Chemical Name: Endosulfan (technical)
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 Endosulfan (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 (2004) Also used by: ♦ US EPA HEAST (1997) ♦ US EPA Region 3 (2004)	6×10^{-3}	0.6 (male) 0.7 (female)	NOEL	100	Based on reduced body weight gain in male and female rats; increased incidence of marked progressive glomerulonephrosis and blood vessel aneurysms in males exposed in diet for 2 years. Study LOEL = 2.9 mg/kg/day (male); 3.8 mg/kg/day (female).
NYS DEC (draft)	6.7×10^{-4}	0.2	NOEL	300	Based on increased serum alkaline phosphatase activity (indicating hepatotoxicity) in male dogs exposed via diet for one year. Study LOEL = 0.65 mg/kg/day.
ATSDR (2000)	2×10^{-3}	0.18	NOEL	100	Based on same study as NYS DEC.

[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 reference dose for endosulfan is reduced body weight gain and increased incidence of kidney toxicity in rats with a NOEL identified at 0.6 mg/kg/d in males. The basis of the NYSDEC and ATSDR reference doses is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (about 0.2 mg/kg/day). The US EPA did not consider the serum biochemical changes observed in the dog study used by the NYSDEC and ATSDR as indicating exposure-related toxicity. The NYSDEC and ATSDR interpreted those results as evidence of subtle liver toxicity. The US EPA and ATSDR each applied an uncertainty factor of 100 to

their NOEL estimates to account for interspecies and intraspecies variability. The NYSDEC included an additional uncertainty factor of 3 to account for uncertainties in the reproductive and developmental toxicity of endosulfan. *In vitro* data suggest that endosulfan may have estrogenic activity and the additional factor of 3 also accounts for uncertainties due to lack of data on *in vivo* estrogenic activity. The lower NOEL identified by the NYS DEC is chosen based on the association of increased serum alkaline phosphatase activity with cellular liver damage. The additional uncertainty factor of 3 to account for endosulfan toxicity database uncertainties accurately reflects the available toxicological information. Therefore, the NYSDEC reference dose (6.7×10^{-4} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for endosulfan technical grade.

As described in the Technical Support Document, the information in this fact sheet is applicable to endosulfan I, endosulfan II, endosulfan sulfate or mixtures of these chemicals.

3. Review Dates

Summary table completion: June, 2004
Toxicity value recommendation: August, 2004

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

NYS DEC (New York State Department of Environmental Conservation). 2004. Draft Human Health Fact Sheet. Ambient Water Quality Value for Endosulfan. 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 03/31/1993. Last revised: 10/01/1994. http://www.epa.gov/iris/subst/index.html

US EPA Region 3 (United States Environmental Protection Agency Region 3). Risk-based Concentration Table. Superfund Technical Support Section. 2004. http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: Endosulfan (technical)
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 (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.*

* 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.

As described in the Technical Support Document, the information in this fact sheet is applicable to endosulfan I, endosulfan II, endosulfan sulfate or mixtures of these chemicals.

3. Review Dates

Summary table completion: June, 2004
Toxicity value recommendation: August, 2004

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 Checked for a Cancer Potency Value

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 (technical)
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 Endosulfan (CAS Number 115-29-7)

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 endosulfan is not available from the authoritative bodies listed in item number 5 (below). Endosulfan 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 endosulfan is 6.7×10^{-4} mg/kg/day. Therefore, a reference concentration of 2.3 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 endosulfan.

As described in the Technical Support Document, the information in this fact sheet is applicable to endosulfan I, endosulfan II, endosulfan sulfate or mixtures of these chemicals.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

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 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: Endosulfan (technical)
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 (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.*

* 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.

As described in the Technical Support Document, the information in this fact sheet is applicable to endosulfan I, endosulfan II, endosulfan sulfate or mixtures of these chemicals.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

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

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 (technical)
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 (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA OPP (1997) ♦ US EPA HEAST (1997)	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 (1996)	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.

[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 doses derived by authoritative bodies 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 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.

As described in the Technical Support Document, the information in this fact sheet is applicable to endrin, endrin aldehyde, endrin ketone or mixtures of these chemicals.

3. Review Dates

Summary table completion: February, 2004
Toxicity value recommendation: April, 2004

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.

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. 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 04/20/88. Last revised: 04/01/91. http://www.epa.gov/iris/index.html.

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 04/21/88.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

WHO (World Health Organization). 2003. Guidelines for drinking water quality, 3rd Ed. World Health Organization, Geneva. http://www.who.int/docstore/water_sanitation_health/GDWQ/draftchemicals/endrin2003.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: Endrin (technical)
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.

As described in the Technical Support Document, the information in this fact sheet is applicable to endrin, endrin aldehyde, endrin ketone or mixtures of these chemicals.

3. Review Dates

Summary table completion: February, 2004
Toxicity value recommendation: April, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification Date: 10/19/88. Last revised: 07/01/93. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 (technical)
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.

As described in the Technical Support Document, the information in this fact sheet is applicable to endrin, endrin aldehyde, endrin ketone or mixtures of these chemicals.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: Endrin (technical)
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 $= 1 \times 10^{-6}$ / 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.

As described in the Technical Support Document, the information in this fact sheet is applicable to endrin, endrin aldehyde, endrin ketone or mixtures of these chemicals.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 (1993)	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
Toxicity value recommendation: July, 2004

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. 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 05/20/1985. Last revised: 06/01/1991. http://www.epa.gov/iris/subst/0408.htm.

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. http://www.epa.gov/reg3hwmd/risk/human/index.htm

WHO (World Health Organization). 2003. Guidelines for drinking water quality, 3rd Ed. World Health Organization, Geneva. http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/ethylbenzene.htm

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: Ethylbenzene
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 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	
US EPA IRIS (2004) ATSDR (1999)	--	--	--	--	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). The US EPA lists ethylbenzene as not classifiable as to human 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

A cancer potency factor for ethylbenzene is not available from the list of authoritative bodies in item 5 (below). Ethyl benzene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an inhalation unit risk based on cancer effects distant from the site of contact (i.e., the respiratory system) exists. A default inhalation-to-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 unit risk. The recommended inhalation unit risk for ethylbenzene is 1×10^{-6} per mcg/m^3. 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
Toxicity value recommendation: March, 2005

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1999. Toxicological Profile for Ethylbenzene. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency verification date: 10/07/1987. Last revised: 08/01/1991.
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: Inhalation
Toxicity: Non-Cancer

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

1. Summary of Available 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 (2004) Also used by: ♦ US EPA Region 3 (2004)	1×10^3	4.3×10^5	NOEL	300	Based on skeletal variations in rats and evidence of slightly reduced litter size in rabbits in developmental toxicity studies in each species. The animals were exposed 6 to 7 hours per day, 7 days per week on gestation days 1 to 19 (rats) and 1 to 24 (rabbits). Study LOEL = 4.3×10^6 mcg/m^3.
CA EPA (2004)	2×10^3	5.7×10^4 (13 ppm)	NOEL	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 = 1.95×10^5 mcg/m^3 (45 ppm).
RIVM (2001)	770	7.7×10^4	NOEL	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 = 1.95×10^5 mcg/m^3 (45 ppm).

[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 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 studies (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 variabilty 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. The US EPA's derivation was published prior to the publication of the chronic toxicity study used by the CA EPA, and the CA EPA NOEL is lower than the LOELs observed in the US EPA and RIVM studies. The CA EPA's estimate of the human equivalent concentration and application of uncertainty factors to a chronic NOEL are consistent with currently-accepted risk assessment practice. Therefore, the CA 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 ethylbenzene.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: October, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2003. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Ethylbenzene. Sacramento, CA: Office of Environmental Health

Assessment, California Environmental Protection Agency.
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.
http://www.rivm.nl/bibliotheek/index-en.html

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 12/20/1990. Last revised: 03/01/1991.
http://www.epa.gov/iris/index.html.

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 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: Ethylbenzene
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 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 (2004)	--	--	--	--	The IRIS chemical file lists ethylbenzene as not classifiable as to human carcinogenicity based on lack of animal bioassays and human 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 $= 1 \times 10^{-6}$ / unit risk.

2. Recommendation and Rationale

An inhalation unit risk for ethylbenzene is not available from the list of authoritative bodies in item 5 (below). 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, 1999) 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. Based on the increased incidence of renal tubular adenomas and carcinomas in male rats, and in the absence of a unit risk from authoritative bodies, the New York State Department of Health derived a unit risk of 1.0×10^{-6} per mcg/m^3 for ethylbenzene using methods consistent with current risk assessment practice. The point of departure was the 95% lower confidence limit on the air concentration associated with a 10% excess risk, 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. 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 ethylbenzene risk specific air concentration calculated from this toxicity value is 1 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: March, 2005

4. References for Summary Table

NTP (National Toxicology Program). 1999. Toxicology and Carcinogenesis Studies of Ethylbenzene (Cas No. 100-41-4) in F344/N Rats and B6C3F_1 Mice (Inhalation Studies). January, 1999. NTP TR 466. NIH Publication No. 99-3956. US Department of Health and Human Services.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Last revised: 08/01/1991. Verification date: 10/07/1987.
http://www.epa.gov/iris/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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
Toxicity value recommendation: March, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment.

Verification date: 11/15/89. Last revised: 07/01/93.
http://www.epa.gov/iris/index.html.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section.
http://www.epa.gov/reg3hwmd/risk/human/index.htm.

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: 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
Toxicity value recommendation: April, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 05/30/90. Last revised: 12/01/90.
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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
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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
Toxicity value recommendation: April, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification Date: 11/15/89. Last revised: 11/01/90. http://www.epa.gov/iris/index.html.

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. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

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: 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
Toxicity value recommendation: April, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment.

Verification Date: 02/07/90. Last revised: 12/01/90.
http://www.epa.gov/iris/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA OPP (1997) ♦ 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. Study LOEL = 0.25 mg/kg/day.
NYS DEC (1997)	1.5×10^{-3}	0.15	NOEL	100	Based on the same study as US EPA IRIS (2004), using an uncertainty factor of 100 instead of 300.
WHO (1993)	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.

[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 and the NYS DEC reference doses are based on the same study. The US EPA used an extra uncertainty factor of 3 for the lack of a chronic toxicity study in a second species. This additional uncertainty factor was not considered necessary by the NYS DEC when deriving the New York State Ambient Water Quality Value for heptachlor. Furthermore, there are chronic studies available in mice exposed to heptachlor (for evaluating cancer effects) as well as studies on reproductive toxicity. Therefore, the database does not appear sufficiently inadequate to justify an additional uncertainty factor of 3. The WHO reference dose is based on a study with heptachlor expoxide, a breakdown product of heptachlor, and not on the parent chemical. The NYS DEC 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.

3. Review Dates

Summary table completion: February, 2004
Toxicity value recommendation: April, 2004

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 Heptachlor. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification Date: 04/16/87. Last revised: 03/01/91.
http://www.epa.gov/iris/index.html

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 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.
http://www.epa.gov/reg3hwmd/risk/human/index.htm.

WHO (World Health Organization). 1993. Guidelines for drinking-water quality, 2nd ed. Vol. 1. Recommendations. Geneva, World Health Organization, pp. 83-84.
http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/heptasum.htm.

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

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).

CA EPA (1999)	2.4×10^{-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., 1×10^{-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 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 CA 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 1.3×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: February, 2004
Toxicity value recommendation: April, 2004

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)).

CA 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.

http://www.oehha.ca.gov/water/phg/allphgs.html.

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification Date: 04/01/87. Last revised: 07/01/93.
http://www.epa.gov/iris/index.html.

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.
http://www.epa.gov/reg3hwmd/risk/human/index.htm.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 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 heptachlor is 1.5×10^{-3} mg/kg/day. Therefore, a reference concentration of 5.2 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 heptachlor.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 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 $= 1 \times 10^{-6}$ / 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 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
Toxicity value recommendation: December, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 04/01/1987. Last revised: 07/01/1993.
http://www.epa.gov/iris/index.html

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.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 (2004) Also used by: • US EPA Region 3 (2003) • US EPA OPP (1997) • US EPA ODW (2002) • NYS DEC (1997)	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.
ATSDR (2002)	5×10^{-5}	0.016	LOEL	300	Based on the same study reviewed in IRIS, except the LOEL was based on minimal hepatic effects (peribiliary lymphocytosis and fibrosis of the liver) in male rats at the lowest dose.
CA EPA (2003)	3×10^{-5}	0.01	LOEL	300	Based on the same study reviewed in IRIS and ATSDR. The identified LOEL is the same as ATSDR except that the body weights were calculated differently.
Health Canada (1993)	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 as used by Health Canada.

[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 hexachlorobenzene is liver toxicity, generally in rats chronically exposed via 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 and determines whether a LOEL point of departure is identified at the lowest dose, or a NOEL is identified at the next-lowest dose. 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). 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 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 to identifying a NOEL at the second-lowest dose (0.08 mg/kg/d). 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 therefore considered the lowest non-zero dose a minimal LOEL. Health Canada and RIVM both identified a NOEL similar to the US EPA point of departure, although their calculations of the effective dose rate in the feeding study differ from the US EPA's and clear documentation of the source of the differences is not available. The US EPA and RIVM applied an uncertainty factor of 100 to account for interspecies and intraspecies variability. 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 significance, but not statistical significance. Health Canada 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, as separate cancer and non-cancer assessments are being made. 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 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
Toxicity value recommendation: August, 2004

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. http://www.atsdr.cdc.gov/toxpro2.html

CA EPA (California Environmental Protection Agency). 2003. Public Health Goal for Hexachlorobenzene in Drinking Water. Division of Drinking Water and Environmental Management. Sacramento, CA. http://www.oehha.ca.gov/water/phg/allphgs.html.

Health Canada, Environment Canada. 1993. Priority Substances List Assessment Report: Hexachlorobenzene. Ottawa, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl2.htm

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. http://www.rivm.nl/bibliotheek/index-en.html

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 05/26/1988. Last revised: 04/01/1991. http://www.epa.gov/iris/index.html.

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 05/05/88.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

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: 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.
CA 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.
CA 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 CA EPA (2002)
CA 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 CA 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 CA EPA are based on increased in incidence of liver tumors or neoplastic nodules in rats or hamsters. The CA 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 CA 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. CA 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 CA EPA (2002) derivation. Of the 3 CA 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 (CA 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 CA EPA (2003) cancer potency estimate based on the 2-generation dietary study are nearly the same, the CA 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 CA 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
Toxicity value recommendation: August, 2004

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. http://www.atsdr.cdc.gov/toxpro2.html

CA 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.

CA EPA (California Environmental Protection Agency). 2003. Public health goal for chemicals in drinking water: hexachlorobenzene. Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/water/phg/allphgs.html

Health Canada, Environment Canada. 1993. Priority Substances List Assessment Report: Hexachlorobenzene. Ottawa, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

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. http://www.rivm.nl/bibliotheek/index-en.html

Toxicology Excellence for Risk Assessment (TERA). 2004. International toxicity estimates for risk database. 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 03/01/1989. Last revised: 11/01/1996. http://www.epa.gov/iris/subst/index.html

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. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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		
--	--	--	--	--	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 hexachlorobenzene is not available from the authoritative bodies listed in item number 5 (below). Hexachlorobenzene 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 hexachlorobenzene is 8×10^{-4} mg/kg/day. Therefore, a reference concentration of 2.8 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 hexachlorobenzene.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: Hexachlorobenzene
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 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	
--	--	--	--	--	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 hexachlorobenzene is not available from the authoritative bodies listed in item number 5 (below). Hexachlorobenzene 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 hexachlorobenzene is 1.0 per mg/kg/day. Therefore, a unit risk of 2.9×10^{-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 3.4×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994 http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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
Toxicity value recommendation: June, 2004

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. http://www.atsdr.cdc.gov/toxprofiles/tp43.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 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: *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).
CA 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 CA 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
Toxicity value recommendation: June, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2004. Toxicity Criteria Database. Office of Exposure and Health Hazard Assessment. http://www.oehha.ca.gov/risk/ChemicalDB/start.asp

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.

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 12/17/86. Last revised: 07/01/93. http://www.epa.gov/iris/index.html.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

5. Authoritative Bodies Checked for a Cancer Potency Value

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
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: *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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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
Toxicity value recommendation: June, 2004

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. 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	$BW^{¾}$ [3]	Based on the same study and toxicological endpoints as US EPA IRIS (2004).
CA 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 CA 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
Toxicity value recommendation: June, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2004. Toxicity Criteria Database. Office of Exposure and Health Hazard Assessment.
http://www.oehha.ca.gov/risk/ChemicalDB/start.asp

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.

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 12/17/86. Last revised: 07/01/93. http://www.epa.gov/iris/index.html.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section.
http://www.epa.gov/reg3hwmd/risk/human/index.htm.

5. Authoritative Bodies Checked for a Cancer Potency Value

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
Toxicity value recommendation: February, 2005

4. References for Summary Table

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
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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994 http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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
Toxicity value recommendation: July, 2004

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. http://www.atsdr.cdc.gov/toxprofiles/tp43.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. 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: *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
Toxicity value recommendation: July, 2004

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. Verification date: 12/17/1986. Last revised: 07/01/1993.
http://www.epa.gov/iris/subst/0163.htm

5. Authoritative Bodies Checked for a Cancer Potency Value

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

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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
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: *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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA ODW (2002) ♦ US EPA OPP (1997) ♦ US EPA HEAST (1997)	3×10^{-4}	0.33	NOEL	1000	Based on liver and kidney toxicity in male and female rats in an 18-week feeding study. Study LOEL = 1.55 mg/kg/day.
ATSDR (2003)	-	-	-	-	Toxicity studies reviewed, but a chronic reference value was not derived.
RIVM (2001)	4×10^{-5}	0.012	LOEL	300	Based on immunological effects in female mice orally exposed for 24 weeks.
NYS DEC (1997)	3×10^{-4}	0.33	NOEL	1000	Based on the same study reviewed in US EPA IRIS (2004).

[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 NYS DEC *gamma*-HCH reference doses is identical with respect to choice of study, species, adverse effect, identification of the point of departure (0.33 mg/kg/day) and uncertainty factor. RIVM based their value on a subchronic study reporting an increased incidence of immunological effects, including increased and then suppressed cellular and humoral immunity responses and histopathologic effects on the thymus. This study reported a very low LOEL dose that RIVM noted was approximately 10 to 100-fold lower than immunotoxicity effect levels reported in earlier short-term exposure studies, raising some question about the validity of the study results. However, the RIVM study duration was somewhat longer than the study used by the US EPA IRIS and

NYSDEC, and immunological endpoints are not routinely assessed, so it is possible that the RIVM LOEL represents a sensitive endpoint. The RIVM study was not available at the time the US EPA considered the reference dose assessment for gamma-HCH. RIVM applied a total uncertainty factor of 300; 10-fold each to account for inter- and intra-species variability and an additional factor of 3 that RIVM considered sufficient to account for the marginal toxic response observed at the LOEL. All of the derivations have some attendant uncertainty since none of them is based on a well-conducted chronic study. There may be somewhat more uncertainty associated with interpretation of the study used by RIVM. However, there is not compelling data to reject the RIVM study result and immunological effects were not evaluated in the 18-week rat study used by the US EPA. Therefore, the RIVM reference dose (4×10^{-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
Toxicity value recommendation: September, 2004

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. http://www.atsdr.cdc.gov/toxprofiles/tp43.html

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for gamma-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. 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 (97-1).

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 01/22/1986. Last revised: 03/01/1988 http://www.epa.gov/iris/subst/0065.htm

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2002. Office of Drinking Water, Drinking Water Standards and Health Advisories. Washinton, 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 10/11/85.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

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: *gamma*-hexachlorocyclohexane (*gamma*-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 *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	
US EPA HEAST (1997) Also used by: ♦ US EPA Region 3 (2003)	7.7×10^{-7}	1.3	linearized multistage model, extra risk	body surface area[2]	Based on liver tumors in a mouse feeding study. (Limited review information available. Value is listed as "Under Review")
CA EPA (2002)	9.1×10^{-7}	1.1	linearized multistage model, extra risk	body surface area[2]	Based on incidence data of liver tumors in a single strain of male mice fed gamma-HCH for 110 weeks.
ATSDR (2003)	-	-	-	-	Suggestive evidence of carcinogenicity in several strains of mice, but not rats, in chronic feeding studies. Insufficient data to assess human carcinogenic potential.
NYS DEC (1997)	1.4×10^{-6}	0.71	linearized multistage model, extra risk	$BW^{3/4}$ [3]	Based on the same tumor data as used by CA 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

All the cancer potency factors derived by authoritative bodies use male and female mouse data sets showing an increased incidence of liver tumors. The CA EPA 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 currently 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
Toxicity value recommendation: July, 2004

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. http://www.atsdr.cdc.gov/toxprofiles/tp43.html

CA EPA (California Environmental Protection Agency). 2002. Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/risk/ChemicalDB/index.asp

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for gamma-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 Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

5. Authoritative Bodies Checked for a Cancer Potency Value

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

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: Inhalation
Toxicity: Non-Cancer

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

1. Summary of Available 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		
--	--	--	--	--	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 *gamma*-HCH is not available from the authoritative bodies listed in item number 5 (below). *gamma*-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 *gamma*-HCH is 4×10^{-5} mg/kg/day. Therefore, a reference concentration of 0.14 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 *gamma*-HCH.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: *gamma*-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 *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	
--	--	--	--	--	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 *gamma*-HCH is not available from the authoritative bodies listed in item number 5 (below). *gamma*-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 *gamma*-HCH is 0.71 per mg/kg/day. Therefore, a unit risk of 2.0×10^{-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 *gamma*-HCH. The risk specific air concentration calculated from this toxicity value is 5.0×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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 Available 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		
ATSDR (1995)	-	-	-	-	Toxicity studies reviewed in Toxicological Profile for Polycyclic Aromatic Hydrocarbons, but a reference value was not derived due to insufficient toxicity data.

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

2. Recommendation and Rationale

No compound-specific reference dose values for indeno[1,2,3-cd]pyrene have been derived by the authoritative bodies from the list in item 5 (see below). An oral reference dose is available for pyrene, which is a chemically similar polycyclic aromatic hydrocarbon that can be used to represent indeno[1,2,3-cd]pyrene with respect to noncancer endpoints. The basis for choosing pyrene as a chemical surrogate for indeno[1,2,3-cd]pyrene is that pyrene is expected to be toxicologically similar, and has the most stringent reference dose available among the polycyclic aromatic hydrocarbons. Therefore, the US EPA reference dose for pyrene (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 indeno[1,2,3-cd]pyrene (see Oral Non-Cancer Toxicity Value Documentation for pyrene).

3. Review Dates

Summary table completion: March, 2004
Toxicity value recommendation: September, 2004

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.

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: 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 Available 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 OSRTI (2004) US EPA Region 3 (2003)	1.37×10^{-6}	0.73	--	--	Based on a relative potency factor of 0.1 applied to US EPA's cancer potency estimate for benzo(a)pyrene, which is based on increased incidence of squamous cell papillomas and carcinomas of the forestomach in mice and of the forestomach, larynx and esophagus in rats.
ATSDR (1995) US EPA IRIS (2004)	-	-	-	-	Human data are not available. Indeno[1,2,3-cd]pyrene produced tumors in mice following lung implants, subcutaneous injection and dermal exposure.

CA EPA (2002)	8.3×10^{-7}	1.2	--	--	Based on a potency equivalency factor of 0.1 applied to the cancer potency factor of 11.5 per mg/kg/day for benzo[a]pyrene. The cancer potency factor for benzo[a] pyrene is based on stomach tumors observed in a 4-6 month feeding study in mice.
RIVM (2001)	5.0×10^{-5}	-- [2]	--	--	Based on a potency equivalency factor of 0.1 applied to a cancer potency factor for benzo(a)pyrene. The cancer potency factor for benzo(a)pyrene is 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., 1×10^{-6} dose), where 1×10^{-6} dose = 1×10^{-6} / cancer potency factor.

[2]No cancer potency factor is reported, as the derivation directly extrapolates from an experimental dose with significant increased incidence above background to the dose associated with a one-in-one million risk; the risk-specific dose is not a lower-bound estimate.

2. Recommendation and Rationale

The cancer potency values for indeno[1,2,3-cd]pyrene are based on benzo(a)pyrene and the application of relative potency factors. The recommended cancer potency value for benzo(a)pyrene is 9.03 per mg/kg/day (see Oral Cancer Toxicity Value Documentation for benzo(a)pyrene). Application of the recommended relative potency factor (0.1) yields a cancer potency factor 0.903 per mg/kg/day, which 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 (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The indeno[1,2,3-cd]pyrene risk specific dose calculated from this toxicity value is 1.1×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: March, 2004
Toxicity value recommendation: February, 2005

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.

CA EPA (California Department of Environmental Protection, Office of Environmental Health Hazard Assessment). 2002. Air Toxics Hot Spots Program Risk Assessment Guidelines: Part II Technical Support Document for Describing Available Cancer Potency Factors. Sacramento, CA.

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 02/07/90. Last revised: 03/01/94. http://www.epa.gov/iris/index.html.

US EPA OSRTI (Office of Superfund Remediation and Technology Innovation). 2004. Provisional Toxicity Value Summary (PPRTV) for Benz[a]anthracene. Office of Superfund Remediation and Technology Innovation. http://hhpprtv.ornl.gov/

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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 Available 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		
--	--	--	--	--	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 indeno[1,2,3-cd]pyrene is not available from the authoritative bodies listed in item number 5 (below). Indeno[1,2,3-cd]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 for a chemically similar surrogate (pyrene) 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 (pyrene) is 0.03 mg/kg/day. Therefore, based on the chemical surrogate and exposure route extrapolation, a 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 indeno[1,2,3-cd]pyrene.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 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 (2002)	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 (PEF) of 0.1. The PEF for indeno[1,2,3-cd]pyrene is based on its ability (relative to benzo[a]pyrene) to induce skin cancer in mice on dermal application and lung tumors in rats exposed by lung implantation.

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 an 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.
--	9.1×10^{-3}	1.1×10^{-4}	--	--	Based on the CA EPA unit risk for benzo[a]pyrene and application of the recommended relative potency factor of 0.1.

[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 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 1.1×10^{-3} per mcg/m^3 (see Inhalation Cancer Toxicity Value Documentation for benzo(a)pyrene). Application of the recommended relative potency factor (0.1) yields a unit risk of 1.1×10^{-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 indeno[1,2,3-cd]pyrene (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The indeno[1,2,3-cd]pyrene risk specific air concentration calculated from this toxicity value is 9.1×10^{-3} mcg/m^3.

3. Review Dates

Summary table completion: November, 2004
Toxicity value recommendation: December, 2004

4. References for Summary Table

CA 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. http://www.oehha.ca.gov/air/cancer_guide/TSD2.html

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

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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 Manganese

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 (2004) ♦ 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	

[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. Recommendation and Rationale

The US EPA values are the only available reference dose estimates for manganese from an authoritative body listed in item 5 (below), and are derived using methods that reflect general consistency with current risk assessment practice. The recommended dietary value of 0.14 mg/kg/d is based on several reviews of typical dietary intake. The US EPA recommends that an additional modifying factor of 3 should be used for oral non-food assessments, including drinking water and soil. 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.

3. Review Dates

Summary table completion: May, 2004
Toxicity value recommendation: August, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 05/12/1995. Last revised: 05/01/1996. http://www.epa.gov/iris/index.html

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 Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: 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
Toxicity value recommendation: August, 2004

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. Verification date: 05/25/1988. Last revised: 12/01/1996.
http://www.epa.gov/iris/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 (2004) Also used by: ♦ US EPA Region 3 (2004)	0.05	50	LOEL	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[2] occupational exposure multiplied by individual work histories in years).
ATSDR (2000)	0.04	18	$BMDL_{10}$[3]	500	Based on the same study as US EPA IRIS (2004).
CA EPA (2004)	0.2	54	LOEL	300	Based on the same study and assessment as US EPA IRIS (2004).
WHO (2000)	0.15	7.2	$BMDL_5$[4]	50	Based on the same study as US EPA IRIS (2004).
NYS DOH (1989)	0.3	150	NOEL	500	Based on pulmonary effects (inflammation) in subchronic studies in monkeys and rabbits. The NOEL is the air concentration corresponding to the inhaled dose at which no pulmonary effects were observed in rats, hamsters, rhesus monkeys and squirrel monkeys.

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

[2]TWA: time weighted average
[3]$BMDL_{10}$: The 95% lower bound on the modeled benchmark concentration associated with 10% incidence of the toxic effect.

[4]$BMDL_5$: The 95% lower bound on the modeled benchmark concentration associated with 5% 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 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. Values based on adequate human data, when available, are typically chosen over values based on animal studies. The WHO and ATSDR values are based on a modeled benchmark air concentration, while the US EPA and CA EPA values use the study LOEL as the point of departure. Modeling of the data where possible to obtain a point of departure is more consistent with current risk assessment practice. The WHO and ATSDR derivations both use a full 10-fold uncertainty factor for intraspecies differences as well as an uncertainty factor of 5 to account for the potential greater sensitivity of children to the effects of manganese. The ATSDR derivation also uses a full 10-fold uncertainty factor to account for database limitations, including 1) the effects of different forms of manganese, 2) database limitations for inhalation exposure, 3) database limitations for reproductive effects in females, and 4) database limitations for developmental effects. A full uncertainty factor of 10 for database deficiencies does not appear fully justified in that there is a considerable database on the human health effects of inhaled manganese, and the lack of information on developmental effects is partly accounted for in the 5-fold uncertainty factor for children. Therefore, the WHO reference concentration (0.15 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
Toxicity value recommendation: December, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2000. Toxicological Profile for Manganese. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. http://www.atsdr.cdc.gov/toxpro2.html#Final

CA EPA (California Environmental Protection Agency). 2004. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Manganese and Manganese Compounds. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. http://www.oehha.ca.gov/air/chronic_rels/AllChrels.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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 09/23/1993. Last revised: 12/01/1993.
http://www.epa.gov/iris/subst/index.html

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

WHO (World Health Organization). 2000. Air Quality Guidelines (2nd Ed.), Chapter 6.8, Manganese. World Health Organization, Copenhagen, Denmark.
http://www.euro.who.int/air/Activities/20020620_1

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: 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
Toxicity value recommendation: December, 2004

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. Verification date: 05/25/1988. Last revised: 12/01/1996. http://www.epa.gov/iris/subst/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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 (inorganic salts)
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 (2004)[2] Also used by: • US EPA Region 3 (2003) (mercuric chloride) • US EPA ODW (2004) (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 and is expressed as Hg^{2+}.
CA EPA (1999)	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. The reference dose is expressed as Hg^{2+}.

RIVM (2001)	2×10^{-3}	0.23	NOEL	100	Based on the same study as CA EPA (1999) except doses were not converted (limited review information available). The reference dose is expressed as Hg^{2+}.

[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]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.

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. 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
Toxicity value recommendation: September, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency). 1999. Public Health Goal for Inorganic Mercury in Drinking Water. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. http://www.oehha.ca.gov/water/phg/allphgs.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. 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 11/16/1988. Last revised: 05/01/1995. http://www.epa.gov/iris/index.html.

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 Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: Mercury (inorganic salts)
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
Toxicity value recommendation: August, 2004

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 Checked for a Cancer Potency Value

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 (2004) Also used by: • US EPA Region 3 (2004) • US EPA HEAST (1997)	0.3	9	LOEL	30	Based on several studies of workers exposed by inhalation showing neurobehavioral impairments (i.e. hand tremors, effects on memory, and autonomic dysfunction).
ATSDR (1999) 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 (2003)	0.09	8.9	LOEL	100	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.

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 as 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 currently-accepted risk assessment practice. The US EPA IRIS applied a total uncertainty factor of 30 including 10-fold to account for the combination of intraspecies 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 100, including 10-fold factors each to account for intraspecies variability and the use of a LOEL. No clear justification is provided by the US EPA IRIS for decreasing the default uncertainty factors for intraspecies variability and use of a LOEL by, in effect, 3-fold each. The CA EPA application of uncertainty factors is more consistent with currently-accepted risk assessment practice. 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 elemental mercury.

3. Review Dates

Summary table completion: September, 2004
Toxicity value recommendation: October, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological Profile for mercury. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. http://www.atsdr.cdc.gov/toxpro2.html

CA EPA (California Environmental Protection Agency). 2003. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Mercury, Inorganic . Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency.
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. http://www.rivm.nl/bibliotheek/index-en.html

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 4/19/1990. Last revised: 06/01/1995.
http://www.epa.gov/iris/subst/index.html

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 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
- Division of Drinking Water and Environmental Management

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

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
Toxicity value recommendation: October, 2004

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. Verification date: 03/03/1994. Last revised: 05/01/1995.
http://www.epa.gov/iris/subst/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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 (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA HEAST (1997) ♦ NYS DEC (1997) ♦ RIVM (2000)	0.06	6	NOEL	100	Based on liver effects (histological alterations) in rats exposed by drinking water for two years. Study LOEL = 53 mg/kg/day (males), 58 mg/kg/day (females).
ATSDR (2000)	0.06	6	NOEL	100	Based on the same data as US EPA IRIS.
Health Canada (1996)	0.05	5	NOEL	100	Based on the same data as US EPA IRIS.
WHO (1996)	6×10^{-3}	6	NOEL	1000	Based on the same data 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 methylene chloride are essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (6 mg/kg/day). Health Canada reported the nominal dose rate of 5 mg/kg/d 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 assessments are being derived separately in the current context, this additional uncertainty factor is considered unnecessary for deriving a reference dose. Therefore, the US EPA IRIS 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 methylene chloride.

3. Review Dates

Summary table completion: April, 2004
Toxicity value recommendation: July, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological Profile for Methylene Chloride. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.
http://www.atsdr.cdc.gov/toxprofiles/tp14.html

Health Canada. 1996. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. Ottawa: Ministry of Supply and Services Canada (including unpublished supporting documentation). H46-2/96-194E (as cited in on-line International Toxicity Estimates for Risk Database (http://www.tera.org/iter/)).

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). 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. 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 11/06/1985. Last revised: 3/01/1988. http://www.epa.gov/iris/subst/0408.htm.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

WHO (World Health Organization). 1996. Guidelines for drinking water quality, 2rd Ed. World Health Organization, Geneva.
http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/dichloromethatefull.htm

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: 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 (2004) Also used by: • US EPA Region 3 (1997) • US EPA HEAST (1997)	1.3×10^{-4}	7.5×10^{-3}	linearized multistage model, extra risk	body surface area[2]	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	$BW^{¾}$ [3]	Based on the same liver tumor data in male mice exposed by drinking water for 2 years as the US EPA derivation
CA EPA (2000) CA EPA (2004)	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 derivation.

[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 form animal to humans is (animal body weight/human body weight)$^{0.25}$.

2. Recommendation and Rationale

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. The US EPA also used data on increased incidence of liver tumors in female mice exposed via inhalation in their derivation of a cancer potency factor. The US EPA used the arithmetic average of the potency estimates based on these two data sets to derive their value. The NYS DEC value is essentially equivalent to the US EPA value based on the drinking water study, except that the NYS DEC applied $BW^{3/4}$ scaling for interspecies extrapolation, rather than body surface area scaling as used by the US EPA. The US EPA justified combining oral and inhalation tumor incidence data by noting that methylene chloride is rapidly absorbed by either route. The NYS DEC chose to use data from the most relevant route of administration to derive an oral potency estimate. The CA EPA 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 Public Health Goal 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 (CA EPA, 2004) regarding their accepted oral cancer potency factor for methylene chloride. The NYS DEC value reflects data from the most relevant exposure route and its derivation is more consistent with currently-accepted risk assessment practice than the US EPA value. Therefore, the NYS DEC cancer potency factor (6.2×10^{-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 1.6×10^{-4} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004
Toxicity value recommendation: July, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency), 2000. Public Health Goals for Chemicals in Drinking Water: Dichloromethane (Methylene chloride, DCM). Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/water/phg/allphgs.html

CA EPA (California Environmental Protection Agency), 2004. Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/risk/ChemicalDB/start.asp

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 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 4/06/1989. Last revised: 2/01/1995. http://www.epa.gov/iris/subst/0408.htm.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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 HEAST (1997) Also used by: ♦ US EPA Region 3 (2004)	3×10^3	6.95×10^5	NOEL	100	Based on liver toxicity in rats exposed by inhalation 6 hours per day, 5 days per week for 2 years. Complete documentation of derivation unavailable.
ATSDR (2000)	1×10^3	3.1×10^4 (8.92 ppm)	NOEL	30	Based on the same study used by US EPA HEAST.
CA EPA (2004)	400	4.9×10^4 (14 ppm)	LOEL	100	Based on formation of COHb[2] 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 (2004)	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]COHb: carboxyhemoglobin
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

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. The US EPA, ATSDR and NYS DOH all base their values on the same chronic rat inhalation study, but they 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 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 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, the US EPA did not adjust their NOEL exposure level for intermittent exposure or pharmacokinetic differences. ATSDR applied a total uncertainty factor of 30, including 10-fold to account for intraspecies variability and 3-fold to account for interspecies 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 assessed separately.

The CA EPA based their derivation on an occupational study where blood carboxyhemoglobin (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. The CA EPA applied a total uncertainty factor of 100, including factors of 10 each accounting for intraspecies 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.

RIVM's value was obtained by direct adoption of a WHO 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 (2004) 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 CA EPA and ATSDR derivations are both generally consistent with currently-accepted risk assessment practice. The CA EPA value is based on data from a well-conducted human study. 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 methylene choride.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: October, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological Profile for methylene chloride. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. http://www.atsdr.cdc.gov/toxpro2.html

CA EPA(California Environmental Protection Agency). 2000. Chronic toxicity summary: methylene chloride. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacremento, CA. http://www.oehha.ca.gov/air/chronic_rels/AllChrels.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). 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

Toxicology Excellence for Risk Assessment (TERA). 2004. International toxicity estimates for risk database. http://www.tera.org/iter/

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.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

WHO (World Health Organization). 2000. Air Quality Guidelines (2nd Ed.). Dichloromethane. World Health Organization, Copenhagen, Denmark.
http://www.euro.who.int/air/Activities/20020620_1

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: 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 (2004) Also used by: ♦ US EPA Region 3 (2004)	2.0	4.7×10^{-7}	Linearized multistage model, extra risk	Applied dose was converted to an internal dose metric using PBPK modeling. Internal dose was adjusted using body surface area[2] to account for species differences in sensitivity	Based on combined lung and liver tumors in female mice from a 2-year inhalation study.
CA EPA (2002)	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 mouse lung tumor data as in same study as used by US EPA IRIS (2004).
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[2] 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 (2004)

NYS DOH (1988)	27	3.7×10^{-8}	Linearized multistage model	A PBPK model was used to compensate for interspecies differences in metabolism by the glutathione pathway; Equal sensitivity of mice and humans assumed.	Based on combined incidence of lung and liver tumors in female mice in same study as used by US EPA IRIS (2004)
Health Canada (1993)	2.2×10^{6} reported as a TC_{05} [3]; linear equivalent risk specific concentration would be = 44	-- [4]	Linearized multistage model	PBPK modeling was used to account for species differences in metabolism	Based on the same mouse lung tumor data as 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} 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. The TC_{05} represents a maximum likelihood estimate rather than a lower-bound estimate.
[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 the same study, which reported an increased incidence of lung and liver tumors in female mice exposed to methylene chloride via inhalation for two years. The Health Canada 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 (2004) 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 generally considered more consistent with current risk assessment practice. Of the two derivations that used PBPK modeling to account for species differences in glutathione metabolism, the US EPA IRIS (2004) derivation used surface area scaling to account for differences in sensitivity between mice and humans to the same delivered dose, whereas the NYS DOH (1988) derivation assumed that humans and mice are equally sensitive to the same delivered dose. The assumption of equal risk (or sensitivity) at equal delivered doses is consistent with the conclusions contained in a US EPA – Food and Drug Administration analysis of cross-species scaling of dose for carcinogen risk assessment (US EPA, 1992). Therefore, the NYS DOH (1988) unit risk (3.7×10^{-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 27 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: September, 2005

4. References for Summary Table

CA 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.
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http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

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 (United States Environmental Protection Agency). 1992. Draft Report: A Cross-Species Scaling Factor for Carcinogen Risk Assessment Based on Equivalence of mg/kg¾/day. Fed. Register 57:24152-24173.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 04/06/1989. Last revised: 02/01/1995.
http://www.epa.gov/iris/index.html.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. 2004.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

5. Authoritative Bodies Checked for a Cancer Potency Value

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: Methyl Ethyl Ketone (2-Butanone)
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
Toxicity value recommendation: March, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 09/10/03. Last revised: 09/26/03. http://www.epa.gov/iris/index.html.

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. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

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: Methyl Ethyl Ketone (2-Butanone)
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
Toxicity value recommendation: April, 2004

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. http://www.atsdr.cdc.gov/toxprofiles/tp29.html.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 09/10/03. Last revised: 09/26/03. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 (2-Butanone)
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
Toxicity value recommendation: October, 2004

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. Agency consensus date: 09/10/2003. Last revised: 09/26/2003.
http://www.epa.gov/iris/index.html.

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 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: Methyl Ethyl Ketone (2-Butanone)
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
Toxicity value recommendation: September, 2004

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. Agency consensus date: 09/10/2003. Last revised: 09/26/2003.
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 (2004) Also used by: ♦ US EPA Region 3 (2004) ♦ US EPA HEAST (1997)	0.05	50	NOEL	1000	Based on neurological toxicity and decreased body weight in male and female rats in a 90-day gavage study. Study LOEL = 175 mg/kg/day.
RIVM (2001)	0.05	--	--	--	Details are not provided for the basis of this value in the available documentation. This value may be for total cresols (total methylphenols), but this is not clear in the available documentation.

[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 reference dose for 2-methylphenol from an authoritative body listed in item 5 (below) for which adequate documentation of the basis for the value is available. The US EPA value is derived using methods that reflect general consistency with current risk assessment practice. The RIVM reference dose is the same as the US EPA value, but is only documented by a reference to an earlier assessment published in Dutch. The RIVM value also may be meant to apply to total cresols, although this is not clear from the documentation. 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 2-methylphenol.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: September, 2004

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/index-en.html

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Last revised: 09/01/1990. Verification date: 08/13/1987. http://www.epa.gov/iris/subst/index.html

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 Checked for Reference Doses

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: 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
Toxicity value recommendation: September, 2004

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. Verification date: 10/05/1989. Last revised: 08/01/1991.
http://www.epa.gov/iris/subst/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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		
--	--	--	--	--	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 2-methylphenol is not available from the authoritative bodies listed in item number 5 (below). 2-Methylphenol 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 2-methylphenol is 0.05 mg/kg/day. 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 2-methylphenol.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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

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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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available Oral Reference Doses for 3-Methyphenol (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 (2004) Also used by: ♦ US EPA Region 3 (2004) ♦ US EPA HEAST (1997)	0.05	50	NOEL	1000	Based on neurological toxicity and decreased body weight in male and female rats in a 90-day gavage study. Study LOEL = 150 mg/kg/day.
RIVM (2001)	0.05	--	--	--	Details on the basis of this value are not provided in the available documentation. This value may be for (total methylphenols), but this is not clear in the available documentation.

[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 reference dose for 3-methylphenol from an authoritative body listed in item 5 (below) for which adequate documentation of the basis for the value is available. The US EPA value is derived using methods that reflect general consistency with current risk assessment practice. The RIVM reference dose is the same as the US EPA value, but is only documented by a reference to an earlier assessment published in Dutch. The RIVM value also may be meant to apply to total cresols, although this is not clear from the documentation. 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 3-methylphenol.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: September, 2004

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/index-en.html

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Last revised: 09/01/1990. Verification date: 08/13/1987. http://www.epa.gov/iris/subst/index.html

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 Checked for Reference Doses

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: 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
Toxicity value recommendation: September, 2004

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. Verification date: 10/05/1989. Last revised: 08/01/1991.
http://www.epa.gov/iris/subst/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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		
--	--	--	--	--	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 3-methylphenol is not available from the authoritative bodies listed in item number 5 (below). 3-Methylphenol 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 3-methylphenol is 0.05 mg/kg/day. 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 3-methylphenol.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 Region 3 (2004)	5×10^{-3}	5	NOEL	1000	Based on central nervous system, respiratory, and systemic (maternal death) effects in a 6-18 day gestation study in rabbits treated by gavage. Study LOEL = 50 mg/kg/day.
RIVM (2001)	0.05	--	--	--	Details are not provided for the basis of this value in the available documentation. This value may be for total cresols (total methylphenols), but this is not clear in the available documentation.

[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 reference dose for 4-methylphenol from an authoritative body listed in item 5 (below) for which adequate documentation on the basis for the value is available. The US EPA value is derived using methods that reflect general consistency with current risk assessment practice. The RIVM reference dose is only documented by a reference to an earlier assessment published in Dutch. The RIVM value also may be meant to apply to total cresols, although this is not clear from the documentation. 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 4-methylphenol.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: September, 2004

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/index-en.html

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.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

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
- Division of Drinking Water and Environmental Management

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

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
Toxicity value recommendation: September, 2004

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. Last revised: 08/01/1991. Verification date: 10/05/1989.
http://www.epa.gov/iris/subst/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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		
--	--	--	--	--	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 4-methylphenol is not available from the authoritative bodies listed in item number 5 (below). 4-Methylphenol 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 4-methylphenol 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 4-methylphenol.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994 http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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		
WHO (1998)	--	--	--	--	Studies were evaluated but data were inadequate to derive a toxicity value.
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 by corn oil gavage for 90 days at the lowest dose tested.
Health Canada (1996)	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 = 300 mg/kg/day.
ATSDR (1996)	--	--	--	--	Studies were evaluated but data were inadequate to derive a toxicity 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 two reference doses for methyl *tert*-butyl ether are essentially identical with respect to choice of study, species and identification of the point of departure (100 mg/kg/day). However, Health Canada interpreted observed effects at the lowest dose as unrelated to exposure and therefore

considered the lowest dose in the study a NOEL. The NYS DOH considered the effects observed at the lowest dose exposure-related and judged the lowest dose to be a minimal LOEL. Both derivations applied a 1000-fold total uncertainty factor to account for interspecies and intraspecies variability and the use of a subchronic study. Health Canada included an additional 10-fold uncertainty factor to account for lack of data on carcinogenicity and minimal effects at the NOEL. The NYS DOH included an addition 3-fold uncertainty factor to account for the use of a minimal LOEL. The additional uncertainty factor included by Health Canada to account for a lack of carcinogenicity data is not applicable in the current context, as separate cancer and non-cancer evaluations are available for methyl *tert*-butyl ether. Therefore the NYS DOH 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
Toxicity value recommendation: August, 2004

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.

Health Canada. 1996. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances (including unpublished supporting documentation). Ottawa: Ministry of Supply and Services Canada. H46-2/96-194E (as cited in on-line International Toxicity Estimates for Risk Database (http://www.tera.org/iter/)).

NYS DEC (New York State Department of Environmental Conservation). 2001. 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.

WHO (World Health Organization). 2003. Guidelines for drinking water quality, 3rd Ed. World Health Organization, Geneva.
http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/MTBEhist.htm

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: Methyl *tert*-butyl ether
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 *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	
US EPA Region 3 (2003)	2.5×10^{-4}	4×10^{-3}	linearized multistage model, extra risk	body surface area[2]	Based on increased incidence of leukemia and lymphoma in female rats exposed by gavage in a 2-year study.
NYS DOH (2000), NYS DEC (2001)	2.9×10^{-4}	3.4×10^{-3}	linearized multistage model, extra risk	$BW^{¾}$ [3]	Based on increased incidence of testicular tumors in male rats exposed by gavage for 2 years
CA EPA (1999)	5.6×10^{-4}	1.8×10^{-3}	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.

Health Canada (1992)	--	--	--	--	Unclassifiable with respect to carcinogenicity in humans
ATSDR (1996)	--	--	--	--	Studies were reviewed but a cancer potency value was not derived.

[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 NYS DOH cancer potency factor (3.4×10^{-3} per mg/kg/d) is an increased incidence of testicular tumors in male rats exposed by gavage for two years. The basis of the US EPA Region 3 cancer potency factor is an increased incidence of leukemia and lymphoma in female rats exposed by gavage for two years. The CA EPA derivation is based on a geometric mean of cancer potency estimates from the data used by the NYS DOH, US EPA, and separate rat data showing an increased incidence of kidney tumors in animals exposed via inhalation for 2 years. The NYS DOH value is based on a well-conducted study and is supported by other animal carcinogenicity data from oral and inhalation exposure, and is derived for the more sensitive carcinogenic endpoint (testicular tumors). The NYS DOH value also uses $BW^{3/4}$ scaling, which is more consistent with current risk assessment practice than the surface area scaling used to derive the US EPA value. The CA EPA derivation reflects data from several studies. Two of these studies, one showing lymphomas/leukemia in female rats exposed by gavage (which is also the basis of the US EPA value), and another showing kidney and testicular tumors in male rats exposed by inhalation, had significant early mortality indicating that the maximum tolerated dose may have been exceeded. Consequently, confidence in the studies used to derive the CA EPA potency factor and the US EPA potency factor is lower than for the study used to derive the NYS DOH value. Therefore, the NYS DOH 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
Toxicity value recommendation: March, 2005

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1996. Toxicological profile for methy t-butyl ether (MTBE). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. http://www.atsdr.cdc.gov/toxprofiles/tp91.html

Health Canada. 1992. Priority substances list, assessment report no. 5, methyl tertiary-butyl ether. Ottawa: Environment Canada, Health and Welfare Canada. http://www.hc-sc.gc.ca/hecs-sesc/exsd/pdf/methyl_tertiary_butyl_ether.pdf

NYS DEC (New York State Department of Environmental Conservation). 2001. Human health fact sheet for Methyl *tert*-butyl ether. 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.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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 *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 (2004) Also used by: ♦ US EPA Region 3 (2004) ♦ ATSDR (1996)	3×10^3	2.6×10^5	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) in a 24-month inhalation study in rats. Study $LOEL_{(HEC)}$ = 1.95×10^6 mcg/m^3.
Health Canada (1992)	reported as tolerable daily intake of 0.03 mg/kg/d human default equivalent[3] = 105 mcg/m^3	300 mg/kg/d inhaled dose in rats human default equivalent[3] = 1.05×10^6 mcg/m^3	NOEL	10,000	Based on neurobehavioral effects in male and female rats in a 90-day inhalation study. A tolerable daily intake of 0.03 mg/kg/d was derived based on default assumptions for rat body weight and respiration rate.
CA EPA (2003)	8×10^3	2.6×10^5 (72 ppm)	NOEL (HEC)[2]	30	Based on 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.

[2]HEC: Human Equivalent Concentration
[3]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.

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

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 and CA EPA derivations are based on a 24-month chronic inhalation study, while the Health Canada value was derived based on a 90-day subchronic study because the chronic study was not available at the time. The US EPA and CA EPA derivations both identify the same NOEL point of departure. The US EPA applied a total uncertainty factor of 100, including a 10-fold factor to account for intraspecies variability and 3-fold factors each to account for interspecies variability and data deficiencies in the chronic study including lack of serum chemistry and urinalysis and limited reporting of motor activity/clinical signs during exposure. The 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 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 (8×10^3 mcg/m^3) is the toxicity value recommended or 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
Toxicity value recommendation: October, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1996. Toxicological Profile for methyl t-butyl ether (MTBE). US Department of Health and Human Services. Atlanta, Georgia: Public Health Service.
http://www.atsdr.cdc.gov/toxpro2.html

CA EPA (California Environmental Protection Agency). 2003. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Methyl *t*-Butyl Ether. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency.
http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html

Health Canada. 1992. Priority Substances List Assessment Report: Methyl tertiary-butyl ether. Ottawa: Environment Canada, Ministry of Public Works and Government Services.
http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 07/21/1993. Last revised: 09/01/1993. http://www.epa.gov/iris/index.html.

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 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: Methyl *tert*-butyl ether
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	
CA 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 CA 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 CA 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. The methyl *tert*-butyl ether risk specific air concentration calculated from this toxicity value is 3.8 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004

Toxicity value recommendation: September, 2004

4. References for Summary Table

CA 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. http://www.oehha.ca.gov/air/cancer_guide/TSD2.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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 (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA ODW (2002) ♦ CA 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.
RIVM (2000)	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.

2. Recommendation and Rationale

The US EPA reference dose is 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. 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 naphthalene.

3. Review Dates

Summary table completion: February, 2004
Toxicity value recommendation: April, 2004

4. References for Summary Table

CA EPA DDWEM (California Environmental Protection Agency Division of Drinking Water and Environmental Management). 2000. Memorandum: Proposed Action Level for Napthalene. Office of Environmental Health Hazard Assessment. Sacramento, California.
http://www.oehha.ca.gov/water/pals/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.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification Date: 12/01/90. Last revised: 09/17/98.
http://www.epa.gov/iris/index.html.

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2002. Office of Drinking Water, Drinking Water Standards and Health Advisories. Washinton, 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.
http://www.epa.gov/reg3hwmd/risk/human/index.htm.

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: 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
Toxicity value recommendation: April, 2004

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.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification Date: 07/01/98. Last revised: 09/17/98. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 (0.2 ppm)	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.
CA EPA (2004)	9	9.4×10^3 (1.8 ppm)	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.

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 CA 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 CA 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 CA 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 CA 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 CA 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
Toxicity value recommendation: October, 2004

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
http://www.atsdr.cdc.gov/toxpro2.html

CA 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. 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency consensus date: 7/1/98. Last revised: 09/17/1998. http://www.epa.gov/iris/subst/index.html

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

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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
- 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 (2004)	--	--	--	--	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).

[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 naphthalene 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
Toxicity value recommendation: October, 2004

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. Agency consensus date: 07/01/1998. Last revised: 09/17/1998. http://www.epa.gov/iris/subst/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2004) ♦ US EPA ODW (2004) ♦ 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.
CA EPA (2001)	0.00112 (as Ni)	1.12	NOEL	1000	Based on early pup mortality observed in three rat drinking water or gavage developmental toxicity studies. The NOEL chosen was an intermediate dose in one of the three studies where no effects were observed at any exposure level (NOEL at highest dose tested = 2.23 Ni mg/kg/day). The lowest LOEL dose in the other two studies was 1.3 Ni mg/kg/day and so the highest NOEL below this LOEL was chosen as the point of departure dose.
Health Canada (1994, 1996a,b)	0.0013 (as Ni)	1.3	LOEL	1000	Based on one of the oral developmental studies in rats used by CA EPA that gave the lowest LOEL among doses tested in the three studies.

TERA (1999)	0.008 (as Ni)	7.6	LOEL	1000	Based on increased incidence of albuminuria (indicating kidney glomerula dysfunction) in female rats exposed via drinking water for six months. The LOEL was the only dose tested.
RIVM (2001) WHO (1998)	0.05 (as Ni)	5	NOEL	100	Limited documentation suggests the value is based on reduced body weight gain, hemoglobin and serum alkaline phosphatase in rats exposed via the diet for six weeks and same study used by US EPA IRIS. Precise identification of critical study is not provided.

[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 bases for the various reference doses for nickel include reduced body weights and organ weights compared to controls in a chronic rat feeding study, reduced weight gain and blood biochemical changes in a subchronic rat feeding study, increased pup mortality in oral reproductive studies in rats and biochemical indications of kidney toxicity in a subchronic drinking water study in rats. The Health Canada value is based on a LOEL for increased pup mortality in a study where animals were exposed for two successive matings. The results in the first generation of pups differed from those in the second generation, with a LOEL in the first generation at the highest dose (32 mg/kg/day). In the second generation, there was not a clear dose-response, with increased pup mortality at the lowest and highest non-zero doses, but not at the intermediate dose. Health Canada interpreted the study LOEL as 1.3 mg/kg/d (the lowest dose group in the second generation). They applied a total uncertainty factor of 1000 to account for interspecies and intraspecies variability and the use of a LOEL. The US EPA derived its value based on a NOEL in the chronic feeding study, applying uncertainty factors of 10 each to account for interspecies and intraspecies variability. In light of the study used by Health Canada and other earlier studies suggesting some effect of maternal nickel exposure on pup survival, an additional factor of 3 was included to account for a limited database indicating potential for reproductive/developmental toxicity at non-maternally-toxic doses. CA EPA's oral non-cancer evaluation for nickel included data from more recent reproductive toxicity studies not available at the time the US EPA and Health Canada made their assessments, along with the study used by Health Canada. The two more recent studies were conducted sequentially by the same researchers as a dose-ranging study and then a larger follow-up study. The dose-ranging study identified a LOEL for increased pup mortality at 2.23 mg/kg/d, the lowest non-zero dose. There was some uncertainty in the dose-response at the lower end of the dose range, as there was not increased mortality observed at the next highest dose. The follow up study used more animals per group and had four non-zero dose groups with the highest dose equal to the LOEL in the dose-ranging study. No effects on pup survival or any other reproductive/developmental effects were observed at any dose (NOEL = highest dose tested = 2.23 mg/kg/d). The CA EPA accepted the lowest LOEL from these studies (the same LOEL used by Health Canada) and then selected the highest NOEL from among the three studies that was lower than their LOEL dose as the point of departure. They applied a total uncertainty factor of

1000 to this dose accounting for interspecies and intraspecies variability as well as a 10-fold factor to adjust for the potential carcinogenicity of soluble nickel by the oral route, having concluded that a quantitative assessment of oral cancer potency for nickel was not possible. WHO appears to base their derivation on the same study used by US EPA IRIS along with a 6-week dietary study that observed the same NOEL dose. The basis for RIVM's value is only described as a "semi-chronic experiment with rats exposed to nickel-sulfate in the diet". It has the same NOEL as the short-term study described by WHO, but that study is reported to have used nickel acetate. (Another supporting subchronic study described by US EPA IRIS also has a NOEL of 5 mg/kg/day, but is described as an oral gavage study using nickel chloride.) Both the WHO and RIVM derivations apply a total uncertainty factor of 100 to account for inter- and intraspecies variability. TERA based their 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, including 10-fold each for inter- and intraspecies variability and an additional 10-fold factor collectively accounting for the use of a subchronic study, the use of a minimal LOEL and an incomplete database. The study used by Health Canada gives the lowest LOEL among the numerous subchronic, chronic and reproductive/develomental oral-dosing studies available for nickel, which might suggest that derivations based on higher NOEL doses would not be sufficiently protective. However, that study and the two more-recent reproductive studies used by the CA EPA appear to lack evidence for 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. The three-fold additional factor applied by the US EPA appears to account for this uncertainty. The TERA derivation might also be protective for these equivocal effects since its additional 10-fold uncertainty factor adjusts the minimal LOEL below the lowest reproductive LOEL, but it is based on a subchronic study that does not allow the evaluation of a dose-response relationship because only one dose was tested. TERA points out that only a single indication of kidney toxicity was observed, that although statistically significant (in females, in males the NOEL dose was 6.9 mg/kg/day) the increases were not large for the affected endpoint, that no baseline comparative data for the quantitative endpoint were provided, that 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 that 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, and suggest that the study is not optimal as the principal study on which to base a chronic oral reference dose. Although WHO and RIVM appear to base their derivations on the same point of departure level (NOEL = 5 mg/kg/day), they do not include an additional uncertainty factor to account for the equivocal reproductive toxicity database. The CA EPA derivation would have been preferred in the current context if the additional 10-fold uncertainty factor for carcinogenicity had not been included, since cancer is being addressed separately, and would have then differed by less than 2-fold from the US EPA IRIS value. Overall, the US EPA IRIS derivation appears to be based on the most reliable chronic dose-response data and includes adequate uncertainty factors to account for limited reproductive 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
Toxicity value recommendation: September, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2001. Public Health Goal for Nickel in Drinking Water. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. http://www.oehha.ca.gov/water/phg/allphgs.html.

Health Canada. 1994. Priority Substances List Assessment Report: Nickel and its compounds. Ottawa, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

Health Canada. 1996a. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. Ottawa: Ministry of Supply and Services Canada. H-46-2/96-194E. (as cited in on-line International Toxicity Estimates for Risk Database (http://www.tera.org/iter/)).

Health Canada. 1996b. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. Ottawa: Ministry of Supply and Services Canada (including unpublished supporting documentation). H46-2/96-194E (as cited in on-line International Toxicity Estimates for Risk Database (http://www.tera.org/iter/)).

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). 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/index-en.html

TERA (Toxicology Excellence for Risk Assessment). 2004. International toxicity estimates for risk database.
http://www.tera.org/iter/

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 07/16/1987. Last revised: 12/01/1996. http://www.epa.gov/iris/index.html.

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 Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. 2004.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

WHO (World Health Organization). 2003. Guidelines for drinking water quality, 3rd Ed. World Health Organization, Geneva.
http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/chemicalsindex.htm

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
Toxicology Excellence for Risk Assessment

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.
CA EPA (2004) CA 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 CA EPA is 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 CA 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 CA 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 CA 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
Toxicity value recommendation: September, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2001. Public health goals for chemicals in drinking water. Nickel. Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/water/phg/allphgs.html

CA 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. http://www.oehha.ca.gov/prop65/pdf/Sept2003StatusReport.pdf

CA EPA (California Environmental Protection Agency). 2004. Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/risk/ChemicalDB/index.asp

Health Canada, Environment Canada. 1994. Priority Substances List Assessment Report: Nickel and its compounds. Ottawa, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

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/subst/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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	NOEL	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 = 5.4 mcg/m^3.
CA EPA (2003)	0.05	1.6	NOEL	30	Based on the same study used by ATSDR (2003). This reference concentration applies to all particulate nickel forms except nickel oxide.
	0.1	30	LOEL	300	Based on pathological changes in the lung, lymph nodes and adrenal glands of rats exposed by inhalation to nickel oxide for 6 hours/day, 5 days/weeks for 104 weeks.
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.

Health Canada (1994) 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 exposed subchronicly via inhalation. 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/m3 adjusted for continuous exposure). Details of the values presented in TERA (2004) are not available.
TERA (2004)	0.2	1.7	$BMCL_{10}$ [2]	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]$BMCL_{10}$: lower bound on the benchmark concentration (lower 95% confidence limit on the dose corresponding to a 10% relative change in the endpoint compared to the control).

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 (NYSDOH 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 detected 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 or insoluble 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, nickel speciation data may seldom be available as part of the evaluation of nickel soil contamination, and since the nickel sulfate LOEL was nearly 10-fold lower than the nickel oxide LOEL, the nickel sulfate NOEL can be applied to all forms. Therefore the CA EPA nickel oxide value will not be considered further.

ATSDR derived a human equivalent concentration from the chronic rat nickel sulfate study based on adjusting for continuous exposure and applying a pharmacokinetic adjustment for relative particulate deposition in the pulmonary region of the respiratory system in rats and humans. CA EPA made the same adjustments, but its relative deposition fraction differed from the ATSDR value by roughly 2-fold. CA EPA based their adjustment on male rats, whereas ATSDR used parameters for females, and the particle size geometric standard deviation employed by the CA EPA was almost 2-fold lower than the value ATSDR used. The particle size geometric standard deviation used by ATSDR is the same value reported in the original study and CA EPA does not provide any rationale for using a different parameter value. TERA's human equivalent concentration derivation was nearly the same as ATSDR's, despite rounding differences due to reporting different numbers of significant digits and using male rather than female parameters. The human equivalent concentration derived by RIVM only accounts for the discontinuous exposure regime and makes no pharmacokinetic adjustment for particle deposition in the lung. Of the four derivations, ATSDR's and TERA's estimates of the human equivalent concentration were more consistent with currently-accepted risk assessment practice and the parameter values reported in the original study.

ATSDR chose the human equivalent concentration at the NOEL as the point of departure, while TERA used a benchmark concentration approach to derive a point of departure. 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. This conclusion was 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, adjusted for continuous exposure and differing particle size distributions in occupational and ambient environments 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 (2004) points out that there are several limitations of the occupational study that may 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. Therefore, the ATSDR 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 inorganic nickel.

3. Review Dates

Summary table completion: September, 2004
Toxicity value recommendation: October, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological Profile for nickel. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. http://www.atsdr.cdc.gov/toxpro2.html

CA EPA(California Environmental Protection Agency). 2000. Chronic toxicity summary: nickel and nickel compounds; nickel oxide. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacremento, CA. http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html

Health Canada, Environment Canada. 1994. Priority Substances List Assessment Report: nickel and its compounds. Ottawa, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

NYS DOH (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). 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/index-en.html

Toxicology Excellence for Risk Assessment (TERA). 2004. International toxicity estimates for risk database.
http://www.tera.org/iter/

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

Division of Drinking Water and Environmental Management
Health Canada
World Health Organization
National Institute of Public Health & Environmental Protection, Netherlands

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.
CA EPA (2002) CA 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 CA 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 CA 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 CA 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
Toxicity value recommendation: October, 2004

4. References for Summary Table

CA 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. http://www.oehha.ca.gov/air/cancer_guide/TSD2.html.

CA EPA (California Environmental Protection Agency). 2004. Toxicity Criteria Database. Nickel subsulfide and Nickel refinery dust. Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/risk/ChemicalDB/index.asp

Health Canada, Environment Canada. 1993. Priority Substances List Assessment Report: Hexachlorobenzene. Ottawa, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency verification date: 04/01/1987. Last revised: 01/01/1991. Verification and last revised dates apply to both nickel refinery dust and nickel subsulfide. http://www.epa.gov/iris/subst/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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		
US EPA IRIS (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA ODW (2002) ♦ US EPA HEAST (1997) ♦ US EPA OPP (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 (2001)	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 (1997)	1×10^{-3}	1.21	NOEL	1000	Based on anemia in male rats in a 12-week feeding study. Study LOEL = 2.4 mg/kg/day.
RIVM (2001)	3×10^{-3}	1	LOEL	300	Based on the same study reviewed in ATSDR.

Health Canada (1987)	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.

[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 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, and thyroid effects in mink. The US EPA based their derivation on a NOEL in a chronic rat feeding study, the CA EPA used a slightly lower NOEL from a subchronic rat feeding study and ATSDR and RIVM used a LOEL from a more recent multigeneration reproductive study in mink. Health Canada used a NOEL from a developmental toxicity study that is equivalent to the chronic rat NOEL to derive its reference dose. The mink LOEL value is approximately the same as the subchronic rat NOEL and is 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. ATSDR used a total uncertainty factor of 1000 to account for interspecies and intraspecies 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. 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.

3. Review Dates

Summary table completion: March, 2004
Toxicity value recommendation: August, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2001. Toxicological profile for pentachlorophenol. Update. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. http://www.atsdr.cdc.gov/toxpro2.html

CA EPA (California Environmental Protection Agency). 1997. Public Health Goal for Pentachlorophenol in Drinking Water. Division of Drinking Water and Environmental Management). Sacramento, CA. http://www.oehha.ca.gov/water/phg/allphgs.html.

Health Canada. 1987. Water Quality and Health. Guidelines for Canadian Drinking Water Quality. Healthy Environments and Consumer Safety. http://www.hc-sc.gc.ca/hecs-sesc/water/dwgsup.htm

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. 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 05/20/1985. Last revised: 02/01/1993. http://www.epa.gov/iris/subst/index.html

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2002. Office of Drinking Water, Drinking Water Standards and Health Advisories. Washinton, 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.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

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: Pentachlorophenol
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 Pentachlorophenol (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 (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA OPP (1997) ♦ ATSDR (2001)	8.3×10^{-6}	0.12	linearized multistage model, extra risk	body surface area[2]	Based on increased incidences of liver, adrenal gland and vascular tumors in females mice exposed via the diet for two years. The cancer potency slope factor is the geometric mean of potency factors derived from two studies using different pentachlorophenol preparations.
CA EPA (1997)	1.2×10^{-5} ---- 1.2×10^{-5}	0.0834 ---- 0.0811	linearized multistage model, extra risk ---- linear extrap. from LED_{10} [3]	$BW^{¾}$ [4] ---- body weight [5]	Based on the same study as US EPA IRIS (2004) except the incidence of liver tumors in male mice fed a single preparation was the data set used to derive the cancer potency slope factor. Two derivations were reported that give very similar results.

[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]LED_{10} = lower bound on the dose associated with 10% increase in the incidence of tumors.
[4]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[5]Factor for dose adjustment from animal to humans appears to be 1, but a scaling factor is not explicitly described for this derivation.

2. Recommendation and Rationale

The cancer potency factors for pentachlorophenol derived by authoritative bodies use male or female mouse tumor incidence data from the same study. The US EPA pooled all tumor data from female mice, arguing that the tumor type of greatest concern were hemangiomas and hemangiosarcomas (vascular lesions) only observed in the female mice. The US EPA also combined the cancer potency factors based on parallel experiments with two different technical preparations of pentachlorophenol. The CA EPA chose to base their derivation on combined liver tumors in male mice exposed to only one of the pentachlorophenol preparations, arguing that those data showed the strongest statistically significant dose-response. None of the derivations is completely consistent with currently-accepted risk assessment practices regarding the extrapolation methods used for animal-to-human dose scaling and high-dose to low-dose extrapolation. If the same scaling factor had been used in both CA EPA derivations, the resulting cancer potency factors would have differed by about 7-fold. Such a large difference is not generally expected between a linearized multistage model extrapolation and a linear LED_{10} extrapolation from the same data set. That discrepancy and the lack of a clear rationale for not applying a scaling factor in the linear LED_{10} derivation create some uncertainty about the actual scaling factor applied in the CA EPA linear LED_{10} derivation. As published, the US EPA derivation reflects the incidence of a known fatal tumor type in humans exposed to xenobiotic chemicals. Therefore, the US EPA cancer potency factor (0.12 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for pentachlorophenol. The pentachlorophenol risk specific dose calculated from this toxicity value is 8.3×10^{-6} mg/kg/day.

3. Review Dates

Summary table completion: April, 2004
Toxicity value recommendation: September, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2001. Toxicological profile for pentachlorophenol. Update. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. http://www.atsdr.cdc.gov/toxpro2.html

CA EPA (California Environmental Protection Agency). 1997. Public Health Goal for Pentachlorophenol in Drinking Water. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. http://www.oehha.ca.gov/water/phg/allphgs.html.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 08/02/1990. Last revised: 07/01/1993.
http://www.epa.gov/iris/subst/index.html

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.

5. Authoritative Bodies Checked for a Cancer Potency Value

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
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
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: Pentachlorophenol
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 Pentachlorophenol (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	
--	--	--	--	--	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 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 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 pentachlorophenol is 0.12 per mg/kg/day. Therefore, a unit risk of 3.4×10^{-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 pentachlorophenol. The risk specific air concentration calculated from this toxicity value is 0.029 mcg/m^3.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: Oral
Toxicity: Non-Cancer

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

1. Summary of Available 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 a surrogate derivation applying a reference dose of 0.04 mg/kg/day for aromatic compounds to all aromatic petroleum hydrocarbons with effective carbon number 9 to 16.

[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

No compound-specific reference dose values for phenanthrene have been derived by the authoritative bodies from the list in item 5 (see below). The RIVM value is based on total petroleum hydrocarbons, which can include a range of hundreds of chemicals with varying degrees of toxicity. Many of the chemicals that comprise total petroleum hydrocarbons are chemically and toxicologically dissimilar to phenanthrene. Thus total petroleum hydrocarbons are not chosen as a surrogate for phenanthrene. An oral reference dose is available for pyrene, which is a chemically similar polycyclic aromatic hydrocarbon that can be used to represent phenanthrene with respect to noncancer endpoints. The basis for choosing pyrene as a chemical surrogate for phenanthrene is that pyrene is expected to be toxicologically similar, and has the most stringent reference dose available among the polycyclic aromatic hydrocarbons. Therefore, the US EPA reference dose for pyrene (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 phenanthrene (see Oral Non-Cancer Toxicity Value Documentation for pyrene).

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: September, 2004

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/index-en.html

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
- Division of Drinking Water and Environmental Management

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

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
Toxicity value recommendation: September, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 05/03/1990. Last revised: 12/01/1990. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 and chronic minimal risk level.

2. Recommendation and Rationale

An inhalation reference concentration for phenanthrene is not available from the authoritative bodies listed in item number 5 (below). Phenanthrene 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 (pyrene) 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 (pyrene) is 0.03 mg/kg/day. Therefore, based on the chemical surrogate and exposure route extrapolation, a 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 phenanthrene.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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

1. 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 Region 3 (2003)	0.3	93	BMDL	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.
Health Canada (2004)	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. NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor; BMDL: 95% lower confidence limit on the maximum likelihood estimate of the dose corresponding to a one standard deviation change in the mean.

2. Recommendation and Rationale

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 (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 exposure 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. 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
Toxicity value recommendation: March, 2004

4. References for Summary Table

Health Canada, Environment Canada. 2004. Health-based Guidance Values for Substances on the 2nd Priority Substances List. Ottawa, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/pdf/Guidance%20Values.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.128-131.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification Date: 08/28/02. Last revised: 09/30/02. http://www.epa.gov/iris/index.html.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

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: 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
Toxicity value recommendation: March, 2004

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.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification Date: 08/28/02. Last revised: 09/30/02. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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		
CA 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 CA 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. CA 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. CA 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, CA 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
Toxicity value recommendation: December, 2004

4. References for Summary Table

CA 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. 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. 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: 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
Toxicity value recommendation: December, 2004

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. Verification date: 08/28/2002. Last revised: 09/30/2002.
http://www.epa.gov/iris/subst/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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		
--	--	--	--	--	No information available.

[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 *n*-propylbenzene is not available. An oral reference dose is available for isopropylbenzene, which is structurally and chemically similar to *n*-propylbenzene. The similarity between the two chemicals provides a basis for using toxicity data for isopropylbenzene to represent *n*-propylbenzene. Therefore, the US EPA reference dose for isopropylbenzene (0.1 mg/kg/day (US EPA IRIS, 2004)) 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
Toxicity value recommendation: July, 2004

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. Agency consensus date: 06/06/1997. Last revised: 08/01/1997.
http://www.epa.gov/iris/subst/0408.htm.

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: *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
Toxicity value recommendation: July, 2004

4. References for Summary Table

5. Authoritative Bodies Checked for a Cancer Potency Value

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: Inhalation
Toxicity: Non-Cancer

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

1. Summary of Available 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		
--	--	--	--	--	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 *n*-propylbenzene is not available from the authoritative bodies listed in item number 5 (below). A reference concentration is available for isopropylbenzene, which is structurally and chemically similar to *n*-propylbenzene. The similarity between the two chemicals provides a basis for using toxicity data for isopropylbenzene to represent *n*-propylbenzene. Therefore, the US EPA reference concentration for isopropylbenzene (400 mcg/m^3 (US EPA IRIS, 2004)) is 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
Toxicity value recommendation: February, 2005

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. Agency consensus date: 06/06/1997. Last revised: 08/01/1997. http://www.epa.gov/iris/subst/0408.htm

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: *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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994 http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 IRIS (2004) Also used by: • US EPA Region 3 • (2004) • US EPA ODW • (2004) • US EPA HEAST (1997)	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
Toxicity value recommendation: September, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 11/15/1989. Last revised: 07/01/1993. http://www.epa.gov/iris/subst/0408.htm.

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 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 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
- 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
Toxicity value recommendation: September, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 02/07/1990. Last revised: 01/01/1991. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 (2004) Also used by: ♦ US EPA Region 3 (2004) ♦ US EPA ODW (2004) ♦ 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.
ATSDR (2003)	5×10^{-3}	0.015	NOEL	3	Based on a sub-sample of the same study population and review as US EPA IRIS (2004).

[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 two selenium reference doses is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (0.015 mg/kg/day). The two derivations are based on the same human epidemiological data and use the same total uncertainty factor of 3 to account for intraspecies variability. 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 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
Toxicity value recommendation: September, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological profile for Selenium. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. http://www.atsdr.cdc.gov/toxpro2.html

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 03/27/1991. Last revised: 09/01/1991. http://www.epa.gov/iris/index.html.

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 WaterU.S. Environmental Protection AgencyWashington, 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. http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: 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
Toxicity value recommendation: September, 2004

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. Verification date: 03/07/1990. Last revised: 07/01/1993. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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
Toxicity value recommendation: February, 2005

4. References for Summary Table

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

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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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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

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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
Toxicity value recommendation: September, 2004

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 07/18/1991. Last revised: 12/01/1996. http://www.epa.gov/iris/index.html.

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. http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: 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
Toxicity value recommendation: September, 2004

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. Verification date: 09/22/1988. Last revised: 06/01/1989. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994 http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 (2004) Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA EPA ODW (2004)	0.01	14	NOEL	1000	Based on liver toxicity in mice exposed by corn oil gavage for 5/7 days/week for a total of 6 weeks and reduced weight gain in rats exposed via drinking water for 90 days. Study LOEL (mice) = 71 mg/kg/day.
US EPA HEAST (1997)	0.1	14	NOEL	100	Based on the same mouse study as used in US EPA IRIS
RIVM (1999)	0.016	16	NOEL	1000	Based on liver toxicity in rats exposed orally for 4 weeks. Study LOEL = 81 mg/kg/day.
WHO (1993)	0.014	14	NOEL	1000	Based on same data as US EPA IRIS.
Health Canada (1995, 1996)	0.014	14	NOEL	1000	Based on same data as US EPA IRIS.
Health Canada (1993)	0.034	170	LOEL	5000	Based on reduced survival, hepatotoxic effects (males), lung congestion and nephrotoxic effects (males and females) in mice exposed by inhalation six hours per day, five days per week for 103 weeks.

[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, WHO and Health Canada (1995, 1996) reference doses for tetrachloroethene are essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (14 mg/kg/day). RIVM based their value on different subchronic oral rat study that also reported liver toxicity and had a very similar point of departure value (16 mg/kg/day). The only source of substantial variation among the values is the use of a total uncertainty factor of 100 by US EPA HEAST, while the other derivations all used 1000. The extra factor of ten accounts for uncertainty due to the use of subchronic data and is appropriate. The Health Canada (1993) reference dose is based on an inhalation study and not chosen for derivation of an oral reference dose, given the availability of good quality oral data. This reference dose also includes an uncertainty factor (5) for limited evidence of carcinogenicity, which is not applicable in the current context since cancer and noncancer endpoints are being evaluated separately. 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 tetrachloroethene.

3. Review Dates

Summary table completion: May, 2004
Toxicity value recommendation: September, 2004

4. References for Summary Table

Health Canada. 1993. Priority Substances List Assessment Report: Tetrachloroethylene. Ottawa: Environment Canada, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

Health Canada. 1995. Water Quality and Health. Guidelines for Canadian Drinking Water Quality. Healthy Environments and Consumer Safety. http://www.hc-sc.gc.ca/hecs-sesc/water/dwgsup.htm

Health Canada. 1996. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances (including unpublished supporting documentation). Ottawa: Ministry of Supply and Services Canada. H46-2/96-194E (as cited in on-line International Toxicity Estimates for Risk Database (http://www.tera.org/iter/)).

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 IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 09/17/1987. Last revised: 03/01/1988. http://www.epa.gov/iris/subst/0106.htm

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 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

WHO (World Health Organization). 2003. Guidelines for drinking water quality, 3rd Ed. World Health Organization, Geneva.
http://www.who.int/docstore/water_sanitation_health/GDWQ/draftchemicals/tetrachloroethylene2003.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: Tetrachloroethene
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 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 (1985a) Also used by: ♦ US EPA (1985b)	2.0×10^{-5}	$0.05\ (mg/kg/day)^{-1}$ as ingested dose	linearized multistage model, extra risk, metabolized dose (20% of ingested dose) & corrected for early deaths	body surface area [2]	Based on hepatocellular carcinomas in female mice exposed by corn oil gavage 5 days/week for 78 weeks, and observed for 90 weeks.
Cal EPA (2001) Also used by: ♦ US EPA Region 3	2.4×10^{-6}	$0.43\ (mg/kg/day)^{-1}$ as ingested dose	linear extrapol. from LED_{10} [3] with PBPK, metabolized dose (79% of ingested dose) & time-to-tumor adjustment	$BW^{¾}$ [4]	Based on hepatocellular carcinomas in both sexes of mice exposed by corn oil gavage 5 days/week for 78 weeks, and observed for 90 weeks.
Clewell et al. (2005)	3.4×10^{-4}	$0.0029\ (mg/kg/day)^{-1}$ as ingested dose	linear extrapol. from LED_{10} [3] using PBPK	1, equal risk at equal internal dose using PBPK models	Based on hepatocellular carcinomas in both sexes of 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] Factor for dose adjustment from animal to humans is $(\text{animal body weight/human body weight})^{0.33}$.
[3] LED_{10}: The lower bound on the dose that causes a 10% increase in the incidence of tumors.
[4] Factor for dose adjustment from animal to humans is $(\text{animal body weight/human body weight})^{0.25}$.

2. Recommendation and Rationale

The US EPA and Cal EPA cancer potency factors are based on the data from the same study showing increased incidence of liver tumors in male and female mice exposed to oral doses of tetrachloroethene for 78 weeks and observed for 12 more weeks. However, Cal EPA and US EPA derivations differed in three areas. (1) The Cal EPA derivation used $BW^{3/4}$ scaling factor for the animal to human extrapolation, which is generally preferred over the body surface area scaling factor used by the US EPA. (2) Cal EPA considered the study length to short to fully assess the carcinogenic potential of tetrachloroethene and used an adjustment factor for study length. US EPA did not use the adjustment factor. The use of this factor is questionable because NTP (1977) designed the mouse study to last 90 weeks. Moreover, a 90-week carcinogenicity study is considered adequate under FIFRA for identifying the carcinogenic potential of pesticides in mice (US EPA, 1998). (3) More important, the Cal EPA derivation includes an assumption that 79% of an ingested dose is metabolized in humans, and this value may greatly overestimate the ability of human to metabolize tetrachloroethene (Clewell et al., 2005). The US EPA derivation analysis used a percentage (20%) that is consistent with experimental data (US EPA, 1985a). A third oral cancer potency factor derived by Clewell et al. (2005) is based on inhalation data, which are typically not used in the derivation of an oral cancer potency factor when adequate data from oral studies are available. Thus, the US EPA cancer potency factor (0.05 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 2×10^{-5} mg/kg/day.

3. Review Dates

Summary table completion: May, 2004
Toxicity value recommendation: August, 2004
Fact sheet revised: May 2006.

4. References for Summary Table

Cal EPA (California Environmental Protection Agency). 2001. Public Health Goal for tetrachloroethylene in drinking water. Office of Environmental Health Hazard Assessment. Sacramento, CA. http://www.oehha.ca.gov/water/phg/pdf/PCEAug2001.pdf

Clewell HJ, Gentry PR, Kester JE, Andersen ME. 2005. Evaluation of physiologically based pharmacokinetic models in risk assessment: an example with perchloroethylene. Crit Rev Toxicol. 35(5):413-433.

US EPA (U.S. Environmental Protection Agency). 1985a. Health Assessment Document for Tetrachloroethylene (Perchloroethylene). Final Report. EPA/600/8-82/005F. Washington, DC: Office of Health Environmental Assessment.

US EPA (U.S. Environmental Protection Agency). 1985b. National Primary Drinking Water Regulations: Volatile Synthetic Organic Chemicals. Final Rule. Federal Register. 50: 46880-46901.

US EPA (U.S. Environmental Protection Agency). 1998. Health Effects Test Guidelines OPPTS 870.4200. Carcinogenicity. EPA 712–C–98–211. Washington, DC: Prevention, Pesticides and Toxic Substances.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: Inhalation
Toxicity: Non-Cancer

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

1. Summary of Available 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		
ATSDR (1997)	270 (0.04 ppm)	2.4×10^4 (3.6 ppm)	LOEL	100	Based on neurobehavioral effects in 60 women exposed to tetrachloroethene in dry cleaning shops and adjusted for continuous exposure.
Health Canada (1993)	only reported as TDI[2] = 0.034 mg/kg/d (would be equivalent to a reference concentration = 120 mcg/m^3 based on adult body weight and daily breathing rate)	only reported as 171 mg/kg/d intake in mice (would be equivalent to 5.97×10^5 mcg/m^3 based on adult body weight and daily breathing rate)	LOEL	5000	Based on reduced survival and liver toxicity in male mice, and lung congestion and kidney toxicity in male and female mice in a 103-week inhalation study.
Health Canada as reported by TERA (2004)	360 based on 5 – 11 year old child body weight and daily breathing rate	3.63×10^5 based on 5 – 11 year old child body weight and daily breathing rate	LOEL	1000	Based on same study as Health Canada (1993) above, but TERA (2004) reports that a reference concentration was derived by Health Canada based on 5 – 11 year old child body weight and breathing rate parameters and a different total uncertainty factor than reported by Health Canada (1993)

WHO (2000) Also used by: ♦ RIVM (2001)	250	2.4×10^4	LOEL	100	Based on renal toxicity in 50 workers chronically exposed to tetrachloroethene in dry-cleaning facilities and adjusted for continuous exposure.
NYS DOH (1997)	100	--	LOEL & NOEL	--	Based on effects on the liver, kidney and central nervous system in human epidemiological (primarily occupational) studies. Recommended reference concentrations for children were extrapolated from adult reference concentrations with an additional uncertainty factor, and the recommended non-cancer ambient air criterion was at the low end of the child reference concentrations.
CA EPA (2003)	35	--	--	--	Based on kidney and liver effects, but further details are unavailable.

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
[2]TDI = tolerable daily intake in mg/kg/d (i.e., a daily dose, not an exposure concentration in air)
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

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 liver, kidney and central nervous system effects observed in human occupational studies or effects on the liver, kidneys and lungs in mice chronically exposed by inhalation. The CA EPA reference concentration is an ambient air criterion developed for the California Toxic Air Contaminant program, and its basis is not clear from the available documentation. Two values have been reported for a tetrachloroethene reference concentration from Health Canada. Health Canada's (1993) documentation under the priority substances program describes a value based on liver, lung and kidney toxicity in mice chronically exposed via inhalation. They only report a tolerable daily intake in mg/kg/d based on converting the discontinuous LOEL air concentration in mice to a daily continuous dose using time-weighting for continuous exposure and default assumptions for body weight and daily breathing rate in mice. They apply a total uncertainty factor of 5000, including 10-fold factors accounting for intra- and interspecies variability and the use of a LOEL. They also include an additional 5-fold factor to account for uncertainties regarding the carcinogenicity of tetrachloroethene. TERA (2004) attributes a different reference concentration to Health Canada, based on the same mouse LOEL, but reporting that the continuous daily LOEL intake in mice was converted to a human equivalent concentration based on default assumptions for body weight and daily breathing

rate in a 5 – 11 year old child. TERA (2004) also reports that a total uncertainty factor of 1000 was applied, including the same 10-fold factors reported by Health Canada (1993), but not including the additional factor of 5 for carcinogenic uncertainty. Values derived with additional uncertainty factors based on carcinogenicity are not chosen in the current context, as non-cancer and cancer risks are being assessed separately. The derivation of a human equivalent concentration based on relative default breathing rates and body weights in rodents and humans is also inconsistent with currently-accepted risk assessment practice for reference concentration dosimetry. The ATSDR, WHO and NYS DOH derivations are all based on liver, kidney and/or central nervous system effects observed in studies where workers were exposed via inhalation. The reference concentrations are mostly based on human LOEL air concentrations with total uncertainty factors ranging from 30 to 100 and have similar values. The NYS DOH derivations include an explicit additional 3-fold uncertainty factor to extrapolate effects in adult workers to children. Therefore, the NYS DOH 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 tetrachloroethene.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: October, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1997. Toxicological Profile for Tetrachloroethylene (PERC). US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. http://www.atsdr.cdc.gov/toxpro2.html

CA EPA(California Environmental Protection Agency). 2003. Tetrachloroethylene (perchloroethylene): Identified as a toxic air contaminant under California's air toxic program (AB 1807) in 1991. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacremento, CA. http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html

Health Canada. 1993. Priority Substances List Assessment Report: Tetrachloroethylene. Ottawa: Environment Canada, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

NYS DOH (New York State Department of Health). 1997. Tetrachloroethene Ambient Air Criteria Document. Final Report. Albany, NY: Center for Environmental Health, Bureau of Toxic Substance Assessment.

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

Toxicology Excellence for Risk Assessment (TERA). 2004. International toxicity estimates for risk database. http://www.tera.org/iter/

WHO (World Health Organization). 2000. Air Quality Guidelines (2nd Ed.). Tetrachloroethylene. World Health Organization, Copenhagen, Denmark. http://www.euro.who.int/air/Activities/20020620_1

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: Tetrachloroethene
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 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	
CA EPA (2002)	0.17	5.9×10^{-6}	linearized multistage model	metabolized dose based on PBPK[2] modeling and assumes 18.5% of inhaled dose is metabolized in humans	Based on increased incidence of liver tumors male mice exposed via inhalation for 103 weeks.
NYS DOH (1997)	1	1×10^{-6}	linearized multistage model and linear extrap. from LED_{10} [3]	metabolized dose based on PBPK[2] modeling or observed urinary metabolites in mice; metabolized dose or air concentration in rats	Based on geometric or arithmetic means of several unit risks calculated from data on increased incidence of liver tumors in male and female mice from same study used by CA EPA, and increased incidence of leukemias in male and female rats exposed via inhalation for 103 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} air concentration $= 1 \times 10^{-6}$ / unit risk.
[2]PBPK: Physiologically-Based Pharmacokinetic
[3]LED_{10}: The lower bound on the dose associated with a 10% increase in tumor incidence.

2. Recommendation and Rationale

The two inhalation unit risks derived by authoritative bodies are based on the same data showing increased incidence of liver tumors in mice exposed to tetrachloroethene via inhalation for 103 weeks.

The NYS DOH value also reflects additional potency derivations based on increased incidence of leukemia in rats exposed via inhalation in the same study. The NYS DOH derivation represents a composite unit risk derived from multiple unit risk estimates from male and female rats and mice using two high-dose to low-dose extrapolation methods and different dose metrics correlating with internal metabolized dose. The CA EPA value is based on a single set of dose-response data in male mice and a single analysis of those data based on modeled metabolized dose and a linearized multistage high-dose to low-dose extrapolation model. The CA EPA analysis includes an assumption of 18.5% as the fraction of inhaled dose that is metabolized in humans without documenting the basis for that assumption. The NYS DOH derivation includes extrapolation methods more consistent with currently accepted risk assessment practice (using linear extrapolation from a modeled LED_{10}) and there is no clear documentation of the basis for the assumption of 18.5% inhaled dose metabolized used by CA EPA. Therefore, the NYS DOH unit risk (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 1 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: September, 2004

4. References for Summary Table

CA 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. http://www.oehha.ca.gov/air/cancer_guide/TSD2.html

NYS DOH (New York State Department of Health). 1997. Tetrachloroethene Ambient Air Criteria Document. Final Report. Albany, NY: Center for Environmental Health, Bureau of Toxic Substance Assessment.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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 (2004) Also used by: ♦ US EPA Region 3 (2004) ♦ US EPA ODW (2004)	0.2	223	NOEL	1000	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.
WHO (1993)	0.22	223	LOEL	1000	Based on increased liver weight in mice exposed by corn oil gavage for 13 weeks.
Health Canada (1996)	0.22	223	NOEL	1000	Based on increased liver weight in mice exposed by corn oil gavage for 13 weeks.
Health Canada (1992)	1.25	125	NOEL	100	Based on unspecified chronic inhalation study in animals exposed 6.5 hours per day, 5 days per week.
Health Canada (1992)	1.07	10.7	NOEL	10	Based on respiratory tract irritation and decreased scores on neurological function tests in humans in six hour inhalation exposures.
RIVM (1999)	0.223	223	LOEL	1000	Based on increased liver weight in mice exposed by corn oil gavage for 13 weeks.

[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 bases for the various reference doses for toluene include similar adverse effects in rats and mice exposed via oral gavage at the same doses in two parallel 13-week studies, with the exception of the Health Canada (1992) values, which are based on inhalation exposure. The values based on inhalation exposure are typically not used for derivation of an oral reference dose, given the availability of good quality oral data. Documentation of the Health Canada (1992) value in animals is also limited, and the Health Canada (1992) value based on a human clinical study uses exposure durations of only six hours, which is usually considered too short for deriving chronic reference doses. The numerical differences among the remaining values are due to variations in the precision used to report the value. The point of departure for both rats and mice was 223 mg/kg/day. The US EPA and Health Canada (1996) considered this dose a NOEL in both rats and mice, while WHO (and RIVM based on the WHO analysis) considered the dose a minimal LOEL in mice due to changes in relative liver weight unaccompanied by any histological changes. Because of the marginal nature of the effect at this dose in mice, the WHO and RIVM chose to use a 10-fold uncertainty factor to account for both extrapolation from a LOEL and from a subchronic study, in essence treating the dose equivalently to a subchronic NOEL as the US EPA had done. The use of an additional factor of 10 for a subchronic NOEL is more consistent with currently accepted risk assessment practice. Therefore, the US EPA IRIS 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 toluene.

3. Review Dates

Summary table completion: May, 2004
Toxicity value recommendation: July, 2004

4. References for Summary Table

Health Canada. 1992. Priority Substances List Assessment Report: Toluene. Ottawa: Environment Canada, Ministry of Public Works and Government Services.
http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

Health Canada. 1996. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. Ottawa: Ministry of Supply and Services Canada (including unpublished supporting documentation). H46-2/96-194E (as cited in on-line International Toxicity Estimates for Risk Database (http://www.tera.org/iter/)).

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 06/20/1990. Last revised: 04/01/1994. http://www.epa.gov/iris/subst/0118.htm

US EPA ODW (United States Environmental Protection Office of Drinking Water). 2004. 2004 Edition of the Drinking Water Standards and Health Advisories. EPA 822-R-04-005.
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.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

WHO (World Health Organization). 1996. Guidelines for drinking water quality, 2rd Ed. World Health Organization, Geneva.
http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/toluenefull.htm

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: 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
Toxicity value recommendation: July, 2004

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.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency verification date: 09/15/1987. Last revised: 02/1/1994.
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 (2004) Also used by: • US EPA Region 3 (2004) • 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 (2000)	300 (0.08 ppm)	3×10^4 (8 ppm)	LOEL	100	Based on alcohol- and age-adjusted color vision impairment in three groups of Croatian workers.
CA EPA (2003)	300	2.6×10^4 (7 ppm)	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.
Health Canada (1992)	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.

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 four derivations based on human data (US EPA IRIS, ATSDR, Health Canada and WHO) all estimate the human equivalent concentration based on an adjustment from non-continuous to continuous exposure. Of those four, three are LOEL points of departure from occupational studies and one (Health Canada) is a NOEL from a volunteer clinical chamber study. The chamber study NOEL is higher than ATSDR's observed occupational LOEL, and Health Canada chose to apply only a 10-fold uncertainty factor to account for intraspecies 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 intraspecies variability and 10-fold for use of a minimal LOEL. The US EPA IRIS applied a total uncertainty factor of 300, including the same 10-fold factors for intraspecies variability and use of a LOEL as applied by ATSDR and an additional 3-fold factor for database deficiencies "including the lack of data and well-characterized laboratory animal exposures evaluating neurotoxicity and respiratory irritation." The WHO's application of uncertainty factors was similar to the US EPA's, with the same 10-fold factors for intraspecies variability and use of a LOEL and an additional 3-fold factor to account for potential effects on the developing central nervous system. 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 intraspecies 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 interspecies 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. The CA EPA reports data published subsequent to the US EPA IRIS analysis that supports this conclusion and also suggests that the basis on which US EPA included an additional 3-fold uncertainty factor for database deficiencies is questionable. The ATSDR and CA EPA derivations are both consistent with currently-accepted risk assessment practices and result in the same reference concentration estimate. When two values are similar in the quality of the data and methods used for their derivation, a value based on appropriate human data, if available, is typically chosen. Therefore, the ATSDR reference concentration (300 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
Toxicity value recommendation: October, 2004

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. http://www.atsdr.cdc.gov/toxpro2.html

CA EPA(California Environmental Protection Agency). 2003. Chronic toxicity summary: Toluene. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacremento, CA. http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html

Health Canada. 1992. Priority Substances List Assessment Report: Toluene. Ottawa: Environment Canada, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification dates: 05/18/1989, 12/11/1991. Last revised: 08/01/1992. http://www.epa.gov/iris/index.html.

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

WHO (World Health Organization). 2000. Air Quality Guidelines (2nd Ed.). Toluene. World Health Organization, Copenhagen, Denmark. http://www.euro.who.int/air/Activities/20020620_1

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: 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
Toxicity value recommendation: September, 2004

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. Verification date: 09/15/1987. Last revised: 02/01/1994. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 (2004)	--	--	--	--	Oral RfD was withdrawn in 1991 pending further review.
US EPA Region 3 (2004)	0.28	25	NOEL	90	Based on liver toxicity (focal hepatocellular alterations) in female rats exposed by inhalation for 12 months and observed 19 months thereafter. The point of departure was obtained from the inhalation NOEL by pharmacokinetic modeling.
US EPA ODW (2004)	0.035				Based on a former US EPA IRIS RfD that has been withdrawn pending a re-evaluation.

[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. Recommendation and Rationale

Detailed documentation for the derivation of the US EPA ODW value was not available. The value is a former US EPA IRIS RfD that was withdrawn on IRIS, but still forms the basis of an extant federal drinking water standard (Maximum Contaminant Level). The US EPA Region 3 value is derived using methods that reflect general consistency with current risk assessment practice. Therefore the US EPA Region 3 reference dose (0.28 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
Toxicity value recommendation: July, 2004

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/subst/index.html

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). 2004. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: 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
Toxicity value recommendation: June, 2004

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.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 08/05/87. Last revised: 9/01/90. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 OSRTI (2004) Also used by: ♦ US EPA Region 3 (2004)	2.2×10^3	0.449 mg/kg in brain, modeled lifetime average daily concentration; human equivalent concentration of 1.99×10^5 mcg/m^3	NOEL	90	Based on neurotoxicity in gerbils in a 3-month inhalation study and PBPK[2] modeling. Animal NOEL = 70 ppm (3.82×10^5 mcg/m^3); LOEL = 210 ppm (1.15×10^6 mcg/m^3)
CA EPA (2003)	1×10^3	3.82×10^5 (70 ppm)	NOEL	300	Based on the same study used by US EPA OSRTI (2004)

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
[2]PBPK: Physiological-Based Pharmacokinetic Modeling

2. Recommendation and Rationale

The reference concentrations for 1,1,1-trichloroethane derived by authoritative bodies from the list in item 5 (below) are based on the same study, but differ in the identification of the point of departure. The US EPA applied a PBPK modeling approach to estimate the internal dose metric associated with the NOEL exposure concentration and the human equivalent exposure concentration associated with NOEL internal dose metric, while the CA EPA used the animal exposure concentration as the NOEL point of departure. The CA EPA applied a total uncertainty factor of 300 to account for inter- and intraspecies variability and the use of a subchronic study. The US EPA applied a total uncertainty value of 90, including the same 10-fold factor for intraspecies variability and a 3-fold factor for database deficiencies. An uncertainty factor for use of a subchronic study was not used because the internal dose metric (i.e., the concentration of 1,1,1-trichloroethane in the brain) was averaged

over the two year lifetime for gerbils. The US EPA also applied a 3-fold factor for interspecies variability based on the use of a PBPK model to relate internal dosimetry in animals and humans to external air concentrations. The US EPA approach, which uses PBPK modeling, is more consistent with currently-accepted risk assessment practice. Therefore the US EPA reference concentration (2.2 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 1,1,1-trichloroethane.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: October, 2004

4. References for Summary Table

CA EPA(California Environmental Protection Agency). 2003. Chronic toxicity summary: methyl chloroform. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacremento, CA. http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html

US EPA OSRTI (Office of Superfund Remediation and Technology Innovation). 2004. Provisional Toxicity Value Summary (PPRTV) for 1,1,1-Trichloroethane. Office of Superfund Remediation and Technology Innovation. http://hhpprtv.ornl.gov/

US EPA Region 3 (United States Environmental Protection Agency Region 3). Risk-based Concentration Table. Superfund Technical Support Section. 2004.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: 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
Toxicity value recommendation: September, 2004

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. Verification date: 08/05/1987. Last revised: 09/01/1990. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 NCEA (2001) Also used by: ♦ US EPA Region 3 (2004)	3×10^{-4}	1	NOEL, LOEL and LED_{10} (human equivalent doses)	3000	Based on a composite point of departure for liver toxicity (changes in liver to body-weight ratio). The points of departure were human equivalent doses obtained by PBPK modeling and included: 1) A NOEL from a six-month drinking water study in mice (1 mg/kg/day), 2) A LOEL from a six week gavage study in mice 1 mg/kg/day), and 3) An LED_{10} from a 14-day gavage study in rats (0.6 mg/kg/day).
US EPA ODW (2004)	7×10^{-3}	--	--	--	Information on derivation not available.
Health Canada (2003)	1.46×10^{-3}	0.146	$BMDL_{10}$	100	Based on increased incidence of heart malformations in rats pups born to females exposed prior to and during gestation via drinking water.
RIVM (1999)	0.05	50	NOEL	1000	Based on renal toxicity in male rats exposed by gavage for 52 weeks. Study LOEL = 250 mg/kg/day.
WHO (1997)	0.0238	71.4	LOEL	3000	Based on minor effects on relative liver weight changes in mice exposed orally for 6 weeks, 5 days/week.

[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; LED 10: The lower bound on the dose that results in a 10% increase in the incidence of an adverse effect; PBPK: physiologically-based pharmacokinetic.

2. Recommendation and Rationale

The basis for the RIVM reference dose for trichloroethene is histological changes in the kidney of male rats exposed via gavage for 52 weeks, while the WHO reference dose is based on increased liver weight and biochemical and histological liver changes in mice orally exposed for 6 weeks. Both studies have limitations. The mouse study was of relatively short duration, and the rat study has methodological limitations including failure to report the survival rate during the study and lack of good laboratory practices. The point of departure estimates are similar from these two datasets. RIVM applied a total uncertainty factor of 100 to account for interspecies and intraspecies variability and an additional factor of 10 to account for database limitations. WHO applied the same uncertainty factor of 100 for inter- and intraspecies variability, but added a factor of 10 to account for limited evidence of carcinogenicity and an additional factor of 3 to account for the use of a subchronic LOEL. The use of an uncertainty factor based on carcinogenic considerations is not applicable in this context, since cancer and noncancer health effects are being treated separately. The US EPA NCEA value is based on a composite point of departure for liver toxicity from three animal studies, whose PBPK-derived points of departure were approximately 1 mg/kg/day as a human-equivalent dose. The original animal data include a 6-month NOEL for liver effects in mice at 18 mg/kg/d, a 6-week LOEL for liver effects in rats of 71.4 mg/kg/d and a 14-day LOEL for liver effects in rats of 50 mg/kg/d. The US EPA NCEA originally applied total uncertainty and modifying factors totaling 5000 to its point of departure. The individual factors were $10^{½}$ for use of subchronic studies, $10^{½}$ for use of a point of departure at the "boundary" of where health effects can begin to be observed, $10^{½}$ for extrapolation for animals to humans, and 50 to account for overall human variation suggested by the phamacokinetic model (US EPA NCEA, 2001). A modifying factor of $10^{½}$ was added to these uncertainty factors to account for differences in background exposure to trichloroethene and its metabolites compared to background exposure in test animals. The document states that a total uncertainty factor of 3000 is recognized by the US EPA as the limit when calculating reference doses using human equivalent concentrations. The executive summary of the document lists a reference dose of 3×10^{-4} mg/kg/day, obtained by application of a factor of 3000 to the point of departure, but does not state in the text the specific values of the individual uncertainty and modifying factors that would result in a total uncertainty factor of 3000. This reference dose is the one listed by the US EPA Region 3. The US EPA derivation of a human-equivalent point of departure via PBPK modeling is expected to result in a more robust estimate and reduce uncertainties related to interspecies variability. However, applying a single set of uncertainty factors to a composite point of departure that represents both effect and non-effect levels from studies of differing duration and quality is a departure from currently accepted risk assessment practice. Even if the composite point of departure was considered to represent a human-equivalent subchronic minimal LOEL, a selection of uncertainty factors following currently accepted risk assessment practice might be expected to yield a total uncertainty factor of 300 or 1000, rather than 3000 or 5000. In reviewing US EPA NCEA (2001), the US EPA Science Advisory Board (US EPA SAB, 2002) was in general agreement that the scientific rationale for the choice of uncertainty factors in the risk assessment was not sufficiently developed. The Health Canada value is based on heart defects observed in rats born to females exposed via drinking water prior to and during pregnancy. The point of departure was estimated using benchmark dose modeling and a total uncertainty factor of 100 was applied to account for inter- and intraspecies variability. The Health Canada derivation is more consistent with currently accepted risk assessment practice and is based on a relevant exposure route and an endpoint that reflects health outcomes observed in human epidemiologic studies of trichloroethene exposure. Therefore, the Health Canada reference dose (1.46×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for trichloroethene.

3. Review Dates

Summary table completion: June, 2004
Toxicity value recommendation: September, 2004

4. References for Summary Table

Health Canada. 2003. Trichloroethylene in drinking water – document for public comment. Healthy Environments and Consumer Safety. http://www.hc-sc.gc.ca/hecs-sesc/water/index.htm

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 NCEA (United States Environmental Protection Agency National Center for Environmental Assessment). 2001. Trichloroethylene Health Risk Assessment: Synthesis and Characterization. External Review Draft. EPA /600/P-01/002A. Office of Research and Development. Washington DC. http://cfpub2.epa.gov/ncea/cfm/nceapubtopics.cfm?ActType=PublicationTopics

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 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

US EPA SAB (United States Environmental Protection Agency Scientific Advisory Board). 2002. Review of draft trichloroethylene health risk assessment: synthesis and characterization: an EPA science advisory board report. EPA-SAB-EHC-03-002. http://www.epa.gov/sab/fiscal03.htm

WHO (World Health Organization). 2003. Guidelines for drinking water quality, 3rd Ed. World Health Organization, Geneva. http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/trichloroethenesum.htm

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: Trichloroethene
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 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	
NYS DEC (1997)	1.75×10^{-4}	5.72×10^{-3}	linearized multistage model, extra risk	$BW^{3/4}$ [2]	Based on the geometric mean of four gavage data sets showing hepatocellular carcinomas in male and female mice exposed for five days per week for 78 or 103 weeks.
Health Canada (1993)	Reported Range: 200 – 600 (TD_{05} [3])	-- [3]	linearized multistage model, extra risk	body weight [4]	Based on testicular tumors in rats exposed orally and lung tumors in mice exposed via inhalation
CA EPA (2002)	7.7×10^{-5}	1.3×10^{-2}	linear extrapol. from the LED_{10} based on PBPK dose metrics[5]	$BW^{¾}$ [2]	Geometric mean of six potency estimates based on liver tumors in orally exposed mice and liver and lung tumors in mice exposed via inhalation.
US EPA ODW (2004)	8.6×10^{-5}	0.0117	--	--	Information on derivation not available.

US EPA NCEA (2001) Also used by: • US EPA Region 3 (2003)	2.5×10^{-6}	0.4	--	--	Based on increased risk for non-Hodgkin's lymphoma in female residents exposed to trichloroethene and other chemicals in a 75-town epidemiology 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]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.25}$.
[3]No cancer potency factor was derived. A range of risk-specific doses was reported as the modeled TD_{05} (= 200 - 600 mg/kg/day), the dose associated with a 5% increase in mean tumor incidence (not a lower-bound estimate). TERA (2004) convention for converting this estimate to a risk-specific dose at 10^{-5} lifetime risk would be to divide the lowest TD_{05} by 5000; this would imply a 10^{-6} risk specific dose of 4×10^{-3} mg/kg/day (not a lower bound estimate).
[4]Factor for dose adjustment from animal to humans is 1.
[5]PBPK: Physiologically-based pharmacokinetic. LED_{10}: The lower bound on the dose associated with a 10% increase in tumor incidence.

2. Recommendation and Rationale

The US EPA NCEA cancer potency factor is the highest of several factors derived by the US EPA in its 2001 draft health assessment document for trichloroethene (US EPA NCEA, 2001). The specific ecological epidemiology study that is the basis of the US EPA NCEA value associates elevated levels of trichloroethene in drinking water with an increased risk for non-Hodgkin's lymphoma. This investigation is limited in that the study population had concomitant exposure to chemicals other than trichloroethene. In addition, the average and highest trichloroethene drinking water concentrations are used to represent the exposure level of the entire cohort. As a result, the potential for exposure misclassification is high, due to lack of individual exposure information such as length of exposure and the quantity of water consumed from the tap. All of the remaining documented cancer potency factors derived by authoritative bodies are based on composite analysis of several oral and/or inhalation studies in mice indicating increased incidence of liver and lung tumors by both exposure routes. Data indicating increased incidence of testicular tumors in orally-exposed rats was also used in the Health Canada potency analysis. The Health Canada analysis did not attempt to derive a single potency factor, and only reported modeled maximum likelihood estimates of the doses associated with 5% incremental increase in tumor incidence, so a lower-bound risk-specific dose estimate cannot be obtained from these estimates. The NYS DEC value is based on a US EPA cancer potency derivation developed for the Great Lakes Water Quality Initiative, with a modification of the interspecies scaling factor from body surface-area to $BW^{3/4}$. However, a derivation by US EPA on the IRIS database was withdrawn pending a complete re-analysis of trichloroethene cancer risk. The CA EPA value incorporates some of the same oral tumor data as the NYS DEC value, but combines those data with liver and lung tumor incidence data from inhalation studies. The use of PBPK modeling by CA EPA allowed the oral and inhalation dose-response data to be treated consistently based on a common internal dose metric appropriate for systemic effects. The inclusion of inhalation data in the CA EPA derivation changes the mean cancer potency estimate by a factor of about 2 from the NYS DEC estimate. Inhalation data are typically not included in the derivation of an oral cancer potency factor if data from adequate oral studies are available. Therefore, the NYS DEC cancer potency factor (5.72×10^{-3} per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for trichloroethene. The trichloroethene risk specific dose calculated from this toxicity value is 1.75×10^{-4} mg/kg/day.

3. Review Dates

Summary table completion: June, 2004
Toxicity value recommendation: August, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2002. Public Health Goal for Trichloroethylene In Drinking Water. Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/water/phg/allphgs.html

Health Canada. 1993. Priority Substances List Assessment Report: Trichloroethylene. Ottawa: Environment Canada, Health Canada. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

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.

Toxicology Excellence for Risk Assessment (TERA). 2004. International toxicity estimates for risk database. http://www.tera.org/iter/

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/subst/index.html

US EPA NCEA (United States Environmental Protection Agency National Center for Environmental Assessment). 2001. Trichloroethylene Health Risk Assessment: Synthesis and Characterization. External Review Draft. EPA /600/P-01/002A. Office of Research and Development. Washington DC. http://cfpub2.epa.gov/ncea/cfm/nceapubtopics.cfm?ActType=PublicationTopics

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. http://www.epa.gov/waterscience/drinking/

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. http://www.epa.gov/reg3hwmd/risk/human/index.htm.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: Inhalation
Toxicity: Non-Cancer

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

1. Summary of Available 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		
US EPA NCEA (2001) Also used by: ♦ US EPA Region 3 (2004)	40	3.8×10^4	LOEL	1000	Based on central nervous system effects in two occupational studies.
RIVM (2001)	200	2×10^5	LOEL	1000	Based on hepatotoxicity in mice in a 30-day inhalation study.
CA EPA (2003)	600 (0.1 ppm)	6.1×10^4 (11.4 ppm)	LOEL	100	Based on central nervous system effects in a different occupational study from the ones used by US EPA NCEA.

[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 trichloroethene derived by authoritative bodies from the list in item 5 (below) are based on central nervous system effects in workers exposed via inhalation, or on liver toxicity in mice exposed by inhalation. The US EPA NCEA and CA EPA both based their derivations on data from occupational studies. CA EPA's point of departure concentration is based on estimated workplace air concentrations while the US EPA points of departure are based on urinary trichloroacetic acid (TCA, a major trichloroethene metabolite) and an assumed constant relationship between urinary TCA concentration and trichloroethene inhalation exposure. Both derivations estimate the human equivalent concentration by adjusting discontinuous occupational exposure to continuous exposure based on relative occupational to daily inhalation rate and 5 days per week to 7 days per week exposure. RIVM based their value on a mouse LOEL for liver toxicity from a 30-day continuous inhalation study. They did not include any pharmacokinetic adjustment to estimate the human equivalent concentration. The human occupational LOELs are lower than the mouse LOEL, and

therefore a reference concentration based on the human data is chosen. The US EPA NCEA applied a total uncertainty factor of 1000, including 10-fold factors each to account for intraspecies variability, use of a subchronic point of departure and use of a LOEL. The CA EPA applied a total uncertainty factor of 100, which differed from the US EPA derivation by not including the 10-fold factor for use of subchronic data. Mean exposure duration in the CA EPA study was 8 years, which was similar to the mean duration reported in one of the US EPA studies (7 years). The exposure duration was not reported in the other US EPA study, but US EPA considered studies with mean exposure duration as long as 16 years to be subchronic. As support for use of the full 10-fold subchronic uncertainty factor, US EPA noted that occupational evidence suggests severity of central nervous system effects increases with increasing duration of exposure. Therefore, the US EPA NCEA reference concentration (40 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
Toxicity value recommendation: October, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2003. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Trichloroethylene. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency.
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.
http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf

US EPA NCEA (United States Environmental Protection Agency National Center for Environmental Assessment). 2001. Trichloroethylene Health Risk Assessment: Synthesis and Characterization. External Review Draft. EPA /600/P-01/002A. Office of Research and Development. Washington DC.
http://cfpub2.epa.gov/ncea/cfm/nceapubtopics.cfm?ActType=PublicationTopics

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 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

***The New York State Department of Health trichloroethene air guideline of 5 mcg/m^3 is not included among the toxicity values considered for use in derivation of trichloroethene soil cleanup objectives, pending completion of the peer review process for the draft Trichloroethene Air Criteria Document, which summarizes the scientific basis of the guideline.**

P:\Sections\TAS\BROWNFIELDS 2003\Summary of Available Inhalation Reference Values (Reviewed and Edited)\Trichloroethene - Noncancer.doc

Chemical Name: Trichloroethene*
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 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 NCEA (2001) Also used by: • US EPA Region 3 (2003)	8.8×10^{-3}	1.1×10^{-4}	--	--	Based on route-to-route extrapolation of an oral cancer potency factor based on increased risk for non-Hodgkin's lymphoma in female residents exposed to trichloroethene and other chemicals in a 75-town epidemiology study.
CA EPA (2002)	0.5	2×10^{-6}	linearized multistage model, extra risk	Metabolized dose from PBPK[2] modeling; also mentions interspecies adjustment based on surface area scaling[3] but not clear how scaling was used	Based on the incidence of lung and liver tumors and lymphomas in male and female mice in several chronic inhalation studies. A best estimate of the unit risk was obtained by taking the geometric mean of the unit risks from four inhalation studies.

Health Canada (1993)	8.2×10^4 reported as a TC_{05}[4]; a linear extrapolation to 10^{-6} risk would yield: 1.6	-- [5]	--	Derivation includes an adjustment based on the relative inhalation volume to body weight for rats vs. humans aged 5 –11 years	Based on the increased incidence of leydig cell tumors in male rats exposed via inhalation for 104 weeks.
WHO (2000)	2.3	4.3×10^{-7}	linearized multistage model	inhaled dose	Based on the same data set used by Health Canada.

[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]PBPK: Physiologically-based pharmacokinetic
[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 associated with a 5% increase in mean tumor incidence (not a lower-bound estimate)
[5]No unit risk was derived.

2. Recommendation and Rationale

The US EPA NCEA unit risk is based on route-to-route extrapolation of the highest of several cancer potency factors derived by the US EPA in its 2001 draft health assessment document for trichloroethene (US EPA NCEA, 2001). The specific ecological epidemiology study that is the basis of the US EPA NCEA value associates elevated levels of trichloroethene in drinking water with an increased risk for non-Hodgkin's lymphoma. This investigation is limited in that the study population had concomitant exposure to chemicals other than trichloroethene. In addition, the average and highest trichloroethene drinking water concentrations are used to represent the exposure level of the entire cohort. As a result, the potential for exposure misclassification is high, due to lack of individual exposure information such as length of exposure and the quantity of water consumed from the tap. The remaining inhalation unit risks derived by authoritative bodies are either based on increased incidence of liver and lung tumors and lymphomas in mice or leydig cell (testicular) tumors in rats exposed via inhalation for about 2 years. The WHO and Health Canada derivations are both based on the rat leydig cell tumor data, but Health Canada only reported a TC_{05} maximum likelihood estimate, so that an upper-bound unit risk value is not available from their analysis. The CA EPA derivation is based on unit risks estimated for several chronic inhalation data sets in mice. The CA EPA used metabolized dose in animals and humans as the interspecies scaling metric, although a statement in the CA EPA documentation also mentions using surface area scaling for interspecies adjustments. There is no further elaboration of the latter statement and it is not clear whether that adjustment refers to a dosimetry adjustment or an allometric scaling adjustment for parameters in the PBPK model. Nevertheless, the use of PBPK dosimetry modeling and a composite unit risk based on several inhalation data sets is expected to provide a more robust unit risk estimate and is more consistent with currently-accepted risk assessment practice. Therefore, the CA EPA unit risk (2.0×10^{-6} per mcg/m^3) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for trichloroethene. The trichloroethene risk specific air concentration

calculated from this toxicity value is 0.5 mcg/m^3.

3. Review Dates

Summary table completion: July, 2004
Toxicity value recommendation: September, 2004

4. References for Summary Table

CA 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. http://www.oehha.ca.gov/air/cancer_guide/TSD2.html

Health Canada. 1993. Priority Substances List Assessment Report: Trichloroethylene. Ottawa: Environment Canada, Ministry of Public Works and Government Services. http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl2.htm

US EPA NCEA (United States Environmental Protection Agency National Center for Environmental Assessment). 2001. Trichloroethylene Health Risk Assessment: Synthesis and Characterization. External Review Draft. EPA /600/P-01/002A. Office of Research and Development. Washington DC. http://cfpub2.epa.gov/ncea/cfm/nceapubtopics.cfm?ActType=PublicationTopics

WHO (World Health Organization). 2000. Air Quality Guidelines (2nd Ed.), Chapter 5.15, Trichloroethylene. World Health Organization, Copenhagen, Denmark. http://www.euro.who.int/air/Activities/20020620_1

5. Authoritative Bodies Checked for a Cancer Potency Value

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

***The New York State Department of Health trichloroethene air guideline of 5 mcg/m^3 is not included among the toxicity values considered for use in derivation of trichloroethene soil cleanup objectives, pending completion of the peer review process for the draft Trichloroethene Air Criteria Document, which summarizes the scientific basis of the guideline.**

Chemical Name: 2-(2,4,5-Trichlorophenoxy)propionic Acid
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 2-(2,4,5-Trichlorophenoxy)propionic Acid (2,4,5-TP) (CAS Number 93-72-1)

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 ODW (2004) • US EPA NCEA (2004)	8×10^{-3}	0.75	NOEL	100	Based on histopathological changes in the livers of male dogs exposed via the diet for two years. Study LOEL = 2.5 mg/kg/day (females).
CA EPA (2003)	9×10^{-4}	0.9	NOEL	1000	Based on the same study as 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.

2. Recommendation and Rationale

The basis for the two reference doses for 2,4,5-TP are essentially identical with respect to choice of study, species and adverse effect. The US EPA and CA EPA apparently make slightly different assumptions about dietary intake in dogs, and so arrive at slightly different points of departure from the average daily dietary NOEL exposure level of 56 parts per million in food. The US EPA applied a total uncertainty factor of 100 to account for interspecies and intraspecies variability. The CA EPA applies the same 100-fold uncertainty factor for those two components, but also includes an additional factor of 10 to account for database uncertainties. Although the database for 2,4,5-TP is somewhat sparse, both the US EPA and CA EPA point out that the chronic dog NOEL is below NOELs observed for developmental effects observed in rats and mice, and is also below another chronic NOEL in rats which was essentially equal to the dog LOEL. The male dog LOEL (2.5 mg/kg/day) appears to represent a sensitive effect as it is equal to or lower than NOELs in rats and female dogs in two well-conducted chronic feeding studies, and in rats and mice in the two developmental studies. It does not appear that database deficiencies are sufficiently large to warrant an additional 10-fold uncertainty factor. Therefore, the US EPA reference dose (8×10^{-3} mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 2,4,5-TP.

3. Review Dates

Summary table completion: September, 2004
Toxicity value recommendation: September, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2003. Public health goals for chemicals in drinking water. Silvex. Office of Environmental Health Hazard Evaluation. Sacramento, CA. http://www.oehha.ca.gov/water/phg/allphgs.html

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 01/21/1988. Last revised: 09/07/1988. http://www.epa.gov/iris/subst/index.html

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 WaterU.S. Environmental Protection AgencyWashington, 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. http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: 2-(2,4,5-Trichlorophenoxy)propionic Acid
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-(2,4,5-Trichlorophenoxy)propionic Acid (2,4,5-TP) (CAS Number 93-72-1)

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 are not available and the available animal cancer bioassay studies are considered to be inadequate because of small numbers of animals, short study duration and no evidence of maximum tolerated dose 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 2,4,5-TP 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
Toxicity value recommendation: September, 2004

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. Verification date: 12/02/1987. Last revised: 08/22/1988. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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-(2,4,5-Trichlorophenoxy)propionic Acid
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 2-(2,4,5-Trichlorophenoxy)propionic Acid (2,4,5-TP) (CAS Number 93-72-1)

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 2,4,5-TP is not available from the authoritative bodies listed in item number 5 (below). 2,4,5-TP 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 2,4,5-TP is 8×10^{-3} mg/kg/day. Therefore, a reference concentration of 28 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 2,4,5-TP.

3. Review Dates

Summary table completion: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 2-(2,4,5-Trichlorophenoxy)propionic Acid
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-(2,4,5-Trichlorophenoxy)propionic Acid (2,4,5-TP) (CAS Number 93-72-1)

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 2,4,5-TP 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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: Oral
Toxicity: Non-Cancer

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

1. Summary of Available Oral Reference Doses for 1,2,4-Trimethylbenzene (CAS Number 95-63-6)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA NCEA (2004) Also used by: ♦ US EPA Region 3 (2003)	0.05	143	NOEL	3000	Based on increased liver and kidney weights, decreased weight gain, and increased serum phosphorus levels in rats exposed orally to 1,3,5-trimethylbenzene by gavage for 90 days. Study LOEL = 429 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 reference dose for 1,2,4-trimethylbenzene is derived by analogy to 1,3,5-trimethylbenzene. The US EPA value is the only available reference dose for 1,2,4-trimethylbenzene 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 (0.05 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,2,4-trimethylbenzene.

3. Review Dates

Summary table completion: May, 2004
Toxicity value recommendation: June, 2004

4. References for Summary Table

US EPA NCEA (National Center for Environmental Assessment). 2003. Toxicological Review of 1,2,4 Trimethylbenzene (Noncancer effects). U.S. Environmental Protection Agency. http://hhpprtv.ornl.gov/Trimethylbenzene124.shtml.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section.

http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: 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
Toxicity value recommendation: June, 2004

4. References for Summary Table

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 (2004) Also used by: ♦ US EPA Region 3 (2003)	6	1.8×10^4	LOEL	3000	Based on study of human exposures that showed increased vertigo, headaches, drowsiness, chronic asthma-like bronchitis, anemia, altered blood clotting in workers exposed up to 10 years.

[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 1,2,4-trimethylbenzene 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 (6 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
Toxicity value recommendation: October, 2004

4. References for Summary Table

US EPA OSRTI (Office of Superfund Remediation and Technology Innovation). 2004. Provisional Toxicity Value Summary (PPRTV) for 1,2,4-Trimethylbenzene. Office of Superfund Remediation and Technology Innovation.
http://hhpprtv.ornl.gov/

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. 2004.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: 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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994 http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: Oral
Toxicity: Non-Cancer

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

1. Summary of Available Oral Reference Doses for 1,3,5-Trimethylbenzene (CAS Number 108-67-8)

Agency	Reference Dose[1] (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA OSRTI (2004) Also used by: ♦ US EPA Region 3 (2004)	0.05	143	NOEL	3000	Based on increased liver and kidney weight and serum phosphorus levels in rats exposed by corn oil gavage 5 days/week for 90 days. Study LOEL = 429 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 NCEA value is the only available reference dose for 1,3,5-trimethylbenzene 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 (0.05 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,3,5-trichlorobenzene.

3. Review Dates

Summary table completion: June, 2004
Toxicity value recommendation: June, 2004

4. References for Summary Table

US EPA OSRTI (Office of Superfund Remediation and Technology Innovation). 2004. Provisional Toxicity Value Summary (PPRTV) for 1,3,5-Trimethylbenzene. SRC TR-03-032/08-04-03. Office of Superfund Remediation and Technology Innovation. Available online at: http://hhpprtv.ornl.gov/

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 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: 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
Toxicity value recommendation: June, 2004

4. References for Summary Table

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 OSRTI (2004) Also used by: ♦ US EPA Region 3 (2003)	6	1.8×10^4	LOEL	3000	Based on study of human exposures that showed increased vertigo, headaches, drowsiness, chronic asthma-like bronchitis, anemia, altered blood clotting in workers exposed up to 10 years.

[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 1,3,5-trimethylbenzene 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 (6 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
Toxicity value recommendation: October, 2004

4. References for Summary Table

US EPA OSRTI (Office of Superfund Remediation and Technology Innovation). 2004. Provisional Toxicity Value Summary (PPRTV) for 1,3,5 Trimethylbenzene. Office of Superfund Remediation and Technology Innovation. http://hhpprtv.ornl.gov/

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section. 2004.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

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: 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
Toxicity value recommendation: February, 2005

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. Verification date: 09/15/1987. Last revised: 02/01/1994. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 (2004) Also used by: ♦ US EPA Region 3 (2004) ♦ US EPA EPA ODW (2004)	3×10^{-3}	0.09 (human equivalent dose)	NOEL	30	Based on polymorphism of liver cells and liver cysts in rats exposed in diet (powder) 4 hours/day for 150 weeks for females and 149 weeks for males. Study LOEL = 0.9 mg/kg/day (human equivalent dose).
ATSDR (2004)	3×10^{-3}	0.09 (human equivalent dose)	NOEL	30	Based on liver cell polymorphism in rats exposed in diet (powder) 4 hours/day for 150 weeks (same study as in 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 two reference doses for vinyl chloride are 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, and a physiologically-based pharmacokinetic 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 intraspecies extrapolation and 3 for interspecies extrapolation). No other reference doses were available from the authoritative bodies listed in item 5 (below), and the US EPA and ATSDR values are derived using methods that reflect general consistency with current risk assessment practice. 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
Toxicity value recommendation: January, 2005

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2004. Toxicological Profile for Vinyl chloride (*Draft for Public Comment*). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. http://www.atsdr.cdc.gov/toxpro2.html.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency consensus date: 07/20/2000. Last revised: 08/07/2000. http://www.epa.gov/iris/subst/1001.htm.

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 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 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: 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 (2004) Also used by: ♦ US EPA Region 3 (2004)	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 (2004) Also used by: ♦ US EPA Region 3 (2004)	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 (2004)	1.3×10^{-6}	0.75 (continuous lifetime adult exposure)	linear extrapol. from LED_{10} [3]	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 (2004)	6.7×10^{-7}	1.5 (continuous lifetime exposure from birth)	linear extrapol. from LED_{10} [3]	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.
RIVM (2000)	6×10^{-6}	-- [4]	linear extrapola-tion	body weight [5]	Based on same study as US EPA IRIS (2004).
Health Canada (1992)	5.1×10^{-6} to 4.9×10^{-5}	--[6]	linear extrapol. from LED_{10} [3]	body surface area [7]	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 [7]	Based on lung and liver tumors in rats exposed by diet for 1001 days.
CA EPA (2000)	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 physiologically-based pharmacokinetic model.
[3]LED_{10} = The 95% lower confidence limit of the dose that produces a 10% increase in tumor incidence.
[4]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)
[5]Factor for dose adjustment from animal to humans is 1.
[6]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.
[7]Factor for dose adjustment from animal to humans is (animal body weight/human body weight)$^{0.33}$.

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 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 presents four possible oral cancer potency values on IRIS - 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 applications only considering continuous adult lifetime exposure and for applications when considering continuous lifetime exposure from birth. RIVM derived a risk-specific dose from the same data set used by the US EPA on 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. Health Canada used the data set for angiocarcinomas in female rats from the same study used by the US EPA, 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 at the US EPA IRIS value, 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} values are derived from the analysis most consistent with currently accepted risk assessment practice. In practice, the values derived by the two methods are nearly identical. Therefore the US EPA 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
Toxicity value recommendation: July, 2004

4. References for Summary Table

CA EPA (California Environmental Protection Agency), 2000. Public health goals for chemicals in drinking water: vinyl chloride. Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/water/phg/allphgs.html

Health Canada. 1992. Water Quality and Health. Guidelines for Canadian Drinking Water Quality. Healthy Environments and Consumer Safety. http://www.hc-sc.gc.ca/hecs-sesc/water/dwgsup.htm

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 IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency consensus date: 07/20/2000. Last revised: 08/07/2000. http://www.epa.gov/iris/subst/1001.htm

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 Checked for a Cancer Potency Value

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: 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
Toxicity value recommendation: December, 2004

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. Agency consensus date: 07/20/2000. Last revised: 08/07/2000. http://www.epa.gov/iris/index.html.

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 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: 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}			
CA 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 CA 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 CA 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 CA 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
Toxicity value recommendation: September, 2004

4. References for Summary Table

CA 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. 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. 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency consensus date: 07/20/2000. Last revised: 08/07/2000. http://www.epa.gov/iris/index.html.

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 Checked for a Cancer Potency Value

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 (2004) Also used by: ♦ US EPA Region 3 (2004) ♦ EPA ODW (2004) ♦ WHO (1993)	0.2	179	NOEL	1000	Based on decreased body weight and increased mortality in rats exposed by corn oil gavage five days per week for 2 years. Study LOEL = 358 mg/kg/day.
RIVM (2001)	0.15	150	LOEL	1000	Based on mild nephropathy in female rats exposed by gavage for 90 days.
Health Canada (1996)	1.5	150	NOEL	100	Based on mild nephropathy in female rats exposed by gavage for 90 days.
EPA OPP (1997)	2	179	NOEL	100	Based on same data as the US EPA IRIS value
WHO (1996)	0.179	179	NOEL	1000	Based on same data as the US EPA IRIS value

Health Canada (1993)	0.14	144	LOEL	1000	Based on maternal (unspecified) and fetal toxicity (skeletal retardation) observed in rats exposed by inhalation on days 7 to 20 of gestation.

[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 three of the xylene reference doses (WHO, EPA IRIS, EPS OPP) is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (179 mg/kg/day). The RIVM and Health Canada (1996) 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, subchronic data is not chosen as the reference dose basis. The Health Canada (1993) reference dose 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 derivation also uses methods that are generally no longer used in current risk assessment practices. The other 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 interspecies and intraspecies 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 total xylenes.

3. Review Dates

Summary table completion: June, 2004
Toxicity value recommendation: September, 2004

4. References for Summary Table

Health Canada. 1993. Priority Substances List Assessment Report: Xylenes. Ottawa: Environment Canada, Ministry of Public Works and Government Services.
http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

Health Canada. 1996. Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. Ottawa: Ministry of Supply and Services Canada (including unpublished supporting documentation). H46-2/96-194E (as cited in on-line International Toxicity Estimates for Risk Database (http://www.tera.org/iter/)).

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). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency consensus date: 01/30/2003. Last revised: 02/21/2003.
http://www.epa.gov/iris/subst/0270.htm

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). 2003 Risk-based Concentration Table. Superfund Technical Support Section. 2004.
http://www.epa.gov/reg3hwmd/risk/human/index.htm

WHO (World Health Organization). 1996. Guidelines for drinking water quality, 2rd Ed. World Health Organization, Geneva.
http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/xylenesfull.htm

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: 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
Toxicity value recommendation: July, 2004

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.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency consensus date: 01/30/2003. Last revised: 02/21/2003. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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: 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 (2004) Also used by: ♦ US EPA Region 3 (2004)	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 (1995)	600 (0.1 ppm)	6.01×10^4 (14 ppm)	LOEL	100	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.
Health Canada (1993)	only reported as TDI[2] = 0.144 mg/kg/d (would be equivalent to a reference concentration = 500 mcg/m^3 based on adult body weight and daily breathing rate)	rat LOEL concentration = 2.5×10^5 mcg/m^3 converted to human equivalent as daily intake of 144 mg/kg/d	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.
Health Canada as reported by TERA (2004)	180 mcg/m^3 based on 5 – 11 year old child body weight and daily breathing rate	1.8×10^5 mcg/m^3 based on 5 – 11 year old child body weight and daily breathing rate	LOEL	1000	Based on same study as Health Canada (1993) above, but TERA (2004) reports that a reference concentration was derived by Health Canada based on 5 – 11 year old child body

					weight and breathing rate parameters and different parameters for rat body weight and daily breathing rate.
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 (2003)	700 (0.2 ppm)	2.2×10^4 (5.1 ppm)	LOEL	30	Based on the same study as used by ATSDR (1995)

[1]Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.
[2]TDI = tolerable daily intake in mg/kg/day (i.e., a daily dose, not an exposure concentration in air)
NOEL: no observed effect level; LOEL: lowest observed effect level; UF: uncertainty factor.

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. Two values have been reported for a xylene reference concentration from Health Canada. Health Canada's (1993) documentation under the priority substances program describes a value based on skeletal effects in offspring of rats exposed during gestation. Unspecified toxicity was also reported in the exposed female rats. Health Canada (1993) only report a tolerable daily intake in mg/kg/d based on converting the LOEL air concentration in rats to a daily dose using default assumptions for body weight and daily breathing rate in rats. A conversion from discontinuous to continuous exposure was not made, although it is not clear from the documentation whether or not exposure was continuous during this developmental study. They apply a total uncertainty factor of 1000, including 10-fold factors accounting for intra- and interspecies variability and the use of a LOEL. TERA (2004) attributes a different reference concentration to Health Canada, based on the same rat LOEL, but reporting that the daily LOEL intake in rats was converted to a human equivalent concentration based on default assumptions for body weight and daily breathing rate in a 5 – 11 year old child and different rat body weight and daily breathing rate parameters. TERA (2004) also reports the same total uncertainty factor of 1000 was applied. 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. 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 based their 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 intraspecies variability, 3-fold to account for interspecies 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 100, including 10-fold for intraspecies variability and 10-fold for use of a LOEL exposure level. The CA EPA applied a total uncertainty factor of 30, including 10-fold for intraspecies 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 include 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 generally more consistent with currently-accepted risk assessment practice than either the ATSDR or CA EPA derivation. Therefore, the US EPA 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
Toxicity value recommendation: October, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. Toxicological Profile for xylenes. US Department of Health and Human Services. Atlanta, Georgia: Public Health Service. http://www.atsdr.cdc.gov/toxpro2.html

CA EPA(California Environmental Protection Agency). 2003. Chronic toxicity summary: xylenes. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacremento, CA.
http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html

Health Canada. 1993. Priority Substances List Assessment Report: Xylenes. Ottawa: Environment Canada, Ministry of Public Works and Government Services.
http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm

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

Toxicology Excellence for Risk Assessment (TERA). 2004. International toxicity estimates for risk database. http://www.tera.org/iter/

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency consensus date: 01/30/2003. Last revised: 02/21/2003. http://www.epa.gov/iris/index.html.

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 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: 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
Toxicity value recommendation: September, 2004

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. Agency consensus date: 01/30/2003. Last revised: 02/21/2003.
http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 (2004) Also used by: • US EPA Region 3 (2004) • US EPA ODW (2004) • US EPA HEAST (1997)	0.3	1.0	LOEL	3	Based on a 47% decrease in erythrocyte superoxide dismutase (ESOD) concentration in adult females after 10 weeks of zinc exposure (zinc gluconate twice daily) in a dietary supplement study. The experimental LOEL of 0.83 mg/kg/day was adjusted to account for background zinc consumption.
RIVM (2001)	0.5	1.0	LOEL	2	Based on the same study and as US EPA IRIS (2004). An outdated ATSDR toxicological profile document is cited as the source of the LOEL value. The current ATSDR profile reports a LOEL of 0.83 mg/kg/day uncorrected for background dietary intake.

[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 two inorganic zinc reference doses is essentially identical with respect to choice of study, species and observed effect level and point of departure (1.0 mg/kg/d). The US EPA applied a total uncertainty factor of 3 to account for the use of a minimal LOEL in sensitive humans and consideration of a substance that is a essential dietary nutrient. RIVM applied a total uncertainty factor of 2, which was considered a sufficient margin of safety, without a clear explanation of the basis for that conclusion. The US EPA derivation is more consistent with current 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-based soil cleanup objective for zinc.

3. Review Dates

Summary table completion: June, 2004
Toxicity value recommendation: September, 2004

4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological profile for Zinc. Atlanta, GA: U.S. Department of Health and Human Services, 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. 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). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 11/06/1991. Last revised: 10/01/1992.
http://www.epa.gov/iris/index.html.

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 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 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

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
Toxicity value recommendation: September, 2004

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. Verification date: 06/15/1990. Last revised: 02/01/1991. http://www.epa.gov/iris/index.html.

5. Authoritative Bodies Checked for a Cancer Potency Value

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 Available 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 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, 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 zinc is 0.3 mg/kg/day. 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: February, 2005
Toxicity value recommendation: February, 2005

4. References for Summary Table

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: 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
Toxicity value recommendation: September, 2004

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. Verification date: 06/15/1990. Last revised: 02/01/1991.
http://www.epa.gov/iris/index.html

5. Authoritative Bodies Checked for a Cancer Potency Value

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