPK models of internal doses when possible, and appropriate use of uncertainty factors given the different points of departure. Good quality human data on which to base a reference dose were not available. Therefore, the US EPA IRIS reference dose (5×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for trichloroethene.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/15/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2009. Public Health Goals for Chemicals. Trichloroethylene. Last accessed (01/15/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/15/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

NYS DOH (New York State Department of Health. 2006. Final Report. Trichloroethene Air Criteria Document. Last accessed (01/15/2018) at http://www.health.ny.gov/environmental/chemicals/trichloroethene/

NTP (National Toxicology Program). 1988. Toxicology and Carcinogenesis Studies of Trichloroethylene (CAS No. 79-01-6) in Four Strains of Rats (ACI, August, Marshall, Osborne-Mendel) (Gavage Studies). Tech Report Series No.273. NIH Publ. No. 88-2525. Last accessed (01/15/2018) at http://ntp.niehs.nih.gov/index.cfm?objectid=0847DDA0-F261-59BF-FAA04EB1EC032B61.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/15/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2012 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/15/2018) at http://water.epa.gov/action/advisories/drinking/upload/dwstandards2012.pdf.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/15/2018) at http://whqlibdoc.who.int/publications/2011/9789241548151_eng.pdf?ua=1

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Trichloroethene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Oral Cancer Potency Values for Trichloroethene (CAS Number 79-01-6)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS* Also used by: ♦ US EPA RSL*	2×10^{-5}	5×10^{-2}	lifetable analysis and weighted linear regression; linear extrapolation from the LED_{01} (2)	--	Based on kidney cancer, liver cancer, and non-Hodgkin's lymphoma in humans. A cancer potency factor based on kidney cancer was estimated from an inhalation unit risk (derived from studies of kidney cancer in French workers) using a PBPK-based $route_{Inhalation}$-to-$route_{Oral}$ extrapolation of internal doses. To obtain the cancer potency factor based on all three cancer types, the kidney-based cancer potency factor was adjusted to account for increased risks of liver and non-Hodgkin's lymphoma observed in other human studies.
NYS DEC (1997)	1.8×10^{-4}	5.7×10^{-3}	linearized multistage model	$BW^{3/4}$ (3)	Recommended value is the geometric mean of four cancer potency factors based on increased incidences of hepatocellular carcinomas in male and female mice exposed via gavage 5 days/week for 78 or 103 weeks.
HC PSAP	4×10^{-3} (4)	200 to 600 (TD_{05}) (4)	linearized multistage model	body weight[5]	Based on increased incidences of testicular tumors in rats chronically exposed via gavage and lung tumors in mice chronically exposed via inhalation.

HC DWQ*	1.2×10^{-3}	8.1×10^{-4}	linearized multistage model	$BW^{3/4}$ (3)	Based on increased incidences of combined tubular cell adenomas and adenocarcinomas of the kidneys in male rats exposed via gavage 5 days/week for 103 weeks.
WHO (2011)*	1.3×10^{-3}	7.8×10^{-4}	linearized multistage model	$BW^{3/4}$ (3)	Based on same dose-response data used by HC DWQ.
CA EPA PHG*	1.7×10^{-4}	5.9×10^{-3}	"best-fit" quantal model; linear extrapolation from the LED_{10}(6)	$BW^{3/4}$ (3)	Recommended value is the geometric mean of four cancer potency factors based on increased incidences of liver tumors in mice chronically exposed via gavage or inhalation and on PBPK estimates of metabolized dose.
CA EPA CPF*	6.7×10^{-5}	1.5×10^{-2}	--	--	Information on derivation not provided by CA EPA CPF.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6}/cancer potency factor.

[2]LED_{01}: 95% lower confidence limit on the effective dose associated with a 1% increase (above background) in cancer incidence.

[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.25}$.

[4]A cancer potency factor was not derived. A range of risk-specific doses was reported as the modeled TD_{05s} (of 200 to 600 mg/kg/day), where TD_{05} is the tumorigenic dose (not a lower-bound estimate) associated with a 5% increase in mean tumor incidence (relative to controls). If 200 mg/kg/day is associated with an increased risk of 0.05, then the dose associated with an increased risk of 1×10^{-6} (a risk level 50,000X lower than 0.05) is 4×10^{-3} mg/kg/day (i.e., 50,000 times lower than 200 mg/kg/day), assuming a linear relationship between risk and dose.

[5]Factor for dose adjustment from animals to humans is 1.

[6]LED_{10}: 95% lower confidence limit on the effective dose associated with a 10% increase (relative to controls) in tumor incidence.

PBPK: physiologically based pharmacokinetic.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

Data from epidemiological studies of good quality are generally preferred over animal studies for estimating the human carcinogenic risk of chemical exposures (US EPA, 2005). The only cancer potency factor for trichloroethene that is based on human studies is that of the US EPA IRIS. More importantly, the cancer potency factor was based on epidemiologic studies that provide convincing evidence of a causal association between trichloroethene exposures and cancer in several well-designed cohort and case-control studies. The strongest epidemiologic evidence consists of reported increased risks of kidney cancer, with more limited evidence for non-Hodgkin's lymphoma and liver cancer. Moreover, the cancer potency factor, although derived from an inhalation unit risk, was estimated using PBPK models and internal doses rather than a default $route_{Inhalation}$-to-$route_{Oral}$ extrapolation based on inhaled daily doses (20 m^3/day) and adult body weights (70 kg). Lastly, the US EPA derivation was peer-reviewed and well documented, and is consistent with generally accepted risk assessment practices. Therefore, the US EPA cancer potency factor (5×10^{-2} per mg/kg/day) is the toxicity value

recommended for use in the derivation of an oral cancer-based soil cleanup objective for trichloroethene. The trichloroethene risk specific dose calculated from this toxicity value is 2×10^{-5} mg/kg/day.[6]

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: August, 2004; revised January, 2018

4. References for Summary Table and Rationale and Recommendation

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/15/2018) at http://www.oehha.ca.gov/water/phg/allphgs.html.

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Adoption of the Revised Air Toxics Hot Spots Program Technical Support Document for Cancer Potency Factors. Last accessed (01/15/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/15/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/15/2018) at http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=95D719C5-1.

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Trichloroethene. Albany, NY: Division of Water.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/15/2018) at https://www.tera.org/iter/

US EPA (United State Environmental Protection Agency). 2005. Guidelines for Carcinogen Risk Assessment. EPA/630/P-03/001F. Last accessed (01/15/2018) at http://www.epa.gov/risk/guidance.htm.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/15/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/.

[6] Trichloroethene is identified by the US EPA as a chemical that causes kidney cancer by a mutagenic mode of action (US EPA IRIS). Age-dependent adjustment factors are incorporated into the derivation of the oral cancer-based SCO to account for increased susceptibility to kidney tumors from early-life exposures.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
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National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
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New York State Department of Health
United States Environmental Protection Agency
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- Office of Drinking Water
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- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Trichloroethene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Trichloroethene (CAS Number 79-01-6)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
General Population					
US EPA IRIS* Also used by: ♦ US EPA RSL* ♦ ATSDR*	2**	190	$HEC_{99,LOAEL}$[2]	100	Based on decreased thymus weight in female mice exposed via drinking water each day for 30 weeks. $Route_{Oral}$-to-$route_{Inhalation}$, high-to-low dose and animal-to-human extrapolations were based on internal dose estimates from PBPK models.
		21	$HEC_{99,BMDL01}$[3,4]	10	Based on increased fetal heart malformations in offspring of rat dams exposed via drinking water on gestations day 1 to 22. $Route_{Oral}$-to-$route_{Inhalation}$, high-to-low dose and animal-to-human extrapolations were based on internal dose estimates from PBPK models.
CA EPA REL	600	6.1×10^4	$LOEL_{ADJ}$[5]	100	Based on central nervous system effects (drowsiness, fatigue, headache) and eye irritation in American workers exposed 8 hours/day, 5 days/week for an average of 8 years.
NYS DOH (2006)*	10	1.1×10^4	LOEL	1000	Based on nervous system effects (motor coordination deficits) in a study of 99 Danish workers exposed to solvents. The dominant exposure for 70 workers was trichloroethene with a mean exposure time of 7.1 years, 35 hours/week and for 25 workers, the dominant exposure was CFC 113 with a mean exposure time of 4.2 years, 15.1 hours/week.
RIVM (2001)	200	2×10^5	LOEL	1000	Based on hepatotoxicity in mice in a 30-day inhalation study.

Childhood-Specific Reference Concentration					
NYS DOH (2006)*	10	1.1×10^4	LOEL	1000	Based on same study and effects used in NYS DOH derivation for the general population.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

[2]$HEC_{99,LOAEL}$: the 99th percentile of human equivalent air concentration (HEC) at which the human internal dose equals the mouse internal dose at the mouse LOEL. It can be interpreted as being the air concentration at which there is 99% likelihood that a randomly selected individual will have an internal dose less than or equal to the internal dose of the rodent at the LOEL.

[3]$HEC_{99,BMDL01}$: the 99th percentile of HEC at which the human internal dose equals the rat internal dose at the $BMDL_{01}$. It can be interpreted as being the air concentration at which there is 99% likelihood that a randomly selected individual will have an internal dose less than or equal to the internal dose of the rodent at the $BMDL_{01}$.

[4]$BMDL_{01}$: 95% lower confidence limit on the benchmark dose associated with a 1% increase (relative to controls) in the incidence of an adverse effect.

[5]$LOEL_{ADJ}$: $NOEL_{OCCUP}$ adjusted for continuous exposure (i.e., $NOEL_{OCCUP}$ x 10 m^3/20 m^3 x 5 days/7 days).

LOEL: lowest-observed-effect level; $LOEL_{OCCUP}$: LOEL based on occupational exposures; UF: uncertainty factor; PBPK: physiologically based pharmacokinetic.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

**The two candidate reference concentrations (point of departure/UF) support a reference concentration of 2 mcg/m^3.

2. Recommendation and Rationale

The available reference concentrations for trichloroethene derived by authoritative bodies from the list in item 5 (below) are based on thymus weight decreases and fetal heart malformations in animals exposed via drinking water, central nervous system effects in workers exposed via inhalation, and liver toxicity in mice exposed via inhalation.

The US EPA IRIS program based its reference concentration on two oral studies in animals, and used animal and human PBPK models for $route_{Oral}$-to-$route_{Inhalation}$, high-to-low dose, and animal-to-human extrapolations. US EPA applied an uncertainty factor of 100 to the $HED_{99,LOAEL}$ for decreased thymus weight in mice to compensate for animal-to-human extrapolation in sensitivity (3), use of a LOEL (10), and human variation in pharmacodynamics (i.e., sensitivity) (3). An uncertainty factor of 3 (rather than 10) was used for animal-to-human extrapolation because PBPK models were used to compensate for pharmacokinetic (but not pharmacodynamic)) differences between animals and humans. An uncertainty factor of 3 (rather than 10) was used for human variation because a probabilistic human PBPK model and the use of $HED_{99,LOAEL}$ as the point of departure compensated for pharmacokinetic (but not for pharmacodynamic) variation among humans. The study on fetal rat heart malformations, however, had many methodological limitations, including the reliability of the technique to identify heart malformations, the lack of a clearly defined dose-response relationship, and apparent deficiencies in the conduct and reporting of the study (NYS DOH, 2006). Additional concerns are raised by the failures of other more recent studies to detect trichloroethene-induced fetal heart malformations in rats, even though the studies used sufficiently high exposure levels and adequate heart dissection techniques (NY DOH, 2006). Collectively, these uncertainties weaken confidence in the usefulness of the study results for use in dose-response assessment. Consequently, NYS DOH (2006) and CA EPA (2009) declined to use the study in the derivation of a reference concentration or dose, respectively.

CA EPA based their reference concentration on subjective data (self-reported symptoms of drowsiness, fatigue, headache, and eye irritation) from an occupational study and used a $LOEL_{ADJ}$ (6.1×10^4 mcg/m^3) as the point of departure based on estimated $LOEL_{OCCUP}$ (1.7×10^5 mg/m^3). CA EPA adjusted for workplace exposures for continuous exposure by adjusting discontinuous occupational exposure to

continuous exposure based on relative occupational (10 m^3) to daily (20 m^3) inhalation rates and 5 days/workweek to 7 days/week exposure. The CA EPA applied a total uncertainty factor of 100 to compensate for the use of a LOEL (10) and human variation (10). They did not use an uncertainty factor for the use of a subchronic study even though the mean duration of occupational exposure was only 8 years (about 11% of a 70-year lifespan).

NYS DOH based their reference concentration on objective data (reduced scores on motor coordination tests, adjusted for confounding by age, neurological disease, arteriosclerotic disease, and alcohol abuse) from an occupational study, and used a point of departure concentration (1.1×10^4 mcg/m^3) based on PBPK modeling. The PBPK model was used to estimate the air concentration (11 mg/m^3, assuming continuous exposure) at which the mean urinary trichloroacetic acid concentration in people environmentally exposed would equal the mean concentration (7.7 mg/L) measured in the urine of workers at the time of neurological testing. In the derivation of reference concentration for adults, NYS DOH used a total uncertainty factor of 1000 to compensate for the use of a LOEL (10) from a subchronic study (10) and human variation (10). An uncertainty factor of 10 for the use of a subchronic study was used to compensate for exposure duration because the mean exposure duration of the affected workers (11 years) is only 16% of a 70-year lifetime.

In their preparation of a trichloroethene air criteria document, NYS DOH recognized the need to separately evaluate the potential health risks to children, and derived a childhood-specific reference concentration. Based on same study and effects used in NYS DOH derivation for the general population. NYS DOH used a total uncertainty factor of 1000 to compensate for the use of a LOEL (10) from a subchronic study (3), human variation (10), and lifestage variability in sensitivity to the same internal dose (3). This last factor was used because of evidence that developing central nervous system of infants and children might be more sensitive than adults to the same internal dose. An uncertainty factor of 3 (rather than 10) for the use of a subchronic study was used to compensate for exposure duration because the mean exposure duration of the affected workers (11 years) is a substantial portion of childhood (e.g., 11 years/18 years), rather than only 16% of a 70-year lifetime.

RIVM based their value on a mouse LOEL for liver toxicity from a 30-day continuous inhalation study. RIVM did not include any pharmacokinetic adjustment to estimate the human equivalent concentration. The use of a 30-day study to derive a chronic reference concentration is not consistent with generally accepted risk assessment practices.

A comparison of the studies used by CA EPA and NYS DOH indicates that the study used by NYS DOH is a better basis for a reference concentration than the study used by CA EPA. Both studies provided biomonitoring data that showed trichloroethene exposures and had similar average lengths of exposure (7.1 and 8 years). However, the study used by NYS DOH included more workers (99 to 19) and used objective measures rather than subjective symptoms of nervous system effects. The study used by CA EPA did not provide dose-response data, whereas the study used by NYS DOH showed a statistically significant trend for increasing severity of motor coordination deficits with increasing exposure duration.

Concomitant exposure to CFC is a significant limitation of the human study used by NYS DOH. Although the neurological potency of CFC 113 is low compared to trichloroethene, and only a small percentage of the cohort was identified as having CFC 113-related effects, the potential confounding effect of CFC 113 exposure on the motor coordination deficits attributed to trichloroethene is not known. The US EPA IRIS derivation was peer-reviewed by national experts and is well documented. It is consistent with generally accepted risk assessment practices for high-to-low dose and animal-to-human extrapolations, including the use of benchmark dose models when possible, animal-to-human extrapolations based on PBPK models of internal doses when possible, and appropriate use of

uncertainty factors given the different points of departure. Therefore, the US EPA IRIS reference concentration (2 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for trichloroethene.

3. Review Dates

Summary table completion: July, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/15/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/15/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

CA EPA (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). 2009. Public Health Goals for Chemicals. Trichloroethylene. Last accessed (01/15/2018) at http://www.oehha.ca.gov/water/phg/allphgs.html.

NYS DOH (New York State Department of Health. 2006. Final Report. Trichloroethene Air Criteria Document. Last accessed (01/15/2018) at http://www.health.ny.gov/environmental/chemicals/trichloroethene/

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/15/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values

Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Trichloroethene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Inhalation Unit Risk Values for Trichloroethene (CAS Number 79-01-6)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS* Also used by: ♦ US EPA RSL*	0.25	4×10^{-6}	lifetable analysis and weighted linear regression; linear extrapolation from the LEC_{01}[(2)]	--	Based on kidney cancer, liver cancer, and non-Hodgkin's lymphoma in humans. A unit risk based on kidney cancer was estimated using a PBPK-model of internal doses and relative risk and exposure estimates derived from studies of kidney cancer in French workers. To obtain the cancer potency factor based on all three cancer types, the kidney-based unit risk was adjusted to account for increased risks of liver and non-Hodgkin's lymphoma observed in other human studies.
CA EPA CPF	0.5	2×10^{-6}	linearized multistage model	body surface area[3] of metabolized doses from PBPK models	Based on the incidence of lung and liver tumors and lymphomas in male and female mice in several chronic inhalation studies. The unit risk is geometric mean of the unit risks from four inhalation studies.

HC (1996a,b)	1.6 [(4)]	8.2 x 10^4 (TC_{05})[4]	multistage model	TC_{05} for rats modified to account for ratio of the daily inhalation volume/body weight of humans aged 5 to 11 years [(12 m^3/day)/27 kg] to rats [(0.11 m^3/day)/0.35 kg]	Based on the increased incidence of testicular tumors in male rats exposed via inhalation for 104 weeks, but based on the number of animals alive at the time of appearance of the first testicular tumor.
WHO	2.3	4.3 x 10^{-7}	linearized multistage model	inhaled dose	Based on the same data set used by HC.
NYS DOH (2006)*	0.3, 1.4, 7.8	3.3 x 10^{-6}, 7.1 x 10^{-7}, 1.3 x 10^{-7}	"best-fit" quantal model; linear extrapolation from $BMDL_{10 \text{ or } 05}$[(5)]	PBPK models of metabolized dose (liver); air concentrations (lymphoma & kidney)	Based on liver tumors in male mice; lymphomas in female mice, or kidney tumors in male rats chronically exposed via inhalation.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million, where 1 x 10^{-6} air concentration = 1 x 10^{-6}/unit risk.

[2]LEC_{01}: 95% lower confidence limit on the effective air concentration dose associated with a 1% increase (above background) in tumor incidence.

[3]Factor for dose adjustment from animals to humans is (animal body weight/human body weight)$^{0.33}$.

[4]A unit risk was not derived. A linear extrapolation to 1 x 10^{-6} risk from TC_{05} (the tumorigenic concentration in air associated with a 5% increase (relative to controls) in mean tumor incidence (not a lower-bound estimate) would yield a risk specific concentration of 1.6 per mcg/m^3.

[5]$BMCL_{10 \text{ or } 05}$: The lower 95% confidence limit on the benchmark air concentration associated with a 10% or 5% increased (relative to control) in the incidence of cancers.

PBPK: physiologically based pharmacokinetic.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

Data from epidemiologic studies of good quality are generally preferred over animal studies for estimating the carcinogenic risk of chemical exposures (US EPA, 2005). The only unit risk for trichloroethene based on human studies is that of US EPA IRIS. More importantly, the estimate was based on epidemiologic studies that provide convincing evidence of a causal association between trichloroethene exposure and cancer in several well-designed cohort and case-control studies. The strongest epidemiologic evidence consists of reported increased risks of kidney cancer, with more limited evidence for non-Hodgkin's lymphoma and liver cancer. Lastly, the US EPA unit risk derivation was peer-reviewed and well documented, and is consistent with generally accepted risk assessment practices. Therefore, the US EPA unit risk (4 × 10^{-6} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for trichloroethene. The trichloroethene risk specific air concentration calculated from this toxicity value is 0.25 mcg/m^3.[(7)]

[7] Trichloroethene is identified by the US EPA as a chemical that causes kidney cancer by a mutagenic mode of action (US EPA IRIS). Age-dependent adjustment factors are incorporated into the derivation of the oral cancer-based SCO to account for increased susceptibility to kidney tumors from early-life exposures.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: August, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA CPF (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Adoption of the Revised Air Toxics Hot Spots Program Technical Support Document for Cancer Potency Factors [06/01/09] Appendix C Updated 2011. Appendix B. Chemical-Specific Summaries of the Information Used to Derive Unit Risk and Cancer Potency Values. Last accessed (01/15/2018) at http://www.oehha.ca.gov/air/hot_spots/tsd052909.html.

HC (Health Canada). 1996a. Health-Based Tolerable Daily Intakes/Concentrations and Tumorigenic Doses/Concentrations for Priority Substances. Last accessed (01/15/2018) at http://publications.gc.ca/site/eng/411636/publication.html

HC (Health Canada). 1996b. Canadian Environmental Protection Act. Priority Substances List. Supporting Documentation: Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances (Unedited Version). Last accessed (01/15/2018) at http://www.tera.org/iter/HCPSL1supportdoc.pdf.

NYS DOH (New York State Department of Health. 2006. Final Report. Trichloroethene Air Criteria Document. Last accessed (01/15/2018) at http://www.health.ny.gov/environmental/chemicals/trichloroethene/.

US EPA (United State Environmental Protection Agency). 2005. Guidelines for Carcinogen Risk Assessment. EPA/630/P-03/001F. Last accessed (01/15/2018) at http://www.epa.gov/risk/guidance.htm.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2000. Air Quality Guidelines for Europe. Last accessed (01/15/2018) at http://www.euro.who.int/en/what-we-publish/abstracts/air-quality-guidelines-for-europe.

5. Authoritative Bodies

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Provisional Peer Reviewed Toxicity Values
Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: 1,2,4-Trimethylbenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for 1,2,4-Trimethylbenzene (CAS Number 95-63-6)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
CA EPA NL	0.05	143	NOEL	3000	Based on increased serum phosphorus levels in rats exposed to 1,3,5-trimethylbenzene by corn oil gavage 5 days/week for 90 days. Study LOEL = 429 mg/kg/day.
US EPA IRIS	0.01	3.5	$BMCL_{1SD}$ [2]	300	Based on decreased pain sensitivity in male rats exposed by inhalation for 6 hours/day, 5 days/week for 90 days.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. UF: uncertainty factor.
[2] The $BMCL_{1SD}$ is the 95% lower confidence limit on benchmark air concentration (BMC) corresponding to a change in the mean equal to one standard deviation (SD) of the control mean. A pharmacokinetic model was used to obtain a human equivalent dose corresponding to the rat 1,2,4-trimethylbenzene blood concentration at the BMCL.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The CA EPA value for 1,2,4-trimethylbenzene uses 1,3,5-trimethylbenzene as a surrogate chemical as both chemicals are alkylated benzenes containing three methyl group substitutions on their benzene rings. The oral reference dose for 1,3,5-trimethylbenzene is based on an adjusted NOEL of 143 mg/kg/day for increased serum phosphorus levels in rats exposed by corn oil gavage 5 days per week for 90 days. A total uncertainty factor of 3000 (10 each to account for animal-to-human extrapolation and human variation, 10 for the use of a subchronic study and an additional 3 for database deficiencies) was applied to the adjusted NOEL.

The US EPA IRIS derived its reference dose for 1,2,4-trimethylbenzene based on neurotoxicity in a subchronic rat inhalation study of 1,2,4-trimethylbenzene. The rationale for this was based on neurotoxicity being the critical toxicological endpoint for trimethylbenzene exposure, and that the neurotoxic endpoints are qualitatively comparable across exposure routes. US EPA IRIS used benchmark modeling to calculate the lower confidence limit on the air concentration corresponding to a change equal to one standard deviation of the control mean. A pharmacokinetic model for 1,2,4-trimethylbenzene was used to obtain a human equivalent dose corresponding to the 1,2,4-

trimethylbenzene blood concentration in rats at the benchmark air concentration. US EPA IRIS applied a total uncertainty factor of 300 to the human equivalent dose (3 for interspecies extrapolation, 10 for intraspecies extrapolation, 3 for use of a subchronic study, and 3 for database deficiencies) to obtain the reference dose.

The US EPA IRIS reference dose is chemical-specific, is based on a sensitive toxicological endpoint, and uses methods more consistent with generally accepted risk assessment practice (benchmark modeling and pharmacokinetic modeling) than the CA EPA derivation, which uses the NOEL/LOEL approach for identifying a point of departure. Therefore, the US EPA IRIS reference dose (0.01 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,2,4-trimethylbenzene.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA NL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Notification Levels for Chemicals in Drinking Water. Last accessed (01/12/2018) at https://oehha.ca.gov/water/notification-levels-chemicals-drinking-water.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (1/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
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- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,2,4-Trimethylbenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 1,2,4-Trimethylbenzene (CAS Number 95-63-6)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	One available animal study is inadequate for evaluating potential carcinogenicity.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for 1,2,4-trimethylbenzene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: May, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations

Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,2,4-Trimethylbenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for 1,2,4-Trimethylbenzene (CAS Number 95-63-6)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA OSRTI Also used by: ♦ US EPA RSL	7	2.2×10^4	$NOEL_{[HEC]}$	3000	Based on decreased clotting time in female rats exposed by inhalation 6 hours/day, 5 days/week for 90 days. Study $LOEL_{[HEC]} = 8.8 \times 10^4$ mcg/m^3
US EPA IRIS	60	18×10^4	$BMCL_{1SD}$ [2]	300	Based on decreased pain sensitivity in rats exposed by inhalation for 6 hours/day, 5 days/week for 90 days.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

[2] The $BMCL_{1SD}$ is the 95% lower confidence limit on benchmark air concentration (BMC) corresponding to a change in the mean equal to one standard deviation (SD) of the control mean. A pharmacokinetic model was used to obtain a human equivalent air concentration corresponding to the rat 1,2,4-trimethylbenzene blood concentration at the BMCL.

NOEL: no observed effect level; LOEL: lowest observed effect level; HEC: human equivalent concentration; UF: uncertainty factor.

2. Recommendation and Rationale

Both the US EPA OSRTI and US EPA IRIS reference concentrations for 1,2,4-trimethylbenzene are based on subchronic inhalation studies in rats. The US EPA OSRTI value is based on blood effects in female rats while the US EPA IRIS value is based on neurotoxicity in male rats. The US EPA OSRTI point of departure (human equivalent concentration) is the time-weighted experimental air concentration at the NOEL multiplied by a default dosimetric adjustment factor of 1, which is used when the blood:gas partition coefficients of a Category 3 gas in the species of interest are unknown. The US EPA IRIS point of departure is based on benchmark modeling to calculate the lower confidence limit on the air concentration corresponding to a change equal to one standard deviation of the control mean. A pharmacokinetic model for 1,2,4-trimethylbenzene was then used to obtain a human equivalent air concentration corresponding to the 1,2,4-trimethylbenzene blood level in rats at

the benchmark air concentration. Both derivations employ uncertainty factors of 3 for interspecies extrapolation and 10 for interspecies extrapolation. The US EPA OSRTI used uncertainty factors of 10 each for use of a subchronic study and database deficiencies, while the US EPA IRIS used a value of 3 for each of these uncertainty factors. The US EPA IRIS derivation is more robust in that it uses up to date methods such as benchmark dose modeling and pharmacokinetic modeling to calculate internal dose metrics, while the US EPA OSRTI derivation uses the NOEL/LOEL approach and a default dosimetric adjustment. Further, the full uncertainty factor of 10 used by the US EPA OSRTI for extrapolation of data from a subchronic study seems unnecessary in light of data indicating that blood and organ concentrations of trimethylbenzenes are similar following repeated versus acute exposures, and that trimethylbenzene isomers would not likely accumulate to an appreciably greater degree following a chronic exposure and lead to effects at lower doses compared to shorter duration studies. Therefore, the US EPA IRIS reference concentration (60 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,2,4-trimethylbenzene.

3. Review Dates

Summary table completion: May, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (1/20/2018) at http://www.epa.gov/iris/.

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund . Last accessed (1/20/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (1/20/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
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World Health Organization

Chemical Name: 1,2,4-Trimethylbenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 1,2,4-Trimethylbenzene (CAS Number 95-63-6)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for 1,2,4-trimethylbenzene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
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California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,3,5-Trimethylbenzene
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for 1,3,5-Trimethylbenzene (CAS Number 108-67-8)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
CA EPA NL	0.05	143	NOEL	3000	Based on increased serum phosphorus levels in rats exposed by corn oil gavage 5 days/week for 90 days. Study LOEL = 429 mg/kg/day.
US EPA OSRTI Also used by: ♦ US EPA RSL	0.01	143	NOEL	10,000	Based on increased liver weight in same study used by CA EPA.
US EPA IRIS	0.01	3.5	$BMCL_{1SD}$ [2]	300	Based on decreased pain sensitivity in rats exposed to 1,2,4-trimethylbenzene by inhalation for 6 hours/day, 5 days/week for 90 days.

[1] Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level.
[2] The $BMCL_{1SD}$ is the 95% lower confidence limit on benchmark air concentration (BMC) corresponding to a change in the mean equal to one standard deviation (SD) of the control mean. A pharmacokinetic model was used to obtain a human equivalent dose corresponding to the rat 1,2,4-trimethylbenzene blood concentration at the BMCL.
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

Both the CA EPA and the US EPA OSRTI reference doses for 1,3,5-trimethylbenzene are based on the same subchronic gavage study in rats. The derivations use the same point of departure (an adjusted NOEL of 143 mg/kg/day), although CA EPA identified the critical effect as increased serum phosphorus levels, while the US EPA OSRTI identified increases in liver weight. Identical uncertainty factors applied by both agencies to the adjusted NOEL were 10 each for inter- and intraspecies extrapolation, and 10 for the use of a subchronic study. CA EPA used an uncertainty factor of 3 for database deficiencies, while the US EPA used a full uncertainty factor of 10, resulting in total uncertainty factors of 3000 and 10,000 respectively. The use of a total

uncertainty factor higher than 3000 is less consistent with generally accepted risk assessment practice as it may ascribe an undue level of toxicity in the absence of data. Therefore the US EPA OSRTI value is not considered further.

In its trimethylbenzene technical support document, the US EPA IRIS derived a candidate reference dose of 0.01 mg/kg/day for 1,3,5-trimethylbenzene based on the same 90-day gavage study used by CA EPA and US EPA OSRTI. This derivation was based on hematological effects and used methods consistent with generally accepted risk assessment practice, such as calculation of a benchmark dose and a dosimetric adjustment based on body weight to the ¾ power. However, the US EPA IRIS derived and chose a 1,3,5-trimethylbenzene reference dose based on neurotoxicity in a subchronic rat inhalation study of 1,2,4-trimethylbenzene. The rationale for this choice was based on neurotoxicity being the critical toxicological endpoint for trimethylbenzene exposure, and that the neurotoxic endpoints are qualitatively comparable across exposure routes and trimethylbenzene isomers. US EPA IRIS used benchmark modeling to calculate the lower confidence limit on the air concentration corresponding to a change equal to one standard deviation of the control mean. A pharmacokinetic model for 1,2,4-trimethylbenzene was used to obtain a human equivalent dose corresponding to the 1,2,4-trimethylbenzene blood concentration in rats at the benchmark air concentration. US EPA IRIS applied a total uncertainty factor of 300 to the human equivalent dose (3 for interspecies extrapolation, 10 for intraspecies extrapolation, 3 for use of a subchronic study, and 3 for database deficiencies) to obtain the reference dose, which is numerically identical to the reference dose they derived based on toxicological endpoints other than neurotoxicity. Both derivations use methods more consistent with generally accepted risk assessment practice (benchmark modeling, body weight scaling and pharmacokinetic modeling) and are preferred over the CA EPA derivation, which uses the NOEL/LOEL approach for identifying a point of departure. Therefore, the US EPA IRIS reference dose (0.01 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,3,5-trimethylbenzene.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: June, 2004; revised January 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA NL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Notification Levels for Chemicals in Drinking Water. Last accessed (01/17/2018) at https://oehha.ca.gov/water/notification-levels-chemicals-drinking-water

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA OSRTI (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). Provisional Peer Reviewed Toxicity Values for Superfund . Last accessed (01/17/2018) at http://hhpprtv.ornl.gov/quickview/pprtv_papers.php.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,3,5-Trimethylbenzene
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for 1,3,5-Trimethylbenzene (CAS Number 108-67-8)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	No data available.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for 1,3,5-trimethylbenzene is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: June, 2004; no revision January, 2018
Toxicity value recommendation: June, 2004; no revision January, 2018

4. References for Summary Table

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: 1,3,5-Trimethylbenzene
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for 1,3,5-Trimethylbenzene (CAS Number 108-67-8)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS	60	18×10^4	$BMCL_{1SD}$ [2]	300	Based on decreased pain sensitivity in rats exposed to 1,2,4-trimethylbenzene by inhalation for 6 hours/day, 5 days/week for 90 days.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

[2] The $BMCL_{1SD}$ is the 95% lower confidence limit on benchmark air concentration (BMC) corresponding to a change in the mean equal to one standard deviation (SD) of the control mean. A pharmacokinetic model was used to obtain a human equivalent air concentration corresponding to the rat 1,2,4-trimethylbenzene blood concentration at the BMCL.

HEC: human equivalent concentration; UF: uncertainty factor.

2. Recommendation and Rationale

The US EPA IRIS reference concentration for 1,3,5-trimethylbenzene is the only available value from an authoritative body listed in item 5 (below). The US EPA IRIS recommends that its reference concentration based on 1,2,4-trimethylbenzene neurotoxicity in a subchronic rat study be used for all trimethylbenzene isomers. The point of departure is based on benchmark modeling to calculate the lower confidence limit on the air concentration corresponding to a change equal to one standard deviation of the control mean. A pharmacokinetic model for 1,2,4-trimethylbenzene was then used to obtain a human equivalent air concentration corresponding to the 1,2,4-trimethylbenzene blood level in rats at the benchmark air concentration. A total uncertainty factor of 300 (3 for interspecies extrapolation, 10 for intraspecies extrapolation, 3 for use of a subchronic study and 3 for database deficiencies) was applied to the human equivalent air concentration to obtain the reference concentration. The reference concentration was derived using methods that reflect consistency with generally accepted risk assessment practices, and the structural chemical and toxicological similarity between the two chemicals provides a basis for using toxicity data for 1,2,4-trimethylbenzene to represent 1,3,5-trimethylbenzene. Therefore the US EPA reference concentration for (60 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,3,5-trimethylbenzene.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; revised January, 2018

4. References for Summary Table and Recommendation and Rationale

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6 & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: 1,3,5-Trimethylbenzene
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for 1,3,5-Trimethylbenzene (CAS Number 108-67-8)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Data suitable for derivation of a chemical-specific inhalation unit risk are not available.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for 1,3,5-trimethylbenzene is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: February, 2005; no revision January, 2018
Toxicity value recommendation: February, 2005; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Vinyl Chloride
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Vinyl Chloride (CAS Number 75-01-4)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL ♦ US EPA ODW	3×10^{-3}	0.09 (human equivalent dose)	NOEL	30	Based on polymorphism of liver cells and liver cysts in rats exposed in the diet (powder) 4 hours/day for 150 weeks (females) and 149 weeks (males). Study LOEL = 0.9 mg/kg/day (human equivalent dose).
ATSDR	3×10^{-3}	0.09 (human equivalent dose)	NOEL	30	Based on liver cell polymorphism in rats exposed in the diet (powder) 4 hours/day for 150 weeks (same study as in US EPA IRIS).
CA EPA PHG*	1×10^{-3}	0.13	NOEL	100	Based on the same study and effects used by US EPA IRIS.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for the reference doses for vinyl chloride is identical with respect to choice of study, species, and adverse effect. The US EPA and the ATSDR derived a human equivalent dose based on the administered (or bioavailable) dose corresponding to the NOEL reported in the study. A physiologically-based pharmacokinetic (PBPK) model was used to estimate the internal dose of reactive metabolites in rats and humans and the relationship between internal metabolite dose and administered (or bioavailable) dose. Although there were slight differences in the assumptions and modeling methods used by the two agencies, identical points of departure and reference doses were derived, after application of the same uncertainty factors (10 for human variability and 3 for animal-to-human

variability). CA EPA PHG used the rat NOEL dose as the point of departure, and applied a default 100 total uncertainty factor to account for human and animal-to-human variability. The US EPA IRIS and ATSDR assessments, which used a PBPK model, are more consistent with generally-accepted risk assessment practices. Therefore the US EPA and ATSDR reference dose (3×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for vinyl chloride.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: January, 2005; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/17/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies (see Table for Internet Websites)

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Vinyl Chloride
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Vinyl Chloride (CAS Number 75-01-4)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS Also used by: ♦ US EPA RSL	1.4×10^{-6}	0.72 (continuous lifetime adult exposure)	linearized multistage model, extra risk	PBPK [2]	Based on the incidence of hepatocellular carcinomas, angiosarcomas, and neoplastic nodules observed in female rats exposed in diet four hours/day for 144 weeks.
US EPA IRIS Also used by: ♦ US EPA RSL	7.1×10^{-7}	1.4 (continuous lifetime exposure from birth)	linearized multistage model, extra risk	PBPK [2]	Based on the incidence of hepatocellular carcinomas, angiosarcomas, and neoplastic nodules observed in female rats exposed in diet four hours/day for 144 weeks.
US EPA IRIS Also used by: • WHO (2011)*	1.3×10^{-6}	0.75 (continuous lifetime adult exposure)	linear extrapola-tion from LED_{10}	PBPK [2]	Based on the incidence of hepatocellular carcinomas, angiosarcomas, and neoplastic nodules observed in female rats exposed in diet four hours/day for 144 weeks.
US EPA IRIS Also used by: • WHO (2011)*	6.7×10^{-7}	1.5 (continuous lifetime exposure	linear extrapola-tion from LED_{10}	PBPK [2]	Based on the incidence of hepatocellular carcinomas,

		from birth)			angiosarcomas, and neoplastic nodules observed in female rats exposed in diet four hours/day for 144 weeks.
RIVM (2001)	6×10^{-6}	-- [3]	linear extrapola-tion	body weight [4]	Based on same study as US EPA IRIS (2004).
HC DWQ	5.1×10^{-6} to 4.9×10^{-5}	-- [5]	linear extrapola-tion from LED_{10}	body surface area [6]	Based on the incidence of hepatocellular angiosarcomas observed in female rats exposed in diet four hours/day for 144 weeks.
US EPA HEAST (1997)	5.3×10^{-7}	1.9	linearized multistage model, extra risk	body surface area [6]	Based on lung and liver tumors in rats exposed by diet for 1001 days.
CA EPA PHG	3.7×10^{-6}	0.27	linearized multistage model on internal dose, extra risk	unclear	Based on lung tumors in female mice exposed via inhalation.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

[2]Dose adjustment from animal to humans is based on back-modeling of internal dose at fixed risk level to oral exposure level via a PBPK model.

[3]No cancer potency factor was derived. The risk specific dose was obtained by linear extrapolation from the lowest tumorigenic dose (not a lower-bound estimate)

[4]Factor for dose adjustment from animal to humans is 1.

[5]No cancer potency factor was derived. The risk specific dose was obtained from the drinking water unit risk range of 5.8×10^{-7} to 5.6×10^{-6} per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day.

[6]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.

LED_{10}: The 95% lower bound on the dose associated with a 10% increase in tumor incidence above background; PBPK model: physiologically-based pharmacokinetic model.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The cancer potency factors derived by authoritative bodies primarily use male and female rat data sets showing an increased incidence of liver tumors (including liver angiosarcomas, a rare tumor type in rats) with dietary exposure. Inhalation studies in rats and mice also show an increased incidence of liver tumors as well as lung tumors, and the CA EPA PHG cancer potency value is based on lung tumor data from an inhalation study with the assumption that the same potency value may be applied to oral exposure. The US EPA IRIS presents four possible oral cancer potency values - two derived using the linear multistage model and two derived using a linear extrapolation from the LED_{10}. For each derivation method, values are presented for continuous adult lifetime exposure and for continuous lifetime exposure from birth. RIVM derived a risk-specific dose from the same data set used by US EPA IRIS, but used a linear extrapolation from the lowest dose with observed increased tumor incidence (not a lower bound on the dose) and did not use an interspecies scaling adjustment. HC DWQ used the data set for angiocarcinomas in female rats from the same study used by US EPA IRIS, but employed the less current body surface area method to scale the doses from animals to humans. The US EPA HEAST value is derived from the same data set as the US EPA IRIS values, but the derivation methodology used has been superceded by the more up-to-date IRIS analysis. The route extrapolation used by CA EPA is not chosen given that data from well-conducted oral studies are available. Although the US EPA IRIS narrative recommends use of the LMS-derived values, the LED_{10}-based values are more consistent with generally-accepted risk assessment practice. In practice, the values derived by the two methods are nearly identical. Therefore, the US EPA IRIS cancer potency factors (0.75 per mg/kg/day for scenarios involving only continuous exposure during the adult lifetime and 1.5 per mg/kg/day for scenarios involving continuous exposure during the entire lifetime from birth) are the toxicity values recommended for use in the derivation of an oral cancer-based soil cleanup objective for vinyl chloride. The vinyl chloride risk specific doses calculated from these toxicity values are 1.3×10^{-6} and 6.7×10^{-7} mg/kg/day respectively.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/17/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC DWQ (Health Canada). Guidelines for Canadian Drinking Water Quality - Technical Documents. Last accessed (01/17/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/water-eau/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA HEAST (United States Environmental Protection Agency, Office of Superfund Remediation and Technology Innovation). 1997. Health Effects Assessment Summary Tables. FY 1997 Update. Last accessed (01/17/2018) at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2877#Download.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/17/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/17/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/17/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies (see Table for Internet Websites)

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Vinyl Chloride
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Vinyl Chloride (CAS Number 75-01-4)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2004)	100	2.5×10^3	NOEL	30	Based route-to-route extrapolation from the incidence of liver cell polymorphisms in a 2-year rat feeding study. Extrapolated LOEL = 2.5×10^4 mcg/m^3.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
[2]HEC: human equivalent concentration
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

2. Recommendation and Rationale

The US EPA value is the only available reference concentration for vinyl chloride from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the reference concentration of 100 mcg/m^3 is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for vinyl chloride.

3. Review Dates

Summary table completion: June, 2004; no revision January, 2018
Toxicity value recommendation: December, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Vinyl Chloride
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Vinyl Chloride (CAS Number 75-01-4)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: • US EPA Region 3 (2004) • US EPA HEAST (1997)	0.11 (continuous lifetime exposure from birth)	8.8×10^{-6}	linearized multistage model, extra risk and linear extrapolation from the LED_{10}[2]	PBPK[3] model	Based on increased incidence of liver tumors in female rats in a 1-year inhalation study.
	0.23 (continuous lifetime exposure during adulthood)	4.4×10^{-6}			
Cal EPA (2002)	0.013	7.8×10^{-5}	linearized multistage model, extra risk	an unspecified metabolic model was used for interspecies dosimetry scaling	Based on the highest unit risk derived from several datasets reporting increased incidence of liver, lung and mammary tumors in rats and mice; the highest unit risk derives from lung tumor data in female mice

RIVM (2001)	reported as 10^{-4} lifetime risk-specific concentration of 3.6; linear extrapolation to 10^{-6} risk would yield: 0.036 [4]	--[5]	linear extrapolation from the observed tumor incidence at the lowest dose with increased incidence	concentration in air	Based on increased incidence of liver tumors rats in the same study and review as US EPA IRIS (2004).

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10^{-6} dose), where 1 x 10^{-6} air concentration = 1 x 10^{-6} / unit risk.
[2]LED_{10} = The 95% lower confidence limit of the dose that produces a 10% increase in tumor incidence.
[3]PBPK: Physiologically-Based Pharmokinetic
[4]The risk-specific concentration reported was a linear extrapolation to a risk level of 10^{-4} from the observed tumor incidence at the lowest dose with a significant increased incidence above controls. This is not a lower-bound estimate.
[5]The only value reported is a non-lower-bound risk-specific concentration; a unit risk was not reported.

2. Recommendation and Rationale

The inhalation unit risks derived by authoritative bodies from the list in item 5 (below) are all based on increased incidence of liver or lung tumors in rats and mice exposed to vinyl chloride via inhalation. The RIVM derivation is a linear extrapolation from the observed tumor incidence at the lowest dose with significantly increased incidence above controls, and does not represent a lower-bound estimate on the risk-specific concentration. The Cal EPA derivation included the use of a metabolic model to account for saturable metabolism of vinyl chloride, but there is no clear description provided in the Cal EPA documentation of the model used or how it was applied to derive internal dose metrics.

The US EPA derivation was based on an extensive data set for liver tumors in rats exposed to vinyl chloride via inhalation and used PBPK modeling to estimate internal dose metrics in rats from airborne exposure concentrations and reverse PBPK modeling to estimate human equivalent air concentrations from internal dose metrics associated with target lifetime risk levels. US EPA also derived unit risk estimates based on a linearized multistage model and a linear extrapolation from the LED_{10}. The two approaches yielded nearly identical unit risk estimates. The US EPA derivation is expected to provide a more robust unit risk estimate, is more clearly documented than the Cal EPA derivation and is more consistent with currently-accepted risk assessment practice. The US EPA derivation also specifically accounts for data suggesting that there is increased sensitivity to vinyl chloride carcinogenicity early in life by increasing the unit risk two-fold for exposures beginning from birth. Therefore, the US EPA unit risks (4.4 x 10^{-6} per mcg/m^3 for scenarios involving only continuous exposure during the adult lifetime and 8.8 x 10^{-6} per mcg/m^3 for scenarios involving continuous exposure during the entire lifetime from birth) are the toxicity values recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for vinyl chloride. The vinyl chloride risk specific air concentrations calculated from these toxicity values are 0.23 and 0.11 mcg/m^3 respectively.

3. Review Dates

Summary table completion: June, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2002. Air Toxics Hot Spots Program Risk Assessment Guidelines: Part II Technical Support Document for Describing Available Cancer Potency Factors. Sacramento, CA. Last accessed (01/17/2018) at http://www.oehha.ca.gov/air/cancer_guide/TSD2.html

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. Last accessed (01/17/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update 9200.6-303 997-1. Washington, DC: Office of Research and Development. Office of Emergency and Remedial Response.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

United States Environmental Protection Agency
- Integrated Risk Information System
- National Center for Environmental Assessment
- Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
- Region 3 Risk-Based Concentrations
- Office of Pesticides
- Office of Drinking Water
- Health Effects Assessment Summary Tables

New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Xylenes
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Available Oral Reference Doses for Xylenes (CAS Number 1330-20-7)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS Also used by: • US EPA RSL • EPA ODW • ATSDR	0.2	179	$NOEL_{ADJ}$	1000	Based on decreased body weight and increased mortality in rats exposed by corn oil gavage 5 days per week for 2 years. $NOEL_{ADJ}$ = 250 mg/kg-day ($NOEL_{EXP}$) x 5 days/7 days = 179 mg/kg-day; $LOEL_{ADJ}$ = 500 mg/kg-day ($LOEL_{EXP}$) x 5 days/7 days = 357 mg/kg/day.
RIVM (2001)	0.15	150	LOEL	1000	Based on mild nephropathy in female rats exposed by gavage for 90 days.
HC PSAP	1.5	150	NOEL	100	Based on mild nephropathy in female rats exposed by gavage for 90 days.
EPA OPP	2	179	$NOEL_{ADJ}$	100	Based on same data as the US EPA IRIS value
WHO (2011)	0.179	179	$NOEL_{ADJ}$	1000	Based on same data as the US EPA IRIS value
CA EPA PHG*	0.25	7.5	LOEL	30	Based on self-reported neurological symptoms in workers exposed to xylene by inhalation.

[1]Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor; ADJ = adjusted (time-weighted); EXP = experimental.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.

2. Recommendation and Rationale

The basis for three of the xylene reference doses ([WHO, US EPA IRIS (also US EPA RSL, EPA ODW, ATSDR), and US EPA OPP] is essentially identical with respect to the choice of study (a two-year study in rats), adverse effect (decreased body weights and increased mortality) and identification of the point of departure ($NOEL_{ADJ}$ = 179 mg/kg/day). The RIVM and HC PSAP reference doses are derived from a

subchronic oral rat study where mild kidney toxicity was observed in females. Since data from well-conducted chronic oral studies are available and are preferred as the basis of a chronic reference dose, the RIVM and HC PSAP derivations were not considered further as the basis for the reference dose. The CA EPA PHG assessment is based on self-reported neurological symptoms in workers exposed to xylenes in air. Although assessments based on human data can be preferred, there are some questions about the quality of this epidemiologic study (including potential self-report bias and mixed solvent exposures). In addition, good quality route-specific animal data are available, making an oral reference dose based on an extrapolation from inhalation data less preferable. The US EPA IRIS, US EPA OPP and WHO values come from essentially equivalent derivations, except that US EPA OPP applied a total uncertainty factor of 100 to the rat NOEL to account for animal-to-human and human variability, while US EPA IRIS and WHO applied an additional factor of 10 to account for database limitations. US EPA IRIS notes in particular that data on chronic neurotoxicity, reproductive toxicity and developmental neurotoxicity are lacking and that these limitations in the database are significant, especially given the acute neurotoxic effects of xylene exposure. Therefore, the additional 10-fold uncertainty appears justified and the US EPA reference dose (0.2 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for xylenes.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/15/2018) at https://www.atsdr.cdc.gov/mrls/mrllist.asp with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA PHG (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Public Health Goals for Chemicals. Last accessed (01/15/2018) at https://oehha.ca.gov/water/public-health-goals-phgs

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/15/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/15/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2012 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/15/2018) at http://water.epa.gov/drink/standards/hascience.cfm.

US EPA OPP (United States Environmental Protection Agency, Office of Pesticide Programs). Pesticide Reregistration Status. Last accessed (01/15/2018) at http://www.epa.gov/opp00001/reregistration/status.htm.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

WHO (World Health Organization). 2011. Guidelines for Drinking-Water Quality, Fourth Edition. Last accessed (01/15/2018) at http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html

5. Authoritative Bodies (see Table for Internet Websites)

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Xylenes
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Xylenes (CAS Number 1330-20-7)

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1995)	--	--	--	--	Studies evaluating the carcinogenicity of xylenes following oral exposure in humans are not available. Mixed results are reported in three long-term animal studies. The limited information and the limitations of the available studies preclude a definitive conclusion regarding the carcinogenicity of mixed xylenes following oral exposure.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for xylenes is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: June, 2004; no revision January, 2018
Toxicity value recommendation: July, 2004; no revision January, 2018

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. Toxicological Profile for Xylene. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. Last accessed (01/17/2018) at https://www.atsdr.cdc.gov/toxprofiledocs/index.html

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

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- Integrated Risk Information System
- National Center for Environmental Assessment
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- Region 3 Risk-Based Concentrations
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New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
- Office of Environmental Health Hazard Assessment

Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Xylenes
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Reference Concentrations for Xylenes (CAS Number 1330-20-7)

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
US EPA IRIS Also used by: ♦ US EPA RSL	100	3.9×10^4	NOEL	300	Based on impaired motor coordination (decreased rotarod performance) in male rats in a 3-month inhalation study. Study LOEL = 7.8×10^4 mcg/m^3.
ATSDR*	200**	6.01×10^4	LOEL	300	Based on an increase of subjective symptoms including anxiety, forgetfulness, inability to concentrate, eye and nasal irritation, dizziness, and sore throats reported by workers exposed to xylenes by inhalation for an average of 7 years.
HC PSAP as reported by TERA (2004)	180	1.8×10^5	LOEL	1000	Based on fetal toxicity (skeletal retardation) in offspring of rats exposed via inhalation during gestation. Unspecified toxicity in maternal rats was also reported at this exposure level. TERA (2004) reports that the reference concentration was derived by Health Canada based on 5 to 11 year old child body weight and breathing rate parameters.

RIVM (2001)	870	8.7×10^5	LOEL	1000	Based on behavioral impairment (indicating an adverse effect on CNS development) in offspring of rats exposed to xylene during pregnancy (limited review information available).
CA EPA REL	700	2.2×10^4	LOEL	30	Based on the same study as used by ATSDR

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

*Agency's toxicity value added or revised during update of fact sheet to support updated soil cleanup objectives for the New York State Brownfield Cleanup Program.
**The ATSDR value is reported as 0.05 parts per million (ppm). For xylenes, 1 ppm = 4.34 mg/m^3.

2. Recommendation and Rationale

The available reference concentrations for mixed xylenes derived by authoritative bodies from the list in item 5 (below) are based primarily on central nervous system effects observed in humans (workers), in rats exposed via inhalation or in offspring of rats exposed by inhalation during gestation. Reference concentrations are also based on skeletal effects observed in offspring of rats exposed via inhalation during gestation. TERA (2004) attributes a reference concentration to HC PSAP, based on a rat LOEL for developmental effects converted to a human equivalent concentration based on default assumptions for body weight and daily breathing rate in rats and in a 5 to 11 year old child. The derivation of a human equivalent concentration based on relative default breathing rates and body weights in rodents and humans is inconsistent with currently-accepted risk assessment practice for reference concentration dosimetry of category 3 gases. RIVM also based their derivation on effects in a developmental study in rats exposed by inhalation during gestation. The LOEL identified in the RIVM study is well above the LOELs in the other derivations and so does not represent a sufficiently sensitive endpoint. The US EPA IRIS based its value on a subchronic rat inhalation study where indications of central nervous system toxicity were observed. The human equivalent concentration was derived based on a default pharmacokinetic adjustment (equal to 1) for the case where the blood:air partitioning coefficient in animals is greater than the human coefficient. They applied a total uncertainty factor of 300, including 10-fold to account for human variability, 3-fold (with a pharmacokinetic adjustment) to account for animal-to-human variability, 3-fold to account for use of a subchronic study and 3-fold for database deficiencies including the lack of a 2-generation reproductive toxicity study. A full 10-fold factor for use of a subchronic study was not considered necessary because evidence from observations made at earlier time points in this study and another study lasting 6 months suggested that changes in the motor function test used in the study did not increase with increasing exposure duration. The ATSDR and CA EPA based their derivations on a study of workers chronically exposed to xylene vapors in air who experienced various subjective symptoms including central nervous system and upper respiratory symptoms. The ATSDR used the 8-hour mean LOEL exposure concentration as the human equivalent concentration without adjusting for continuous exposure, while the CA EPA adjusted this level for continuous exposure based on the fraction of the daily inhalation rate attributed to a 8-hour workday and

5 days/week exposure. The ATSDR applied a total uncertainty factor of 300, including 10-fold for human variability, 10-fold for use of a LOEL exposure level and an additional factor of 3 to account for the lack of studies evaluating chronic neurotoxicity. The CA EPA applied a total uncertainty factor of 30, including 10-fold for human variability and 3-fold for use of a LOEL. The default uncertainty factor for use of a LOEL was decreased based on the generally mild adverse effects observed and the low prevalence (<50%) observed. The subjective symptoms reported, including effects on balance and cognitive ability, are indicative of adverse central nervous system effects that are more appropriately accounted for with a full 10-fold factor for use of a LOEL as applied by ATSDR. However, ATSDR's lack of adjustment for discontinuous weekday exposure is not consistent with currently-accepted risk assessment practice. The US EPA derivation is more consistent with generally-accepted risk assessment practices than either the ATSDR or CA EPA derivation. Therefore, the US EPA IRIS reference concentration (100 mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for mixed xylenes.

3. Review Dates

Summary table completion: June, 2004; revised January, 2018
Toxicity value recommendation: October, 2004; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/15/2018) at http://www.atsdr.cdc.gov/toxpro2.html, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

CA EPA REL (California Environmental Protection Agency, Office of Environmental Health Hazard Assessment). Air Toxics Hot Spots Risk Assessment Guidelines: Noncancer Reference Exposure Levels. Last accessed (01/15/2018) at http://www.oehha.ca.gov/air/hot_spots/rels_dec2008.html.

HC PSAP (Health Canada). Priority Substances Assessment Program. Last accessed (01/15/2018) at http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/index-eng.php.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/15/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

TERA (Toxicology Excellence for Risk Assessment). International Toxicity Estimates for Risk (ITER). Last accessed (01/15/2018) at https://www.tera.org/iter/

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/15/2018) at https://www.epa.gov/risk/regional-screening-levels-rsls-generic-tables

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Xylenes
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Xylenes (CAS Number 1330-20-7)

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Human data are not available, animal data are inadequate for an assessment of the carcinogenic potential of xylenes.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for xylenes is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: June, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/20/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment

Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Zinc
Exposure Route: Oral
Toxicity: Non-Cancer

New York State Department of Health
Oral Non-Cancer Toxicity Value Documentation

1. Summary of Oral Reference Doses for Inorganic Zinc

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS* Also used by: ♦ US EPA RSL ♦ US EPA ODW	0.3	0.91	$LOEL_{TOTAL}$	3	Based on decreases in erythrocyte Cu-Zn-superoxide dismutase (ESOD) activity in healthy adult male and female volunteers in four studies.
ATSDR*	0.3 [2]	0.83	$NOEL_{SUP}$	3	Based on decreases in ESOD activity in 18 women given zinc supplements twice daily (50 mg supplemental zinc/day, or 0.83 mg supplemental zinc/kg/day (assuming a 60-kg mean body weight for healthy women) for a 10-week period. The study was one of the studies used by US EPA IRIS.
RIVM (2001)	0.5	1.0	$LOEL_{TOTAL}$	2	Based on same study and effect as ATSDR, but background zinc consumption was added to the $LOEL_{SUP}$ of 0.83 mg/kg/day to obtain the $LOEL_{TOTAL}$ of 1 mg/kg/day. An outdated 1994 ATSDR Toxicological Profile for Zinc is cited as the source of the $LOEL_{TOTAL}$. The current 2005 ATSDR profile uses a $NOEL_{SUP}$ of 0.83 mg/kg/day.

[1]Agencies use different terms for the reference dose, including acceptable daily intake or dose, tolerable daily intake, and chronic minimal risk level.
[2]ATSDR accepted the intermediate-duration minimal risk level of 0.3 mg/kg/day as the chronic minimal risk level.

NOEL: no-observed-effect level; $NOEL_{SUP}$: NOEL based on supplemental dose; LOEL: lowest-observed-effect level; $LOEL_{TOTAL}$: LOEL based on total dose (supplemental + background doses); UF: uncertainty factor.

*New addition to fact sheet.

2. Recommendation and Rationale

The US EPA reference dose for zinc is based on four subchronic studies that identified effect levels of 0.81 mg/kg/day (two studies), 0.94 mg/kg/day (one study), and 0.99 mg/kg/day (one study). The four

studies had similar methodologies and observed effects, thus, the average of the effect levels was identified as the $LOEL_{TOTAL}$ (0.81+0.94+0.99=2.74/3=0.91 mg/kg/day). The dose conversion factor was based on reference adult body weights for the appropriate gender. Total dose was derived from estimations from the FDA Total Diet Study for 1982-1986 plus supplemental dose. US EPA used a total uncertainty factor of 3 to compensate for human variation. US EPA noted that for zinc, and other nutritionally required elements, it is important that the reference dose not be set at a value that would suggest that people should consume diets with insufficient zinc, and the use of an uncertainty factor greater than 3 would place some sensitive humans in the possible position of either exceeding the reference dose or not obtaining sufficient zinc.

The basis for the ATSDR and RIVM reference doses is essentially identical with respect to choice of study, species, observed effect level, and point of departure (0.83 or 1.0 mg/kg/day). ATSDR identified the point of departure as a $NOEL_{SUP}$ (0.83 mg/kg/day). ATSDR used an uncertainty factor of 3 to compensate for human variation. A larger factor for sensitive populations was not believed necessary, as women already represent a sensitive population with regards to changes in iron status. RIVM applied a total uncertainty factor of 2 to the $NOEL_{TOTAL}$, which was considered a sufficient margin of safety, without a clear explanation of the basis for their choice.

The three derivation are based on nearly the same point-of-departure doses and uncertainty factors resulting in similar reference doses (0.3 or 0.5 mg/kg/day). The US EPA derivation of the reference dose is well documented and was peer-reviewed. It is based on a more comprehensive set of data that the derivations of ATSDR and RIVM. It is consistent with generally accepted risk assessment practices for essential elements (as zinc is). Therefore, the US EPA reference dose (0.3 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for zinc

3. Review Dates

Summary table completion: June, 2004; updated December, 2011; no revision January, 2018
Toxicity value recommendation: September, 2004; updated December, 2011; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

ATSDR (Agency for Toxic Substances and Disease Registry). 1994. Toxicological Profile for Zinc (superseded by 2005 Update). Atlanta, GA: United States Department of Health and Human Services, Public Health Service.

ATSDR (Agency for Toxic Substances and Disease Registry). Minimal Risk Levels. Last accessed (01/02/2018) at http://www.atsdr.cdc.gov/toxpro2.html, with supporting documentation at http://www.atsdr.cdc.gov/toxprofiles/index.asp.

RIVM (National Institute of Public Health & Environmental Protection, Netherlands). 2001. Re-Evaluation of Human-Toxicological Maximum Permissible Risk Levels. RIVM Rapport 711701025. Last accessed (01/02/2018) at http://www.rivm.nl/bibliotheek/rapporten/711701025.html.

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/02/2018) at http://www.epa.gov/iris/.

US EPA ODW (United States Environmental Protection Agency, Office of Drinking Water). 2011 Edition of the Drinking Water Standards and Health Advisories. Last accessed (01/02/2018) at http://water.epa.gov/action/advisories/drinking/drinking_index.cfm#dw-standards.

US EPA RSL (United States Environmental Protection Agency, Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites). Last accessed (01/02/2018) at http://www.epa.gov/reg3hwmd/risk/human/rb-concentration_table/index.htm.

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
- Integrated Risk Information System
- Office of Drinking Water
- Office of Pesticide Programs
- Office of Superfund Remediation and Technology Innovation
  - Health Effects Assessment Summary Tables
  - Provisional Peer Reviewed Toxicity Values
- Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites

World Health Organization

Chemical Name: Zinc
Exposure Route: Oral
Toxicity: Cancer

New York State Department of Health
Oral Cancer Toxicity Value Documentation

1. Summary of Available Oral Cancer Potency Values for Inorganic Zinc

Agency	Risk Specific Dose[1] (mg/kg/day)	Cancer Potency Factor $(mg/kg/day)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Human data are not available. Available animal studies provide no convincing evidence of carcinogenicity.

[1]The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

2. Recommendation and Rationale

An oral cancer potency factor for zinc is not available.*

* Chemicals may lack a cancer potency factor because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a dose-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of a cancer potency factor.

3. Review Dates

Summary table completion: June, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System

National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)
Region 3 Risk-Based Concentrations
Office of Pesticides
Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
New York State Department of Environmental Conservation
Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

Chemical Name: Zinc
Exposure Route: Inhalation
Toxicity: Non-Cancer

New York State Department of Health
Inhalation Non-Cancer Toxicity Value Documentation

1. Summary of Inhalation Reference Concentrations for Inorganic Zinc

Agency	Reference Concentration[1] (mcg/m^3)	Point of Departure		UF	Summary
		Air Concentration (mcg/m^3)	Basis		
--	--	--	--	--	Data suitable for derivation of a chemical-specific reference concentration are not available.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration in air, and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for zinc is not available from the authoritative bodies listed in item number 5 (below). Zinc is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure. The recommended oral reference dose for zinc is 0.3 mg/kg/day, and is based on blood effects. A default $route_{Oral}$-to-$route_{Inhalation}$ extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m^3 of air per day was used to derive a reference concentration from the reference dose. Therefore, a reference concentration of 1.0×10^3 mcg/m^3 based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for zinc.

3. Review Dates

Summary table completion: June, 2004; updated December, 2011; no revision January, 2018
Toxicity value recommendation: September, 2004; updated December, 2011; no revision January, 2018

4. References for Summary Table and Recommendation and Rationale

5. Authoritative Bodies

Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency, Office of Environmental Health Hazard Assessment
Health Canada
National Institute of Public Health & Environmental Protection, Netherlands (RIVM)
New York State Department of Environmental Conservation
New York State Department of Health
United States Environmental Protection Agency
  Integrated Risk Information System
  Office of Drinking Water

Office of Pesticide Programs
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Health Effects Assessment Summary Tables
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Regions 3, 6, & 9 Regional Screening Levels for Chemical Contaminants at Superfund Sites
World Health Organization

Chemical Name: Zinc
Exposure Route: Inhalation
Toxicity: Cancer

New York State Department of Health
Inhalation Cancer Toxicity Value Documentation

1. Summary of Available Inhalation Unit Risk Values for Inorganic Zinc

Agency	Risk Specific Air Concentration[1] (mcg/m^3)	Unit Risk $(mcg/m^3)^{-1}$	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Human data are not available. Available animal studies provide no convincing evidence of carcinogenicity.

[1]The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1×10^{-6} dose), where 1×10^{-6} air concentration $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for zinc is not available.*

* Chemicals may lack a unit risk because their carcinogenic potency has not been studied, because studies of their carcinogenic potency did not show a concentration-related increase in cancer incidence or because some evidence of carcinogenic potency has been observed, but the quality of the studies or the data do not allow quantitative estimation of unit risk.

3. Review Dates

Summary table completion: September, 2004; no revision January, 2018
Toxicity value recommendation: September, 2004; no revision January, 2018

4. References for Summary Table

US EPA IRIS (United States Environmental Protection Agency, Integrated Risk Information System). Last accessed (01/15/2018) at http://www.epa.gov/iris/.

5. Authoritative Bodies

United States Environmental Protection Agency
Integrated Risk Information System
National Center for Environmental Assessment
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed Toxicity Values)

Region 3 Risk-Based Concentrations
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Office of Drinking Water
Health Effects Assessment Summary Tables
New York State Department of Health
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Agency for Toxic Substances and Disease Registry
California Environmental Protection Agency
Office of Environmental Health Hazard Assessment
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands