

**Appendix A. Fact Sheets Containing a Summary of Data Used to Identify Toxicity Values ( Reference Dose, Reference Concentration, Oral Potency Factor, and Inhalation Unit Risk) Used in the Calculation of Soil Cleanup Objectives Based on the Potential for Chronic Toxicity in Adults and Children from Chronic Exposures to Soil Contaminants.**

## Table of Contents<sup>1</sup>

Chemical Name: Acenaphthene .....	4
Chemical Name: Acenaphthylene .....	12
Chemical Name: Acetone .....	20
Chemical Name: Aldrin .....	28
Chemical Name: Anthracene .....	37
Chemical Name: Arsenic .....	45
Chemical Name: Barium .....	56
Chemical Name: Benz[a]anthracene .....	65
Chemical Name: Benzene .....	74
Chemical Name: Benzo[a]pyrene .....	85
Chemical Name: Benzo[b]fluoranthene .....	96
Chemical Name: Benzo[g,h,i]perylene .....	107
Chemical Name: Benzo[k]fluoranthene .....	115
Chemical Name: Beryllium .....	125
Chemical Name: <i>n</i> -Butylbenzene .....	135
Chemical Name: <i>sec</i> -Butylbenzene .....	143
Chemical Name: <i>tert</i> -Butylbenzene .....	151
Chemical Name: Cadmium .....	159
Chemical Name: Carbon Tetrachloride .....	171
Chemical Name: Chlordane (technical) .....	183
Chemical Name: Chlorobenzene .....	193
Chemical Name: Chloroform .....	203
Chemical Name: Chromium (III) .....	216
Chemical Name: Chromium (VI) .....	225
Chemical Name: Chrysene .....	237
Chemical Name: Copper .....	246
Chemical Name: Cyanide .....	255
Chemical Name: p,p'-Dichlorodipenyldichloroethane (4,4'-DDD) .....	264
Chemical Name: p,p'-Dichlorodipenyldichloroethylene (4,4'-DDE) .....	272
Chemical Name: p,p'-Dichlorodipenyltrichloroethane (4,4'-DDT) .....	280
Chemical Name: Dibenz[a,h]anthracene .....	288
Chemical Name: Dibenzofuran .....	297
Chemical Name: 1,2-Dichlorobenzene .....	305
Chemical Name: 1,3-Dichlorobenzene .....	314
Chemical Name: 1,4-Dichlorobenzene .....	322
Chemical Name: 1,1-Dichloroethane .....	334
Chemical Name: 1,1-Dichloroethene .....	342
Chemical Name: 1,2-Dichloroethane .....	352
Chemical Name: <i>cis</i> -1,2-Dichloroethene .....	365
Chemical Name: <i>trans</i> -1,2-Dichloroethene .....	374
Chemical Name: Dieldrin .....	382
Chemical Name: 1,4-Dioxane .....	392
Chemical Name: Endosulfan (technical) .....	400
Chemical Name: Endrin (technical) .....	409
Chemical Name: Ethylbenzene .....	418
Chemical Name: Fluoranthene .....	428
Chemical Name: Fluorene .....	436
Chemical Name: Heptachlor .....	444

<sup>1</sup> Chemicals listed alphabetically, fact sheets presented in this order oral reference dose, oral cancer potency factor, inhalation reference concentration, inhalation unit risk. Only the first page of each chemical is listed.

Chemical Name: Hexachlorobenzene .....	454
Chemical Name: <i>alpha</i> -Hexachlorocyclohexane ( <i>alpha</i> -HCH).....	465
Chemical Name: <i>beta</i> -Hexachlorocyclohexane ( <i>beta</i> -HCH) .....	474
Chemical Name: <i>delta</i> -Hexachlorocyclohexane ( <i>delta</i> -HCH).....	483
Chemical Name: <i>gamma</i> -hexachlorocyclohexane ( <i>gamma</i> -HCH) .....	491
Chemical Name: Indeno[1,2,3-cd]pyrene .....	501
Chemical Name: Manganese .....	512
Chemical Name: Mercury (inorganic salts).....	521
Chemical Name: Mercury (elemental) .....	526
Chemical Name: Methylene Chloride .....	531
Chemical Name: Methyl Ethyl Ketone (2-Butanone) .....	545
Chemical Name: 2-Methylphenol .....	553
Chemical Name: 3-Methylphenol .....	561
Chemical Name: 4-Methylphenol .....	569
Chemical Name: Methyl <i>tert</i> -butyl ether .....	577
Chemical Name: Naphthalene .....	588
Chemical Name: Nickel .....	597
Chemical Name: Pentachlorophenol .....	614
Chemical Name: Phenanthrene .....	624
Chemical Name: Phenol .....	632
Chemical Name: <i>n</i> -Propylbenzene .....	640
Chemical Name: Pyrene .....	648
Chemical Name: Selenium .....	656
Chemical Name: Silver .....	664
Chemical Name: Tetrachloroethene .....	672
Chemical Name: Toluene .....	685
Chemical Name: 1,1,1-Trichloroethane .....	695
Chemical Name: Trichloroethene.....	703
Chemical Name: 2-(2,4,5-Trichlorophenoxy)propionic Acid .....	717
Chemical Name: 1,2,4-Trimethylbenzene.....	725
Chemical Name: 1,3,5-Trimethylbenzene.....	733
Chemical Name: Vinyl Chloride .....	741
Chemical Name: Xylenes .....	752
Chemical Name: Zinc.....	763

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

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

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

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

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

**2. Recommendation and Rationale**

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

**3. Review Dates**

Summary table completion: July, 2004  
 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: 04/01/1994.  
<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 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). 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: Acenaphthene**  
**Exposure Route: Oral**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Oral Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Human and animal data are not available.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for acenaphthene is not available.

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

**3. Review Dates**

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

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

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

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

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

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

**2. Recommendation and Rationale**

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

**3. Review Dates**

Summary table completion: February, 2005  
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: Acenaphthene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

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

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for acenaphthene is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005

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: Acenaphthylene**  
**Exposure Route: Oral**  
**Toxicity: Non-Cancer**

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

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

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

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

**2. Recommendation and Rationale**

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

**3. Review Dates**

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

**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: Acenaphthylene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

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

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

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for acenaphthylene is not available.

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

**3. Review Dates**

Summary table completion: September, 2004

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: 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

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**Chemical Name: Acenaphthylene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

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

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

<sup>1</sup>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 acenaphthylene is not available from the authoritative bodies listed in item number 5 (below). Acenaphthylene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure and for which an oral reference dose for a chemically similar surrogate (acenaphthene) based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for the chemical surrogate (acenaphthene) is 0.06 mg/kg/day. Therefore, based on the chemical surrogate and exposure route extrapolation, a reference concentration of 210 mcg/m<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for acenaphthene.

**3. Review Dates**

Summary table completion: February, 2005

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: Acenaphthylene**  
**Exposure Route: Inhalation**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Inhalation Cancer Toxicity Value Documentation**

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

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for acenaphthylene is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005  
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: Acetone**  
**Exposure Route: Oral**  
**Toxicity: Non-Cancer**

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

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

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

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

**2. Recommendation and Rationale**

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

**3. Review Dates**

Summary table completion: April, 2004  
Toxicity value recommendation: June, 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. <http://www.epa.gov/iris/index.html>. Verification date: 5/29/03. Last revised: 07/31/03.

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: Acetone**  
**Exposure Route: Oral**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Oral Cancer Toxicity Value Documentation**

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

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

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for acetone is not available.\*

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

**3. Review Dates**

Summary table completion: April, 2004  
Toxicity value recommendation: June, 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: 05/29/2003. Last revised: 07/31/2003.  
<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

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

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

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

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
ATSDR (2002)	3 x 10 <sup>4</sup>	2.97 x 10 <sup>6</sup>	LOEL	100	Based on neurological effects in a 6 week human study.

<sup>1</sup>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 ATSDR value is the only available reference concentration for acetone from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore the US EPA reference concentration (30,000 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for acetone.

**3. Review Dates**

Summary table completion: May, 2004

Toxicity value recommendation: October, 2004

**4. References for Summary Table**

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

**5. Authoritative Bodies Checked for Reference Doses**

United States Environmental Protection Agency  
Integrated Risk Information System A-24



National Center for Environmental Assessment  
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed  
Toxicity Values)  
Region 3 Risk-Based Concentrations  
Office of Pesticides  
Office of Drinking Water  
Health Effects Assessment Summary Tables  
New York State Department of Health  
New York State Department of Environmental Conservation  
Agency for Toxic Substances and Disease 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: Acetone**  
**Exposure Route: Inhalation**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Inhalation Cancer Toxicity Value Documentation**

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

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

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An inhalation unit risk for acetone is not available.\*

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

**3. Review Dates**

Summary table completion: May, 2004  
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: 05/29/2003. Last revised: 07/31/2003. <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

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

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

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

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA Region 3 (2003)</li> <li>◆ US EPA OPP (1997)</li> <li>◆ US EPA ODW (2002)</li> <li>◆ US EPA HEAST (1997)</li> </ul>	3 x 10 <sup>-5</sup>	0.025	LOEL	1000	Based on increased liver-to-body weight ratio and liver histopathological changes in male and female rats in a 2-year dietary study.
WHO (2003)  Also used by: <ul style="list-style-type: none"> <li>◆ Health Canada (1994)</li> </ul>	1 x 10 <sup>-4</sup>	0.025	NOEL	250	Based on NOELs of 1 mg/kg in diet of dogs and 0.5 mg/kg in diet of rats, equivalent to 0.025 mg/kg/day in both species. Limited information is available on the precise studies and points of departure used to obtain the reference dose.
ATSDR (2002)	3 x 10 <sup>-5</sup>	0.025	LOEL	1000	Based on same study and analysis as US EPA IRIS (2004).
RIVM (2001)	1 x 10 <sup>-4</sup>	0.025	LOEL	250	Based on liver toxicity in rats in same study as US EPA IRIS (2004), and on liver toxicity in dogs in a 25-month dietary study.

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

## 2. Recommendation and Rationale

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

## 3. Review Dates

Summary table completion: February, 2004

Toxicity value recommendation: March, 2004

## 4. References for Summary Table

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

Health Canada. 1994. 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. p.244-248.

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

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment.

Verification date: 12/18/85. Last revised: 03/01/88.

<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 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). 2003. Guidelines for drinking water quality, 3<sup>rd</sup> Ed. World Health Organization, Geneva.  
[http://www.who.int/docstore/water\\_sanitation\\_health/GDWQ/draftchemicals/aldrindieldrin2003.pdf](http://www.who.int/docstore/water_sanitation_health/GDWQ/draftchemicals/aldrindieldrin2003.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

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

**New York State Department of Health**  
**Oral Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA Region 3 (2003)</li> <li>◆ US EPA OPP (1997)</li> <li>◆ CA EPA (2004)</li> </ul>	5.8 x 10 <sup>-8</sup>	17	linearized multistage model, extra risk	body surface area <sup>2</sup>	Chronic dietary studies showed aldrin increased the incidence of liver tumors in both sexes of three strains of mice. There was no sex or strain effect. The cancer potency factor is the geometric mean of three separate cancer potency factors; each derived from a different dose response dataset.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

**2. Recommendation and Rationale**

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

**3. Review Dates**

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

#### 4. References for Summary Table

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

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: 03/22/87. 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: Aldrin**  
**Exposure Route: Inhalation**  
**Toxicity: Non-Cancer**

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

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

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

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

**2. Recommendation and Rationale**

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

**3. Review Dates**

Summary table completion: February, 2005  
 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: Aldrin**  
**Exposure Route: Inhalation**  
**Toxicity: Cancer**

**New York State Department of Health  
 Inhalation Cancer Toxicity Value Documentation**

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

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

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

**2. Recommendation and Rationale**

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

**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: Anthracene**  
**Exposure Route: Oral**  
**Toxicity: Non-Cancer**

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

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

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>♦ US EPA Region 3 (2003)</li> <li>♦ US EPA ODW (2002)</li> <li>♦ US EPA HEAST (1997)</li> </ul>	0.3	1,000	NOEL	3000	Based on a lack of treatment-related effects in male and female mice in a 90-day gavage study. The NOEL was assigned to the highest dose tested.
RIVM (2001)	0.04	NA	NA	NA	Based on RIVM's evaluation of total petroleum hydrocarbons and its designation of anthracene as a non-carcinogenic aromatic containing 9 to 16 carbons.

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

**2. Recommendation and Rationale**

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

**3. Review Dates**

Summary table completion: February, 2004  
Toxicity value recommendation: March, 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 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 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: Anthracene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

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

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

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

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

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

**3. Review Dates**

Summary table completion: March, 2004  
Toxicity value recommendation: March, 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: 01/01/91.  
<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: Anthracene**  
**Exposure Route: Inhalation**  
**Toxicity: Non-Cancer**

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

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

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

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

**2. Recommendation and Rationale**

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

**3. Review Dates**

Summary table completion: February, 2005  
 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: Anthracene**  
**Exposure Route: Inhalation**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Inhalation Cancer Toxicity Value Documentation**

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

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for anthracene is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005  
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: Arsenic**  
**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 Arsenic**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA HEAST (1997)</li> <li>◆ US EPA ODW (2002)</li> <li>◆ US EPA Region 3 (2003)</li> </ul>	$3 \times 10^{-4}$	$8 \times 10^{-4}$	NOEL	3	Based on hyperpigmentation, keratosis and possible vascular complications from chronic drinking water exposure to humans. The NOEL was based on an arithmetic mean of a range of arsenic concentrations and also includes an estimation of arsenic exposure from food intake. The NOEL of 0.009mg/L and LOEL of 0.17 mg/L (reported in a later study of the same cohort by the same investigators) were adjusted to 0.0008 mg/kg/day and 0.014 mg/kg/day, respectively, assuming 4.5L water consumed per day and 55 kg human body weight.
ATSDR (2000)	$3 \times 10^{-4}$	$8 \times 10^{-4}$	NOEL	3	Based on same study and analysis as US EPA IRIS (2004).
RIVM (2001)	0.001	$2.1 \times 10^{-3}$	NOEL	2	Based on critical effects on the skin in humans and derived from the World Health Organization PTWI <sup>2</sup> for arsenic of 0.015 mg/kg/week for adults of 70 kg of body weight. The daily equivalent (0.0021 mg/kg/d) was considered a NOEL by the Health Council of the Netherlands.

<sup>1</sup>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.

<sup>2</sup>PTWI: provisional maximum tolerable weekly intake

## 2. Recommendation and Rationale

The basis for the two reference doses for arsenic is skin effects in human populations chronically exposed to elevated arsenic in drinking water. There is limited documentation of the specific data providing the basis of the RIVM reference dose, and RIVM chose to apply an uncertainty factor of 2 to the NOEL point-of-departure, while US EPA and ATSDR applied an uncertainty factor of 3. The US EPA notes that an uncertainty factor of 3 accounts for the lack of data addressing reproductive toxicity as well as human intraspecies variability. An uncertainty factor of 3 is considered more consistent with accepted risk assessment practices of United States health agencies. Therefore, the US EPA reference dose ( $3 \times 10^{-4}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for arsenic.

## 3. Review Dates

Summary table completion: April, 2004

Toxicity value recommendation: June, 2004

## 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2000. Toxicological profile for arsenic. 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.

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: 11/15/90. Last revised: 02/01/93.  
<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

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

**New York State Department of Health**  
**Oral Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA Region 3 (2003)</li> <li>◆ US EPA HEAST (1997)</li> <li>◆ ATSDR (2000)</li> <li>◆ CA EPA (2002)</li> </ul>	6.7 x 10 <sup>-7</sup>	1.5	linearized multistage model (time and dose related formulation)	--	Estimated from the increased incidence of skin cancer observed in Taiwanese populations consuming drinking water with elevated levels of inorganic arsenic.
Health Canada (1993) (see also TERA, 2004)	3.6 x 10 <sup>-7</sup>	-- <sup>2</sup>	linear extrap. from TD <sub>05</sub> <sup>2</sup>	--	Based on same data as US EPA IRIS (2004), incorporating background rates of skin cancer for Canadians.
Health Canada (1989)	8.0 x 10 <sup>-7</sup>	-- <sup>3</sup>	linearized multistage model (time and dose related formulation)	--	Based on same data and model as US EPA IRIS (2004), taking into account incidence stratified by age group and greater drinking water ingestion rates among Taiwanese compared to North Americans.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where



$1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>No cancer potency factor was derived. The risk specific dose was obtained by linear extrapolation from the modeled TD<sub>05</sub> (= 0.84 mg/L in drinking water, assuming 1.5 L/d water consumption and 70 kg adult body weight), the dose associated with a 5% increase in mean tumor incidence (not a lower-bound estimate; TERA, 2004)

<sup>4</sup>No cancer potency factor was derived. The risk specific dose was obtained from the drinking water unit risk of  $3.6 \times 10^{-5}$  per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day.

## 2. Recommendation and Rationale

The US EPA and Health Canada cancer potency factors are based on increased incidence of skin tumors among Taiwanese populations consuming drinking water containing elevated levels of inorganic arsenic. Documentation on the specific methods and assumptions used to derive the Health Canada (1989) estimates of potency is limited. Both agencies used a time and dose-related formulation of the multistage model, but differed in assumptions regarding background skin cancer rates. The US EPA value is based on the upper-bound estimate of the modeled dose-response slope at low doses, while the Health Canada (1993) value is a linear extrapolation to the low dose region from a maximum likelihood estimate of the dose at 5% incremental risk. Although the difference between the two values is relatively small, the use of Canadian background skin cancer rates may be less appropriate than those assumed for the US population. The US EPA low-dose extrapolation methodology is also more consistent with current risk assessment practice in that it estimates a lower-bound on the dose at one in one-million risk, while the Health Canada (1993) extrapolation uses a central tendency (maximum likelihood) estimate. Therefore, the US EPA cancer potency factor (1.5 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for arsenic. The arsenic risk specific dose calculated from this toxicity value is  $6.7 \times 10^{-7}$  mg/kg/day.

## 3. Review Dates

Summary table completion: April, 2004

Toxicity value recommendation: June, 2004

## 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2000. Toxicological Profile for Arsenic. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

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

Health Canada. 1989. 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. 1993. Priority Substances List Assessment Report: Arsenic and its Compounds. Ottawa: Environment Canada, Ministry of Public Works and Government Services.  
<http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm>

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. 9200.6-303 997-1).

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: 02/03/94. Last revised: 04/10/98.  
<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

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

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

**1. Summary of Available Inhalation Reference Concentrations for Inorganic Arsenic**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
CA EPA (2000)	0.03	33	LOEL	1,000	Based on a reduction in fetal weight and increased incidence of intrauterine growth retardation and skeletal malformations in mice exposed to arsenic trioxide for 4 hours per day on gestational days 9-12.
RIVM (2001)	1.0	10	LOEL	10	RIVM decided the most critical effect after chronic inhalation exposure of humans is lung cancer. Study LOEL = 10 mcg/m <sup>3</sup> , based on the incidence of lung cancer in smelter workers.

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

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

**2. Recommendation and Rationale**

The reference concentrations for arsenic derived by authoritative bodies from the list in item 5 (below) are based on developmental effects in mice exposed to arsenic trioxide during gestation and lung cancer among workers exposed to arsenic from smelters. The RIVM value is based on a carcinogenic endpoint, which is not relevant in the current context since cancer and non-cancer endpoints are being evaluated separately. Therefore, the CA EPA reference concentration (0.03 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for arsenic.

**3. Review Dates**

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

#### 4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2000. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Arsenic and Arsenic Compounds. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency.  
[http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](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

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

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2004)	2.3 x 10 <sup>-4</sup>	4.3 x 10 <sup>-3</sup>	Absolute-risk linear model	--	Based on the incidence of lung cancer in males occupationally exposed to arsenic at two different smelters. A geometric mean was estimated for each smelter cohort from 2 or 3 calculated unit risks. The final estimate is the geometric mean of these two values. The increase in age-specific lung cancer mortality rate was assumed to be a function only of cumulative exposure.
CA EPA (2002)	3.0 x 10 <sup>-4</sup>	3.3 x 10 <sup>-3</sup>	Relative risk model	--	Based on lung tumor incidence from human occupational exposure (one of the cohorts used in US EPA IRIS (2004)) and adjusted for interaction with tobacco smoking.
Health Canada (1992)	7.8 reported as TC <sub>05</sub> <sup>2</sup> ; linear equivalent risk specific concentration = 1.6 x 10 <sup>-4</sup>	-- <sup>3</sup>	--	--	Estimated from the standardized mortality ratios for respiratory cancer from one of the same study cohorts as US EPA IRIS (2004).

WHO (2000)	$6.6 \times 10^{-4}$	$1.5 \times 10^{-3}$	Linearized multistage model	--	WHO reviewed available literature of the incidence of lung cancer in smelter workers and decided that a safe level for inhalation exposure cannot be recommended. At an air concentration of $1 \text{ mcg/m}^3$ , an estimate of lifetime risk is $1.5 \times 10^{-3}$ (based on pooling several unit risk estimates from the cohorts used by US EPA as well as an additional cohort).
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<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6} \text{ dose} = 1 \times 10^{-6} / \text{cancer potency factor}$ .

<sup>2</sup>TC<sub>05</sub> = The concentration in air (expressed in  $\text{mcg/m}^3$ ) associated with a 5% increase in incidence or mortality due to tumors.

<sup>3</sup>The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported, but would be equal to  $1 \times 10^{-6}$  divided by the  $10^{-6}$  risk-specific concentration.

## 2. Recommendation and Rationale

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

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

[http://www.oehha.ca.gov/air/cancer\\_guide/TSD2.html](http://www.oehha.ca.gov/air/cancer_guide/TSD2.html)

Health Canada. 1992. Priority Substances List Assessment Report: Arsenic and its compounds: 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: 02/03/1994. Last revised: 04/10/1998.

<http://www.epa.gov/iris/subst/>

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 (2<sup>nd</sup> Ed.), Chapter 6.1, Arsenic. World Health Organization, Copenhagen, Denmark.

[http://www.euro.who.int/air/activities/20050223\\_4](http://www.euro.who.int/air/activities/20050223_4)

## **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: Barium**  
**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 Barium**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA Region 3 (2004)</li> <li>◆ US EPA ODW (2004)</li> <li>◆ US EPA HEAST (1997)</li> </ul>	0.07	0.21	NOEL	3	The NOEL is based on the absence of blood pressure-related effects in epidemiological and experimental studies in humans. Evidence from animal studies suggests that the kidney is the toxic endpoint. Kidney effects were not investigated in human studies; however the NOEL from human studies is lower than in animal studies, and is thought to be more appropriate for derivation of a reference dose.
CA EPA (2003)	0.07	0.2	NOEL	3	Based on the same study used by US EPA (2004).
WHO (2001)	0.02	0.2	NOEL	10	Based on the same study used by US EPA (2004).
RIVM (2001)	0.02	0.2	NOEL	10	Based on the same study used by US EPA (2004).
Health Canada (1990)	0.02 <sup>2</sup>	0.2 <sup>2</sup>	NOEL	10	Based on the same study used by US EPA (2004).



<sup>1</sup>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.

<sup>2</sup>A reference dose was not derived. The point of departure and the reference dose were derived from water concentrations assuming a 70 kg person drinks 2 liters of water per day.

## 2. Recommendation and Rationale

The basis for the various reference doses for barium is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (0.2 mg/kg/day). The point of departure is based on epidemiological and experimental studies of hypertension in humans related to barium exposure. The US EPA IRIS and CA EPA chose to apply a 3-fold total uncertainty factor to this human NOEL to account for additional intraspecies variability beyond that already represented by the population-based epidemiological study in adults, including possible increased sensitivity in children. The WHO and Health Canada applied a default 10-fold uncertainty factor to account for intraspecies variability, and although a detailed justification is not available, the RIVM 10-fold uncertainty factor also appears to represent the default value. The epidemiological study on which all the reference doses are based was a population-based study of over 2000 men and women aged 18 – 75+ who had lived in the community for more than 10 years, and the US EPA concluded that this group was likely to include sensitive subgroups such as persons with low dietary calcium intake and persons unusually sensitive to barium toxicity. They also concluded that some study participants were likely to have had elevated barium exposure as children, when, based on animal data, absorption of ingested barium may be increased compared to adults. However, no data are presented to support these suppositions. The human experimental study used by US EPA IRIS as another basis of their reference dose was conducted with male volunteers with a mean age of 39.5 years, and so is less likely to represent human variability in sensitivity than the population-based study. Given the uncertainty in the degree to which the human studies reflected responses of sensitive subpopulations to barium toxicity, a full 10-fold uncertainty factor for intraspecies variability is chosen. Therefore, the WHO 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 inorganic barium.

## 3. Review Dates

Summary table completion: August, 2004

Toxicity value recommendation: September, 2004

## 4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2003. Public Health Goal for Barium 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. 1990. 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>

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: 2/18/1998. Last revised: 3/30/98.  
<http://www.epa.gov/iris/subst/0408.htm>.

RIVM. 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 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). 2001. Concise International Chemical Assessment Document 33: Barium and Barium Compounds. World Health Organization, Geneva.  
<http://whqlibdoc.who.int/publications/2001/9241530332.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  
Division of Drinking Water and Environmental Management  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

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

**New York State Department of Health**  
**Oral Cancer Toxicity Value Documentation**

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

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

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

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

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

**3. Review Dates**

Summary table completion: August, 2004  
 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: 2/18/1998. Last revised: 3/30/1998.  
<http://www.epa.gov/iris/subst/0408.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  
Division of Drinking Water and Environmental Management  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

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

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

**1. Summary of Available Inhalation Reference Concentrations for Inorganic Barium**

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

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

<sup>2</sup>US EPA HEAST (1997) lists 800 mcg/m<sup>3</sup> as an experimental NOEL but provides no detail on the derivation of the assumed point of departure as implied by the reference concentration and the value of the uncertainty factor.

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

**2. Recommendation and Rationale**

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

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

### **3. Review Dates**

Summary table completion: November, 2004

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.

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: Barium**  
**Exposure Route: Inhalation**  
**Toxicity: Cancer**

**New York State Department of Health  
 Inhalation Cancer Toxicity Value Documentation**

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

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

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An inhalation unit risk for barium is not available.\*

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

**3. Review Dates**

Summary table completion: November, 2004  
 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: 2/18/1998. Last revised: 3/30/1998.  
<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  
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: Benz[a]anthracene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

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

Agency	Reference Dose <sup>1</sup> (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.

<sup>1</sup>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 benz[a]anthracene 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 benz[a]anthracene with respect to noncancer endpoints. The basis for choosing pyrene as a chemical surrogate for benz[a]anthracene 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 benz[a]anthracene (see Oral Non-Cancer Toxicity Value Documentation for pyrene).

**3. Review Dates**

Summary table completion: February, 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

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**Chemical Name: Benz[a]anthracene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA OSRTI (2004) US EPA Region 3 (2003)	1.37 x 10 <sup>-6</sup>	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.
US EPA IRIS (2004) ATSDR (1995)	--	--	--	--	Human data are not available. Benz[a]anthracene produced tumors in mice exposed dermally, orally by gavage, and by injection, but a potency factor was not derived.
CA EPA (2002)	8.3 x 10 <sup>-7</sup>	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)	$5.0 \times 10^{-5}$	-- <sup>3</sup>	--	--	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).
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<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>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 benz[a]anthracene 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 benz[a]anthracene (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The benz[a]anthracene risk specific dose calculated from this toxicity value is  $1.1 \times 10^{-6}$  mg/kg/day.

## 3. Review Dates

Summary table completion: February, 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

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**Chemical Name: Benz[a]anthracene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

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

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

<sup>1</sup>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 benz[a]anthracene is not available from the authoritative bodies listed in item number 5 (below). Benz[a]anthracene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure and for which an oral reference dose 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<sup>3</sup> 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<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benz[a]anthracene.

**3. Review Dates**

Summary table completion: February, 2005

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: Benz[a]anthracene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2002)	9.1 x 10 <sup>-3</sup>	1.1 x 10 <sup>-4</sup>	--	--	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 benz[a]anthracene is based on its ability (relative to benzo[a]pyrene) to induce lung adenomas via intraperitoneal administration in newborn mice.
--	9.1 x 10 <sup>-3</sup>	1.1 x 10 <sup>-4</sup>	--	--	Based on the CA EPA unit risk for benzo[a]pyrene and application of the recommended relative potency factor of 0.1.

<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> air concentration), where 1 x 10<sup>-6</sup> concentration = 1 x 10<sup>-6</sup> / inhalation unit risk.

**2. Recommendation and Rationale**

The unit risk values for benz[a]anthracene are based on benzo(a)pyrene and the application of relative potency factors. The recommended unit risk value for benzo(a)pyrene is 1.1 x 10<sup>-3</sup> per mcg/m<sup>3</sup> (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 x 10<sup>-4</sup> per mcg/m<sup>3</sup>, which is the



toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for benz[a]anthracene (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The benz[a]anthracene risk specific air concentration calculated from this toxicity value is  $9.1 \times 10^{-3}$  mcg/m<sup>3</sup>.

### 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](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: Benzene**  
**Exposure Route: Oral**  
**Toxicity: Non-Cancer**

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

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

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA Region 3 (2003)</li> <li>◆ US EPA ODW (2004)</li> </ul>	$4 \times 10^{-3}$	1.2	BMDL	300	Based on route-to-route extrapolation of the results of benchmark dose modeling of decreased lymphocyte counts in male and female workers exposed by inhalation for an average of 6.4 years. Study LOEL = 1.2 mg/kg/day.
NYS DEC (1997)	$7.1 \times 10^{-4}$	0.71	NOEL	1000	Based on hematological effects (leukopenia and erythrocytopenia ) in female rats in a six month gavage study. Study LOEL = 35.7 mg/kg/day.

<sup>1</sup>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 NYS DEC derived its reference dose based on hematological effects in a subchronic gavage study in rats, while the US EPA derived a reference dose base on route-to-route extrapolation of air concentrations resulting in blood changes in humans exposed by inhalation in the workplace. The US EPA derivation uses benchmark dose modeling that is consistent with current risk assessment practice. In addition, the US EPA value is based on human data, which is often chosen over animal data, even if the animal data are route specific. Therefore the US EPA reference dose ( $4 \times 10^{-3}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer soil cleanup objective for benzene.

### 3. Review Dates

Summary table completion: March, 2004  
Toxicity value recommendation: April, 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 Benzene. 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: 01/23/02. Last revised: 04/17/03.  
<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: Benzene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2003)	1.8 x 10 <sup>-5</sup>	0.055	linear extrapolation model	--	Benzene is a known human carcinogen based on epidemiology studies that provide clear evidence of a causal association between benzene exposure in the workplace and acute nonlymphocytic leukemia. The cancer potency factor is based on the inhalation unit risk derived from a study of occupationally exposed workers, assuming an inhalation absorption factor of 50% compared to ingestion.
NYS DEC (1997)	3.4 x 10 <sup>-5</sup>	0.029	various	--	The cancer potency factor is derived from the geometric mean of maximum likelihood estimates of cancer potency from two epidemiology studies
CA EPA (2004)	1 x 10 <sup>-5</sup>	0.1	weighted cumulative dose relative risk model	--	Based on same study as the US EPA IRIS value, but using a different model for high to low dose extrapolation. Value derived in 1988.

Health Canada (1986)	4.3 x 10 <sup>-6</sup> to 4.7 x 10 <sup>-5</sup>	-- <sup>2</sup>	linearized multistage model	body surface area <sup>3</sup>	Two potency estimates were derived based on 1) leukemia and lymphoma in female mice exposed for two years by gavage and 2) oral cavity squamous cell carcinomas in male rats exposed for two years by gavage.
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<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>No cancer potency factor was derived. The range of risk specific doses was obtained from the drinking water unit risks of 6.1 x 10<sup>-7</sup> to 6.7 x 10<sup>-6</sup> per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day.

<sup>3</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

## 2. Recommendation and Rationale

The various cancer potency factors for benzene are all based on the increased incidence of leukemia in occupationally exposed workers breathing benzene, with the exception of the Health Canada value, which is based on two different carcinogenic endpoints from animal studies exposed via oral gavage. Route-specific toxicity estimates from animal data would generally be chosen over estimates based on route extrapolation from animal data. However, when potency estimates based on adequate data from human studies are available, these may be chosen over estimates based on route-specific animal data, unless there is information to suggest that route-to-route extrapolation is not scientifically valid. The human data for benzene is therefore chosen over the route specific animal data to estimate cancer potency. Of the estimates based on human data, the US EPA IRIS cancer potency factor (0.055 per mg/kg/day) is based on more current and generally accepted risk assessment methods, and is therefore the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for benzene. The benzene risk-specific dose calculated from this toxicity value is 1.8 x 10<sup>-5</sup>.

## 3. Review Dates

Summary table completion: May, 2004

Toxicity value recommendation: May, 2004

## 4. References for Summary Table

CA EPA (California Environmental Protection Agency). Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. Cancer Potency Values. Technical Support Document for Describing Available Cancer Potency Factors. 2002.

<http://www.oehha.org/water/phg/pdf/BenzeneFinPHG.pdf>

Health Canada. 1986. 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>

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined

Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Benzene. Albany, NY: Division of Water.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency consensus date: 01/3/2000. Last revised: 04/17/2003.  
<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: Benzene**  
**Exposure Route: Inhalation**  
**Toxicity: Non-Cancer**

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

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

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2003)	30	8.2 x 10 <sup>3</sup>	BMCL <sup>2</sup>	300	Based on decreased lymphocyte count in a human occupational study where exposure duration ranged from 0.7 to 16 years (mean = 6.3 years).
CA EPA (2004)	60	600	NOEL	10	Based on the absence of hematological effects in 303 male refinery workers occupationally exposed to benzene for 1-21 years (mean = 7.4 years).

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

<sup>2</sup>BMCL: 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). For the continuous endpoint, a default assumption was used that a modeled response of one standard deviation change from the control mean is approximately equivalent to a 10% increased risk.

**2. Recommendation and Rationale**

The two reference concentrations for benzene derived by authoritative bodies from the list in item 5 (below) are both based on hematological effects in studies of workers exposed to benzene. The US EPA estimated a lower bound on a benchmark concentration associated with 10% incremental increased risk for reduced lymphocyte count, while the CA EPA derived their point of departure based on an average exposure concentration that was without hematological effects in a different occupational study. The US EPA applied a total uncertainty factor of 300, including 10-fold to account for intraspecies variability, and 3-fold each to account for the use of a subchronic study, the use of a benchmark dose that US EPA considered equivalent to a marginal LOEL and database deficiencies including the lack of a 2-generation reproductive and a developmental study. The CA EPA applied a total uncertainty factor of 10 to account for intraspecies variability. They considered the study duration to be chronic since about one-third of the cohort had more than 10 years exposure. The US EPA derivation, which uses the benchmark dose methodology, is more consistent with currently-accepted risk assessment practice. Therefore the US EPA reference concentration (30 mcg/m<sup>3</sup>) is the toxicity

value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benzene.

### 3. Review Dates

Summary table completion: May, 2004

Toxicity value recommendation: October, 2004

### 4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2004. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Benzene. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency.  
[http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](http://www.oehha.ca.gov/air/chronic_rels/AllChrels.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: 01/23/2002. Last revised: 04/17/2003.  
<http://www.epa.gov/iris/subst/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: Benzene**  
**Exposure Route: Inhalation**  
**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2003)	0.13 to 0.45	2.2 x 10 <sup>-6</sup> to 7.8 x 10 <sup>-6</sup>	low-dose linearity; the unit risks are maximum likelihood estimates rather than upper bound estimates	--	Based on the incidence of leukemia in several studies following a cohort of workers occupationally exposed to benzene and considering several analyses estimating benzene exposure in this cohort.
CA EPA (2002)	0.03	2.9 x 10 <sup>-5</sup>	linear non-threshold model for human data; linearized multistage model for animal data	--	Based on a value recommended from a range of assessments based on human epidemiological data (including the same data used by US EPA IRIS) and oral and inhalation animal bioassay data. The selected value is an upper bound estimate from human epidemiologic data and was recommended for the Proposition 65 program in 1988.
CA EPA (2004)	0.065	-- <sup>3</sup>	--	--	Updated risk-specific inhalation intake for the Proposition 65 program. Details of derivation are not available.

WHO (2000)	0.17	$6.0 \times 10^{-6}$	Multiplicative risk model, cumulative exposure	--	The geometric mean of the range of estimates from two occupational studies (of the same cohort as US EPA IRIS (2004)) of the excess lifetime risk of leukemia at an air concentration of $1 \mu\text{g}/\text{m}^3$ .
Health Canada (1991)	$1.5 \times 10^{+4}$ reported as a $\text{TC}_{05}^2$ ; linear equivalent risk specific concentration = 0.3	--	--	--	Based on one of the studies reviewed in US EPA IRIS (2004). The Health Canada $\text{TC}_{05}^2$ estimate was based on one cohort in which the observed and expected numbers of deaths due to leukemia were small and for which there were few actual measurements of concentrations of benzene in the workplace.
RIVM (2001)	0.2	-- <sup>3</sup>	--	--	Based on direct adoption of the lower end of the range of risk-specific concentrations developed by the EU Working Group evaluation for ambient air. This value is also the WHO risk-specific concentration rounded to one significant digit. Limited derivation information available.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>  $\text{TC}_{05}$  = The concentration in air (expressed in  $\text{mcg}/\text{m}^3$ ) associated with a 5% increase in incidence or mortality due to tumors. The  $\text{TC}_{05}$  represents a maximum likelihood estimate rather than a lower-bound estimate.

<sup>3</sup> The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported, but would be equal to  $1 \times 10^{-6}$  divided by the  $10^{-6}$  risk-specific concentration.

## 2. Recommendation and Rationale

The unit risks and/or risk-specific concentrations derived by authoritative bodies are largely based on the increased incidence of leukemia in human occupational exposure studies. One of the CA EPA derivations also included risk-specific concentrations based on increased incidence of tumors at several anatomical sites (including leukemias) in mice and rats exposed orally or by inhalation. All of the analyses apply some form of linear-low dose extrapolation model to the epidemiological data, assuming a non-threshold mode of action for the cancers observed in the occupational cohort. A range of unit risk estimates results from the exact form of the extrapolation model used and assumptions used to estimate exposure in the occupational cohort. The CA EPA (2002) represents an upper-bound unit risk estimate of the same analysis used by US EPA IRIS where unit risks were reported as maximum

likelihood estimates rather than upper bounds. That CA EPA value was recommended as the unit risk for the California Proposition 65 program in 1988, but a subsequent update of the Proposition 65 (CA EPA, 2004) values reports a risk-specific air concentration that is roughly two-fold higher, without any supporting details documenting the basis of the revision. The WHO value is a geometric mean of a range of unit risks based on the same analyses used by US EPA IRIS. The RIVM risk-specific concentration was selected from the lower end of a range of risk-specific concentration values derived by the EU Working Group – that value is the WHO risk-specific concentration rounded to one significant figure – but details of their derivation are not available. Health Canada's value is a TC<sub>05</sub> maximum likelihood value, that if extrapolated linearly to 1 x 10<sup>-6</sup> lifetime risk would also be in the range reported by US EPA IRIS. Although CA EPA (2002) documents a range of risk estimates similar to that reported by US EPA IRIS, the basis of the specific recommended unit risk value chosen in that document and of the subsequent revised value (CA EPA, 2004) is not clearly documented. The upper end of the US EPA IRIS unit risk range is close to the CA EPA values and its derivation is more transparent. Therefore, the upper end of the US EPA IRIS unit risk range (7.8 x 10<sup>-6</sup> per mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for benzene. The benzene risk specific air concentration calculated from this toxicity value is 0.13 mcg/m<sup>3</sup>.

### 3. Review Dates

Summary table completion: May, 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](http://www.oehha.ca.gov/air/cancer_guide/TSD2.html)

CA EPA (California Environmental Protection Agency). 2004. 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 Assessment Section. Office of Environmental Health Hazard Assessment.

<http://www.oehha.ca.gov/prop65/pdf/June2004StatusRpt.pdf>

Health Canada. 2000. Priority Substances List Assessment Report: Benzene. 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. Agency consensus date: 9/30/1998. Last revised: 01/19/2000

<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. 2004.  
<http://www.epa.gov/reg3hwmd/risk/human/index.htm>

WHO (World Health Organization). 2000. Air Quality Guidelines (2nd Ed.), Chapter 5.2, Benzene. World Health Organization, Copenhagen, Denmark.  
[http://www.euro.who.int/air/activities/20050223\\_4](http://www.euro.who.int/air/activities/20050223_4)

## **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: Benzo[a]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 Benzo[a]pyrene (CAS Number 50-32-8)**

Agency	Reference Dose <sup>1</sup> (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.

<sup>1</sup>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 benzo[a]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 benzo[a]pyrene with respect to noncancer endpoints. The basis for choosing pyrene as a chemical surrogate for benzo[a]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 benzo[a]pyrene (see Oral Non-Cancer Toxicity Value Documentation for pyrene).

**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). 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

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**Chemical Name: Benzo[a]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 Benzo[a]pyrene (CAS Number 50-32-8)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2003)	1.4 x 10 <sup>-7</sup>	7.3	Three different modeling procedures were applied to the mouse data; a fourth procedure was applied to the rat data	body surface area <sup>2</sup> used in at least one case	Based on increased incidence of squamous cell papillomas and carcinomas of the forestomach in mice and of the forestomach, larynx and esophagus in rats. Cancer potency factor based on a geometric mean of four slope factors obtained by differing modeling procedures.
RIVM (2001)	5.0 x 10 <sup>-6</sup>	-- <sup>3</sup>	linear extrap. from the TD <sub>LO</sub> <sup>4</sup>	body weight	Based on tumor development in a variety of organs and tissues in an oral (gavage) rat study (limited methodology information available).
CA EPA (2002)	8.3 x 10 <sup>-8</sup>	12	linearized multistage model, extra risk	not specified, but parallel inhalation analysis used body surface area <sup>2</sup> scaling	Based on the same mouse study as in US EPA IRIS, but using only 1 form of extrapolation model.

CA EPA (1997)	1.1 x 10 <sup>-7</sup> -- 1.1 x 10 <sup>-7</sup>	9.5 -- 9.03	linearized multistage model, extra risk  --  linear extrap. from LED <sub>10</sub> <sup>5</sup>	BW <sup>¾</sup> 6	Based on same mouse study as used by US EPA IRIS and CA EPA (2002) for development of drinking water public health goal.
Health Canada (1986)	5.7 x 10 <sup>-7</sup>	-- <sup>7</sup>	linearized multistage model	body surface area <sup>2</sup>	Based on increased incidence of forestomach tumors in a long term feeding study in mice (same as one of the studies used by US EPA IRIS)

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>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.

<sup>4</sup>TD<sub>LO</sub> = The lowest experimental dose that produces a significant increase in tumor incidence above background incidence.

<sup>5</sup>LED<sub>10</sub> = The 95% lower confidence limit of the dose that produces a 10% increase in tumor incidence.

<sup>6</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.25</sup>.

<sup>7</sup>No cancer potency factor was derived. The risk specific dose was obtained from the drinking water unit risk of 5 x 10<sup>-5</sup> per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day.

## 2. Recommendation and Rationale

All the cancer potency factors derived by the US EPA, CA EPA and Health Canada are based on forestomach tumors in mice and rats, with the exception that one of the studies included in the US EPA derivation also showed increased incidence of tumors in the larynx and esophagus. The study used by RIVM reported increased forestomach and liver tumor incidence, but also observed tumors in several other tissues. RIVM's derivation procedure does not produce a lower-bound estimate on the risk-specific dose and is not consistent with currently accepted risk assessment practice for interspecies dose scaling from animals to humans. The one US EPA IRIS and the three CA EPA cancer potency factors are all within less than 2-fold of each other, and the potency factor corresponding to the Health Canada drinking water unit risk is somewhat lower than these values. However, the CA EPA drinking water derivation that uses a linear extrapolation from the LED<sub>10</sub> and BW<sup>¾</sup> dose scaling is more consistent with current risk assessment practice than the other CA EPA derivation or the US EPA and Health Canada derivations. Therefore, the CA EPA (1997) cancer potency factor (9.03 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for benzo[a]pyrene. The benzo[a]pyrene risk specific dose calculated from this toxicity value is 1.1 x 10<sup>-7</sup> mg/kg/day.



### 3. Review Dates

Summary table completion: April, 2004

Toxicity value recommendation: September, 2004

### 4. References for Summary Table

CA EPA (California Environmental Protection Agency). 1997. Public Health Goal for Benzo(a)pyrene in drinking water. Sacramento, CA: Office of Environmental Health Hazard Assessment.  
<http://www.oehha.ca.gov/water/phg/allphgs.html>

CA EPA (California Environmental Protection Agency). 2002. Technical Support Document for Describing Available Cancer Potency Factors, December. Sacramento, CA: Office of Environmental Health Hazard Assessment, Air Toxicology and Epidemiology Section.  
[http://www.oehha.ca.gov/air/cancer\\_guide/TSD2.html](http://www.oehha.ca.gov/air/cancer_guide/TSD2.html)

Health Canada. 1986. 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 IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 12/04/1991. Last revised: 11/01/1994.  
<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      A-89 Hazard Assessment

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

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**Chemical Name: Benzo[a]pyrene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

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

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

<sup>1</sup>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 benzo[a]pyrene is not available from the authoritative bodies listed in item number 5 (below). Benzo[a]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<sup>3</sup> 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<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benzo[a]pyrene.

**3. Review Dates**

Summary table completion: February, 2005  
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: Benzo[a]pyrene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
WHO (2002)	1.12 x 10 <sup>-5</sup>	8.7 x 10 <sup>-2</sup>	Linearized multistage model, extra risk	--	Based on the increased incidence of lung cancer in workers exposed to coke-oven emissions, assuming the benzo(a)pyrene content of coke oven emissions is 0.71%.
Health Canada (1994) (see also TERA, 2004)	1.6 x 10 <sup>3</sup> reported as TC <sub>05</sub> <sup>2</sup> ; linear equivalent risk specific concentration = 0.032	-- <sup>3</sup>	Linearized multistage model, extra risk	not specified	Based the increased incidence of respiratory tract tumors in hamsters exposed by inhalation for 4.5 hours per week, for 7 days a week for the first 10 weeks, then 3 hours per day for the remaining 96 weeks.
CA EPA (2002)	9.1 x 10 <sup>-4</sup>	1.1 x 10 <sup>-3</sup>	Linearized multistage model, extra risk	body surface area <sup>4</sup>	Based on the same inhalation study used by Health Canada (1994)
NYS DOH (1990)	1.7 x 10 <sup>-3</sup>	6 x 10 <sup>-4</sup>	Linearized multistage model, extra risk	body surface area <sup>4</sup>	Based digestive tract and respiratory tract tumors in hamsters in the same inhalation study used by Health Canada (1994).
US EPA Region 3 (2004)	1.1 x 10 <sup>-3</sup>	8.8 x 10 <sup>-4</sup>	Linearized multistage model	body surface area <sup>4</sup>	Based on the same inhalation study used by Health Canada (1994).

<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> air concentration), where 1 x 10<sup>-6</sup> concentration = 1 x 10<sup>-6</sup> / inhalation unit risk.

<sup>2</sup> TC<sub>05</sub> = The concentration in air (expressed in mcg/m<sup>3</sup>) associated with a 5% increase in incidence or mortality due to tumors.

<sup>3</sup>No cancer potency factor was derived. The risk specific air concentration was obtained by linear extrapolation from the modeled TC<sub>05</sub> (TERA, 2004).

<sup>4</sup>Factor for dose adjustment from animal to human is (human body weight/animal body weight)<sup>0.33</sup>.

## 2. Recommendation and Rationale

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

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

Health Canada, CA EPA, NYS DOH and the US EPA base their values on the same inhalation study in hamsters. Health Canada derived a TC<sub>05</sub>, which cannot be directly compared to the other estimates because it represents the maximum likelihood estimate on the risk-specific air concentration rather than a 95% lower bound.

The unit risk estimates derived by the CA EPA, NYS DOH and US EPA all use body surface area to scale the doses from animals to humans. The CA EPA and NYS DOH derivations omit results from the highest exposure group due to a high incidence of mortality. The US EPA derivation fitted the linearized multistage model to the incidence data for malignant pharyngeal and laryngeal tumors only, and included the highest exposure group. However, benign and malignant tumors are usually combined in current risk assessment practice to account for the possibility that benign tumors may progress to become malignant.

The CA EPA and NYS DOH unit risk values are numerically similar. The CA EPA and NYS DOH derivations differ from one another in that the CA EPA used a lower hamster inhalation rate for calculating the hamster inhaled dose that was based on a more up-to-date allometric equation for estimating animal inhalation rates from body weight. Therefore the CA EPA unit risk ( $1.1 \times 10^{-3}$  per mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for benzo[a]pyrene. The benzo[a]pyrene risk specific air concentration calculated from this toxicity value is  $9.1 \times 10^{-4}$  mcg/m<sup>3</sup>.

## 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. Technical Support Document for Describing Available Cancer Potency Factors. Sacramento, CA: Office of Environmental Health Hazard Assessment, Air Toxicology and Epidemiology Section.

[http://www.oehha.ca.gov/air/cancer\\_guide/TSD2.html](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>

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

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, 2<sup>nd</sup> Ed. WHO Regional Office for Europe, Copenhagen.  
[http://www.euro.who.int/air/activities/20050223\\_4?language=French](http://www.euro.who.int/air/activities/20050223_4?language=French)

## **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: Benzo[b]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 Benzo[b]fluoranthene (CAS Number 205-99-2)**

Agency	Reference Dose <sup>1</sup> (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.

<sup>1</sup>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 benzo[b]fluoranthene 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 benzo[b]fluoranthene with respect to noncancer endpoints. The basis for choosing pyrene as a chemical surrogate for benzo[b]fluoranthene 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 benzo[b]fluoranthene (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: Benzo[b]fluoranthene**  
**Exposure Route: Oral**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Oral Toxicity Value Documentation**

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

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA OSRTI (2004) US EPA Region 3 (2003)	1.37 x 10 <sup>-6</sup>	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. Benzo[b]fluoranthene produced tumors in mice after lung implantation, intraperitoneal or subcutaneous injection, and skin painting.

CA EPA (2002)	$8.33 \times 10^{-7}$	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)	$5.0 \times 10^{-5}$	-- <sup>2</sup>	--	--	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).

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>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 benzo[b]fluoranthene 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 benzo[b]fluoranthene (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The benzo[b]fluoranthene risk specific dose calculated from this toxicity value is  $1.1 \times 10^{-6}$  mg/kg/day.

## 3. Review Dates

Summary table completion: March, 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.

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: Benzo[b]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 Benzo[b]fluoranthene  
(CAS Number 205-99-2)**

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

<sup>1</sup>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 benzo[b]fluoranthene is not available from the authoritative bodies listed in item number 5 (below). Benzo[b]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 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<sup>3</sup> 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<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benzo[b]fluoranthene.

**3. Review Dates**

Summary table completion: February, 2005

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: Benzo[b]fluoranthene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2002)	9.1 x 10 <sup>-3</sup>	1.1 x 10 <sup>-4</sup>	--	--	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 benzo[b]fluoranthene 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)	2.7 x 10 <sup>4</sup> reported as TC <sub>05</sub> <sup>2</sup> ; linear equivalent specific concentration = 0.53	-- <sup>3</sup>	--	--	Based on reported TC <sub>05</sub> 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 0.06. The relative potency factor for benzo(b)fluoranthene is based on its ability (relative to benzo[a]pyrene) to induce lung tumors in rats exposed by lung implantation.
--	9.1 x 10 <sup>-3</sup>	1.1 x 10 <sup>-4</sup>	--	--	Based on the CA EPA unit risk for benzo[a]pyrene and application of the recommended relative potency factor of 0.1.

<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> air concentration), where 1 x 10<sup>-6</sup> concentration = 1 x 10<sup>-6</sup> / inhalation unit risk.

<sup>2</sup>TC<sub>05</sub> = The concentration in air (expressed in mcg/m<sup>3</sup>) associated with a 5% increase in incidence or mortality due to tumors.

<sup>3</sup>No cancer potency factor was derived. The risk specific air concentration was obtained by linear extrapolation from the modeled TC<sub>05</sub>.

## 2. Recommendation and Rationale

The unit risk values for benzo[b]fluoranthene are based on benzo(a)pyrene and the application of relative potency factors. The recommended unit risk value for benzo(a)pyrene is 1.1 x 10<sup>-3</sup> per mcg/m<sup>3</sup> (see Inhalation Cancer Toxicity Value Documentation for benzo(a)pyrene). Application of the recommended relative potency factor (0.1) yields an unit risk of 1.1 x 10<sup>-4</sup> per mcg/m<sup>3</sup>, which is the toxicity value recommended for use in the derivation of a inhalation cancer-based soil cleanup objective for benzo[b]fluoranthene (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The benzo[b]fluoranthene risk specific air concentration calculated from this toxicity value is 9.1 x 10<sup>-3</sup> mcg/m<sup>3</sup>.

## 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](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

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**Chemical Name: Benzo[g,h,i]perylene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

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

Agency	Reference Dose <sup>1</sup> (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.
RIVM (2001)	0.03	-	-	-	Based on RIVM's evaluation of total petroleum hydrocarbons and its designation of benzo[g,h,i]perylene as a non-carcinogenic aromatic with equivalent carbon number > 16 to 35.

<sup>1</sup>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**

No compound-specific reference dose values for benzo[g,h,i]perylene 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 benzo[g,h,i]perylene. Thus total petroleum hydrocarbons are not chosen as a surrogate for benzo[g,h,i]perylene. An oral reference dose is available for pyrene, which is a chemically similar polycyclic aromatic hydrocarbon that can be used to represent benzo[g,h,i]perylene with respect to noncancer endpoints. The basis for choosing pyrene as a chemical surrogate for benzo[g,h,i]perylene 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 benzo[g,h,i]perylene (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.

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.

### 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: Benzo[g,h,i]perylene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

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

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

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

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

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

**3. Review Dates**

Summary table completion: September, 2004

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

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**Chemical Name: Benzo[g,h,i]perylene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

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

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

<sup>1</sup>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 benzo[g,h,i]perylene is not available from the authoritative bodies listed in item number 5 (below). Benzo[g,h,i]perylene 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<sup>3</sup> 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<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benzo[g,h,i]perylene.

**3. Review Dates**

Summary table completion: February, 2005  
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: Benzo[g,h,i]perylene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

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

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

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

**2. Recommendation and Rationale**

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

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

**3. Review Dates**

Summary table completion: February, 2005

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: Benzo[k]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 Benzo[k]fluoranthene (CAS Number 207-08-9)**

Agency	Reference Dose <sup>1</sup> (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.

<sup>1</sup>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 benzo[k]fluoranthene 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 benzo[k]fluoranthene with respect to noncancer endpoints. The basis for choosing pyrene as a chemical surrogate for benzo[k]fluoranthene 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 benzo[k]fluoranthene (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: Benzo[k]fluoranthene**  
**Exposure Route: Oral**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Oral Cancer Toxicity Value Documentation**

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

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA OSRTI (2004) US EPA Region 3 (2003)	1.37 x 10 <sup>-5</sup>	0.073	--	--	Based on a relative potency factor of 0.01 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. Benzo[k]fluoranthene produced tumors in mice after lung implantation, intraperitoneal injection, and when administered with a promoting agent in skin-painting studies.
CA EPA (2002)	8.33 x 10 <sup>-7</sup>	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)	$5.0 \times 10^{-5}$	-- <sup>2</sup>	--	--	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).

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>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 benzo[k]fluoranthene 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 (0.01) yields a cancer potency factor 0.0903 per mg/kg/day, which is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for benzo[k]fluoranthene (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The benzo[k]fluoranthene risk specific dose calculated from this toxicity value is  $1.1 \times 10^{-5}$  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

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**Chemical Name: Benzo[k]fluoranthene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for Benzo[k]fluoranthene  
(CAS Number 207-08-9)**

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

<sup>1</sup>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 benzo[k]fluoranthene is not available from the authoritative bodies listed in item number 5 (below). Benzo[k]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 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<sup>3</sup> 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<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for benzo[k]fluoranthene.

**3. Review Dates**

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

**4. References for Summary Table**

**5. Authoritative Bodies Checked for Reference A-120 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: Benzo[k]fluoranthene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Benzo[k]fluoranthene (CAS Number 207-08-9)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2002)	9.1 x 10 <sup>-3</sup>	1.1 x 10 <sup>-4</sup>	--	--	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 benzo[k]fluoranthene is based on its ability (relative to benzo[a]pyrene) to induce lung tumors in rats exposed by lung implantation.
Health Canada (1994)	4.0 x 10 <sup>4</sup> reported as TC <sub>05</sub> <sup>2</sup> ; linear equivalent specific concentration = 0.8	-- <sup>3</sup>	--	--	Based on reported TC <sub>05</sub> 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 0.04. The relative potency factor for benzo(k)fluoranthene is based on its ability (relative to benzo[a]pyrene) to induce lung tumors in rats exposed by lung implantation.

--	$9.1 \times 10^{-2}$	$1.1 \times 10^{-5}$	--	--	Based on the CA EPA unit risk for benzo[a]pyrene and application of the recommended relative potency factor of 0.01.
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<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  air concentration), where  $1 \times 10^{-6}$  concentration =  $1 \times 10^{-6}$  / inhalation unit risk.

<sup>2</sup>TC<sub>05</sub> = The concentration in air (expressed in mcg/m<sup>3</sup>) associated with a 5% increase in incidence or mortality due to tumors.

<sup>3</sup>No cancer potency factor was derived. The risk specific air concentration was obtained by linear extrapolation from the modeled TC<sub>05</sub>.

## 2. Recommendation and Rationale

The unit risk values for benzo[k]fluoranthene are based on benzo(a)pyrene and the application of relative potency factors. The recommended unit risk value for benzo(a)pyrene is  $1.1 \times 10^{-3}$  per mcg/m<sup>3</sup> (see Inhalation Cancer Toxicity Value Documentation for benzo(a)pyrene). Application of the recommended relative potency factor (0.01) yields a unit risk of  $1.1 \times 10^{-5}$  per mcg/m<sup>3</sup>, which is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for benzo[k]fluoranthene (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The benzo[k]fluoranthene risk specific air concentration calculated from this toxicity value is  $9.1 \times 10^{-2}$  mcg/m<sup>3</sup>.

## 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](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/ps11.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: Beryllium**  
**Exposure Route: Oral**  
**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for Inorganic Beryllium**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA Region 3 (2004)</li> <li>◆ US EPA ODW (2004)</li> <li>◆ US EPA HEAST (1997)</li> </ul>	2 x 10 <sup>-3</sup>	0.46	BMDL <sub>10</sub> <sup>2</sup>	300	Based on small intestinal lesions in dogs in a 172-week dietary study.
ATSDR (2002)	2 x 10 <sup>-3</sup>	0.56	BMDL <sub>10</sub> <sup>2</sup>	300	Based on the same study used by US EPA (2004).
CA EPA (2003)	1.5 x 10 <sup>-4</sup>  --  2 x 10 <sup>-4</sup>	1.5  --  0.2	NOEL  --  BMDL <sub>05</sub> <sup>2</sup>	1000	Based on the same study used by US EPA (2004).

<sup>1</sup>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.

<sup>2</sup>BMDL<sub>x</sub> = The 95% lower confidence bound on the modeled benchmark dose associated with an excess lifetime risk of the observed effect of X%.

**2. Recommendation and Rationale**

The basis for the various reference doses for inorganic beryllium is essentially identical with respect to choice of study, species and adverse effect. The US EPA IRIS, ATSDR and one of the CA EPA derivations used a benchmark dose approach to estimate a lower-bound point of departure associated with either a 5 or 10% excess lifetime risk of the observed effect (intestinal lesions). The CA EPA also identified a NOEL point of departure from the same study. In the principal study, dogs were exposed via the diet to one of four non-zero doses. The CA EPA identified the second-lowest dose level in females as the NOEL. However, there were no statistically significant effects observed in dogs of either sex at the next highest dose (1.1 mg/kg/day in males, 1.3 mg/kg/day in females), so that the

choice of the next-lower dose as the NOEL is questionable. Both CA EPA derivations apply a total uncertainty factor of 1000, including a factor of 10 to account for intraspecies variability, a factor of 3 to account for interspecies variability (based on the site-of-contact nature of the lesions, therefore not requiring an adjustment for pharmacokinetic variability), a factor of 3 to account for database deficiencies and an additional factor of 10 to address uncertainties regarding the carcinogenicity of beryllium via ingestion. The additional 10-fold factor for carcinogenicity is not applicable in the current context as cancer and non-cancer effects are being addressed separately. The US EPA IRIS and ATSDR derivations are essentially equivalent, although the estimates of the BMDL<sub>10</sub> differ slightly. Both apply the same total uncertainty factor of 300 (10-fold each to account for intraspecies and interspecies variability and an additional 3-fold to account for database deficiencies). Therefore, the US EPA reference dose ( $2 \times 10^{-3}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for inorganic beryllium.

### 3. Review Dates

Summary table completion: August, 2004

Toxicity value recommendation: September, 2004

### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological profile for beryllium. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. <http://www.atsdr.cdc.gov/toxpro2.html>

CA EPA (California Environmental Protection Agency). 2003. Public Health Goal for beryllium and beryllium compounds in Drinking Water. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. <http://www.oehha.ca.gov/water/phg/allphgs.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. Agency consensus date: 03/26/1998. Last revised: 04/03/1998. <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 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). 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  
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Agency for Toxic Substances and Disease Registry  
California Environmental Protection Agency  
Division of Drinking Water and Environmental Management  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

**Chemical Name: Beryllium**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for Inorganic Beryllium**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2004)	$1.4 \times 10^{-7}$	7	--	--	Oral cancer potency factor for beryllium oxide based on human occupational exposure. Very limited documentation available.
CA EPA (2004)	$3.3 \times 10^{-10}$	3000	--	--	Oral cancer potency factor for beryllium sulfate. Very limited documentation available.
US EPA IRIS (2004)	--	--	--	--	Based on limited animal studies, data were considered inadequate to derive an oral cancer potency value.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

The two cancer potency factors derived by CA EPA are reported on the Toxicity Criteria Database for specific beryllium compounds (beryllium oxide and beryllium sulfate). Both values are derived by CA EPA by reference to a 1987 health assessment of beryllium prepared by the US EPA (US EPA, 1987). The CA EPA only provides a table extracted from that document as the basis for their values. An oral cancer potency factor that was previously published on US EPA IRIS was based on a lifetime study of rats exposed to beryllium sulfate in drinking water. This may have been the same value cited by CA EPA for beryllium sulfate (3000 per mg/kg/d), but the value on IRIS was withdrawn because the tumor incidence did not differ significantly between control and exposed animals and because adequate data



to develop a quantitative oral assessment were not available. Neither of the CA EPA values is chosen for use in the derivation of a soil cleanup objective for several reasons including the lack of documentation explaining the basis of the two CA EPA compound-specific cancer potency factors, the current US EPA assessment concluding that data are inadequate to derive an oral cancer potency factor and the large difference in potency between beryllium sulfate and beryllium oxide suggesting that an assessment of oral cancer potency should be compound specific. The CA EPA drinking water program has published another beryllium cancer potency factor for use in deriving a public health goal for drinking water (CA EPA, 2003). However, that value is an inhalation cancer potency factor that is only applied to estimate the cancer risk associated with inhaling aerosols from drinking water containing beryllium, not the risk associated with beryllium ingestion. That value is therefore not chosen as an oral cancer potency factor for use in the derivation of a soil cleanup objective. Therefore, an oral cancer potency factor for oral beryllium exposure is not available.

### 3. Review Dates

Summary table completion: August, 2004

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. Beryllium and Beryllium Compounds. 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/index.asp>

US EPA (United States Environmental Protection Agency). 1987. Health Assessment Document for Beryllium. Office of Health and Environmental Assessment. Washington DC. EPA/600/8-84/026F

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency consensus date: 03/26/1998. Last revised: 04/03/1998.

<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

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

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

**1. Summary of Available Inhalation Reference Concentrations for Inorganic Beryllium**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2004)	0.02	0.2	LOEL	10	Based on beryllium sensitization in workers and progression to chronic beryllium disease.
CA EPA (2001)	7 x 10 <sup>-3</sup>	0.2	LOEL	30	Based on the same study as US EPA IRIS (2004).

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

LOEL: lowest observed effect level; UF: uncertainty factor

**2. Recommendation and Rationale**

The reference concentrations for beryllium derived by authoritative bodies from the list in item 5 (below) are both based on the same occupational study which documented beryllium sensitization (an immune response) and progression to chronic beryllium disease (a chronic inflammatory lung lesion) among workers exposed occupationally by inhalation for an average of six years. The reference concentrations are based on the same point of departure, but differ in the choice of the uncertainty factors. The US EPA applied an uncertainty factor of 3 (rather than a full 10) to account for the use of a LOEL, based on the sensitive nature of the subclinical effect (beryllium sensitization). The US EPA also used an uncertainty factor of 3 for database deficiencies, citing the poor quality of the monitoring data in the principal study, and did not use an intraspecies uncertainty factor based on the conclusion that 1 to 5% of the population is susceptible to chronic beryllium disease and that the workers in the principal study constituted the most sensitive subpopulation. The CA EPA used a full uncertainty factor of 10 for use of a LOEL and also applied an uncertainty factor of 3 for intraspecies variation, based on their conclusion that even though a sensitive population (i.e., beryllium-sensitized workers) may have been identified by the principal study, additional factors may also determine beryllium sensitivity. Given that chronic beryllium disease (which is made more likely by beryllium sensitization) is a debilitating and irreversible condition, retention of an uncertainty factor of at least 3

for intraspecies variation and 10 for use of a LOEL are more consistent with current risk assessment practices. Therefore, the CA EPA reference concentration ( $7 \times 10^{-3}$  mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for beryllium.

### 3. Review Dates

Summary table completion: November, 2004

Toxicity value recommendation: December, 2004

### 4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2001. Chronic Reference Exposure Levels: Chronic Toxicity Summary for Beryllium and Beryllium Compounds. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency.  
[http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](http://www.oehha.ca.gov/air/chronic_rels/AllChrels.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: 03/26/1998. Last revised: 04/03/1998  
<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>

### 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: Beryllium**  
**Exposure Route: Inhalation**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Inorganic Beryllium**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>♦ US EPA Region 3 (2004)</li> <li>♦ CA EPA (2002)</li> </ul>	4.2 x 10 <sup>-4</sup>	2.4 x 10 <sup>-3</sup>	relative risk	--	Based on the incidence of lung cancer in males occupationally exposed to beryllium.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

**2. Recommendation and Rationale**

The US EPA unit risk is the only available value from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore, the US EPA unit risk (2.4 x 10<sup>-3</sup> per mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of a inhalation cancer-based soil cleanup objective for beryllium. The beryllium risk specific air concentration calculated from this toxicity value is 4.2 x 10<sup>-4</sup> mcg/m<sup>3</sup>.

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

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 03/26/1998. Last revised: 04/03/1998.  
<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 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: *n*-Butylbenzene**  
**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*-Butylbenzene (CAS Number 104-51-8)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
--	--	--	--	--	No information available.

<sup>1</sup>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*-butylbenzene is not available. An oral reference dose is available for isopropylbenzene, which is structurally and chemically similar to *n*-butylbenzene. The similarity between the two chemicals provides a basis for using toxicity data for isopropylbenzene to represent *n*-butylbenzene. 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*-butylbenzene.

**3. Review Dates**

Summary table completion: March, 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

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**Chemical Name: *n*-Butylbenzene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for *n*-Butylbenzene (CAS Number 104-51-8)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	No information available.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for *n*-butylbenzene is not available.\*

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

**3. Review Dates**

Summary table completion: March, 2004  
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

P:\Sections\TAS\BROWNFIELDS 2003\Summary of Available Reference Values (Reviewed and Edited)\n-Butylbenzene-Cancer.doc

**Chemical Name: *n*-Butylbenzene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for *n*-Butylbenzene  
(CAS Number 104-51-8)**

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

<sup>1</sup>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*-butylbenzene 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*-butylbenzene. The similarity between the two chemicals provides a basis for using toxicity data for isopropylbenzene to represent *n*-butylbenzene. Therefore, the US EPA reference concentration for isopropylbenzene (400 mcg/m<sup>3</sup> (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*-butylbenzene.

**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

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

**Chemical Name: *n*-Butylbenzene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for *n*-Butylbenzene (CAS Number 104-51-8)**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for *n*-butylbenzene is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005

Toxicity value recommendation: February, 2005

**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

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

**Chemical Name: *sec*-Butylbenzene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for *sec*-Butylbenzene (CAS Number 135-98-8)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
--	--	--	--	--	No information available.

<sup>1</sup>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 *sec*-butylbenzene is not available. An oral reference dose is available for isopropylbenzene, which is structurally and chemically similar to *sec*-butylbenzene. The similarity between the two chemicals provides a basis for using toxicity data for isopropylbenzene to represent *sec*-butylbenzene. Therefore, the US EPA reference dose for (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 *sec*-butylbenzene.

**3. Review Dates**

Summary table completion: March, 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

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**Chemical Name: *sec*-Butylbenzene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for *sec*-Butylbenzene (CAS Number 135-98-8)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	No information available.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for *sec*-butylbenzene is not available.\*

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

**3. Review Dates**

Summary table completion: March, 2004  
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

P:\Sections\TAS\BROWNFIELDS 2003\Summary of Available Reference Values (Reviewed and Edited)\sec-Butylbenzene-Cancer.doc

**Chemical Name: *sec*-Butylbenzene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for *sec*-Butylbenzene  
(CAS Number 135-98-8)**

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

<sup>1</sup>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 *sec*-butylbenzene 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 *sec*-butylbenzene. The similarity between the two chemicals provides a basis for using toxicity data for isopropylbenzene to represent *sec*-butylbenzene. Therefore, the US EPA reference concentration for isopropylbenzene (400 mcg/m<sup>3</sup> (US EPA IRIS, 2004)) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *sec*-butylbenzene.

**3. Review Dates**

Summary table completion: February, 2005

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

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

**Chemical Name: *sec*-Butylbenzene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for *sec*-Butylbenzene (CAS Number 135-98-8)**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for *sec*-butylbenzene is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005

Toxicity value recommendation: February, 2005

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

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

**Chemical Name: *tert*-Butylbenzene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for *tert*-Butylbenzene (CAS Number 98-06-6)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
--	--	--	--	--	No information available.

<sup>1</sup>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**

An oral reference dose for *tert*-butylbenzene is not available. An oral reference dose is available for isopropylbenzene, which is structurally and chemically similar to *tert*-butylbenzene. The similarity between the two chemicals provides a basis for using toxicity data for isopropylbenzene to represent *tert*-butylbenzene. 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 *tert*-butylbenzene.

**3. Review Dates**

Summary table completion: March, 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

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



**Chemical Name: *tert*-Butylbenzene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for *tert*-Butylbenzene (CAS Number 98-06-6)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	No information available.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for *tert*-butylbenzene is not available.\*

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

**3. Review Dates**

Summary table completion: March, 2004  
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  
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Health Effects Assessment Summary Tables  
New York State Department of Health  
New York State Department of Environmental Conservation  
Agency for Toxic Substances and Disease 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:** *tert*-Butylbenzene

**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 *tert*-Butylbenzene  
(CAS Number 98-06-6)**

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

<sup>1</sup>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 *tert*-butylbenzene 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 *tert*-butylbenzene. The similarity between the two chemicals provides a basis for using toxicity data for isopropylbenzene to represent *tert*-butylbenzene. Therefore, the US EPA reference concentration for isopropylbenzene (400 mcg/m<sup>3</sup> (US EPA IRIS, 2004)) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *tert*-butylbenzene.

**3. Review Dates**

Summary table completion: February, 2005

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

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**Chemical Name: *tert*-Butylbenzene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for *tert*-Butylbenzene (CAS Number 98-06-6)**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for *tert*-butylbenzene is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005

Toxicity value recommendation: February, 2005

**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

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

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

**1. Summary of Available Oral Reference Doses for Inorganic Cadmium**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA Region 3 (2003)</li> <li>◆ US EPA ODW (2004)</li> </ul>	5 x 10 <sup>-4</sup> (water)  1 x 10 <sup>-3</sup> (food)	0.005  0.01	NOEL  NOEL	10  10	Based on the highest level of cadmium in the human renal cortex not associated with significant proteinuria, obtained from many studies on the toxicity of cadmium in both humans and animals.
ATSDR (1999)	2.0 x 10 <sup>-4</sup>	0.0021	NOEL	10	Based on renal effects (proteinuria) in humans in Japan who consumed food containing elevated cadmium levels.
RIVM (2001)	5.0 x 10 <sup>-4</sup>	0.001	LOEL	2	Based on the same study reviewed in ATSDR (1999) except RIVM concluded that human data demonstrated that kidney damage will be prevented if cadmium levels in the renal cortex and urine are below 50 mg/kg and 2.5 mcg/g creatinine, respectively, and that these cadmium levels are likely to be reached following a lifetime exposure to a dose of 0.001 mg/kg/day.
CA EPA (1999)	1.0 x 10 <sup>-5</sup>	0.001	LOEL	100	Based on tubular damage indicated by the appearance of small proteins in the urine in an epidemiological study of a cross sectional sample of the adult Belgian population.

WHO (1993)	$1 \times 10^{-3}$	--	--	--	Based on identification of a weekly cadmium intake of 7 mcg/kg (equivalent to 0.001 mg/kg/day) that will lead to a renal cortex cadmium concentration of 50 mg/kg, and that this kidney cadmium concentration is without appreciable risk. Documentation on actual derivation is limited.
NYS DEC (1997)	$7.0 \times 10^{-4}$	--	--	--	The reference dose is the average of 5 values derived by NYS DOH (0.0007 mg/kg/day), US EPA (0.0005 mg/kg/day), US FDA (0.0008 mg/kg/day), WHO (0.0010 mg/kg/day) and ATSDR (0.0007 mg/kg/day).
Health Canada (1986)	$6 \times 10^{-4}$ to $7 \times 10^{-4}$ <sup>2</sup>	--	--	--	Based on multicompartamental model for cadmium distribution in the body and the conclusion that a daily intake of 0.04 to 0.05 mg would lead to only 0.1 percent of the population reaching the critical cadmium concentration of 0.2 mg/g in the renal cortex after 50 years. Documentation on actual derivation is limited.

<sup>1</sup>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.

<sup>2</sup>A reference dose was not calculated. The range of reference doses was obtained from the daily intakes of 0.04 to 0.05 mg/day assuming a 70 kg adult body weight.

## 2. Recommendation and Rationale

The basis for the various cadmium reference doses is dietary exposure associated with kidney toxicity in humans, but the specific human data and assumptions used to derive a reference dose value differ among the authoritative bodies. The US EPA IRIS values and several of the values that were averaged to derive the NYS DEC value are based on a critical concentration of 200 ug cadmium/g of human kidney cortex associated with minimal renal tubule dysfunction (initially manifested clinically as proteinuria) in the general population and a cadmium pharmacokinetic model that predicts the chronic cadmium intake that will result in a specific cadmium level in the kidney cortex. This cadmium concentration in kidney cortex reflects data from many studies on cadmium exposure and kidney toxicity in human populations and in laboratory animals and is considered to represent a NOEL body burden by many authoritative bodies. The US EPA modified its reference dose based on assumed differences in cadmium absorption from drinking water vs. food to derive separate values for those two media. Documentation on the derivation of the WHO and the Health Canada value is limited. The



ATSDR, RIVM and CA EPA values are derived based on single studies reporting cadmium dietary intake in relation to proteinuria. The Japanese study forming the basis of the ATSDR value used a regression model to estimate that a daily intake of approximately 0.002 mg/kg/day in food resulted in prevalence of proteinuria approximately equal to the control (non-exposed) levels, while RIVM interpreted the same study results as representing an effect level at one-half of that daily intake. RIVM commented that this level was very nearly a NOEL, and therefore applied an uncertainty factor of 2 to derive a reference dose. CA EPA chose a level of 50 mcg cadmium/g kidney weight (i.e., one-fourth the critical value recognized by the US EPA) as a LOEL based on a different population-based study. ATSDR notes that different assumptions regarding dietary cadmium absorption, the shape of the kidney concentration distribution at a given intake level and the cutoff level used to define proteinuria all may influence the estimate of cadmium body burden associated with kidney toxicity. Given the substantial database supporting 200 mcg Cd/g kidney weight as a NOEL or perhaps a minimal LOEL, 50 mcg/g may in fact not be a clear effect level. Even if the intake level taken by RIVM as a LOEL is considered a NOEL, an uncertainty factor of 2 does not appear to account for uncertainties regarding human variability. Additionally, given the quantitative uncertainties in epidemiologic studies, a derivation that is representative of the range of study results is generally chosen over a point estimate from a single epidemiology study. The NYS DEC value is reflective of several similar analyses that derive a cadmium reference dose based on the well-documented critical concentration of 200 mcg Cd/g kidney cortex. Therefore, the NYS DEC reference dose ( $7 \times 10^{-4}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for cadmium.

### 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). 1999. Toxicological profile for cadmium. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

CA EPA (California Environmental Protection Agency). 1999. Public Health Goal for Cadmium 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. 1986. 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>

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

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 249-257. <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: 05/25/88. Last revised: 02/01/94. <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: Cadmium**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for Inorganic Cadmium**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (1999)	$2.6 \times 10^{-6}$	0.38	linearized multistage model, extra risk	BW <sup>3/4</sup> <sup>2</sup>	Based on the increased incidence of leukemia in rats exposed to cadmium in the diet.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.25</sup>.

**2. Recommendation and Rationale**

The CA EPA cancer potency factor 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, CA EPA cancer potency factor (0.38 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for cadmium. The cadmium risk specific dose calculated from this toxicity value is  $2.6 \times 10^{-6}$  mg/kg/day.

**3. Review Dates**

Summary table completion: May, 2004

Toxicity value recommendation: June, 2004

**4. References for Summary Table**

CA EPA (California Environmental Protection Agency). 1999. Public Health Goal for Cadmium in Drinking Water. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. <http://www.oehha.ca.gov/water/phg/allphgs.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: Cadmium**  
**Exposure Route: Inhalation**  
**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for Inorganic Cadmium**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA Region 3 (2004a, b)	0.2	--	--	--	Based on kidney toxicity in exposed workers. Very limited information available.
CA EPA (2003)	0.02	0.5	NOEL	30	Based on kidney and respiratory toxicity in workers exposed to cadmium by inhalation. The NOEL (1.4 mcg/m <sup>3</sup> ) was adjusted to a human equivalent concentration that accounts for occupational ventilation rates and continuous exposure. Study LOEL = 21 mcg/m <sup>3</sup> .
NYS DOH (1990)	0.02	200 mcg cadmium/g kidney cortex;  biokinetic modeling relates this body burden to total daily intake of 14.3 mcg cadmium	LOEL	5	Based on a collective evaluation of epidemiologic evidence for kidney toxicity in workers exposed to cadmium. Assumes 15% of total cadmium exposure not from food and water is allocated to airborne exposure.

<sup>1</sup>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. Recommendation and Rationale

The reference concentrations for cadmium derived by authoritative bodies from the list in item 5 (below) are all based on kidney toxicity (and in one case also respiratory toxicity) in exposed workers. Documentation of the detailed derivation of the US EPA value is not available. The CA EPA derivation is based on estimated air exposure levels in a single epidemiologic study, while the NYS DOH value is based on the weight of epidemiologic evidence suggesting that subtle kidney toxicity effects are associated with kidney Cd levels of 200 mcg/g kidney cortex. The two derivations result in the same reference concentration. The value based on the weight of epidemiological evidence may better represent the range of effects and exposures associated with cadmium-induced renal toxicity in humans. Therefore, the NYS DOH reference concentration (0.02 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for cadmium.

## 3. Review Dates

Summary table completion: September, 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 Cadmium and cadmium compounds. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency.  
[http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html)

NYS DOH (New York State Department of Health). 1990. Ambient Air Criteria Document: Cadmium. Albany, NY: Bureau of Toxic Substance Assessment.

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

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004b. Risk assessment issue paper for: Derivation of a provisional subchronic RfC for Cadmium (CASRN 7440-43-9). 96-015/03-20-96.

## 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

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

**New York State Department of Health**  
**Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Inorganic Cadmium**

Agency	Risk Specific Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Cancer Potency Factor (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2004)	5.6 x 10 <sup>-4</sup>	1.8 x 10 <sup>-3</sup>	two stage model, extra risk	--	Based on evidence of lung, tracheal, and bronchus cancer deaths in workers exposed to cadmium by inhalation.
CA EPA (2002)	2.4 x 10 <sup>-4</sup>	4.2 x 10 <sup>-3</sup>	poisson regression model and lifetable analysis	--	Based on the same study used by US EPA IRIS (2004).
Health Canada (1994)	5.1 reported as a TC <sub>05</sub> <sup>2</sup> ; linear equivalent risk specific concentration = 1.0 x 10 <sup>-4</sup>	-- <sup>3</sup>	linearized multistage model, extra risk	scaled based on default breathing rates and body weights of rats and humans	Based on an increased incidence of lung tumors in rats exposed by inhalation 23 hours per day for 18 months.
NYS DOH (1990)	5 x 10 <sup>-4</sup>	2.0 x 10 <sup>-3</sup>	linear average relative risk model	---	Based on the same study used by US EPA IRIS (2004).

<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> concentration = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>TC<sub>05</sub> = The concentration in air (expressed in mcg/m<sup>3</sup>) associated with a 5% increase in incidence or mortality due to tumors. The TC<sub>05</sub> represents a maximum likelihood estimate rather than a lower-bound estimate.

<sup>3</sup>The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported, but would be equal to 1 x 10<sup>-6</sup> divided by the 10<sup>-6</sup> risk-specific concentration.

**2. Recommendation and Rationale**



The inhalation unit risks derived by authoritative bodies from the list in item 5 (below) are based on increased incidence of lung tumors in human occupational studies or in rats exposed by inhalation for 18 months. Health Canada derived an inhalation risk-specific concentration from the rat study, but only reported a maximum likelihood  $TC_{05}$  that does not provide a lower-bound estimate on the risk specific concentration. The Health Canada derivation also used an interspecies scaling procedure based on inhaled dose and body weight scaling which is not consistent with currently-accepted risk assessment practice.

The US EPA, CA EPA and NYS DOH derivations are all based on the same occupational lung cancer data for cadmium smelter workers. Small differences in the unit risks are due to use of different dose-response models. The CA EPA derivation accounts for the influence of a healthy-worker effect on expected lung-cancer mortality, while the US EPA and NYS DOH derivations do not. Therefore, the CA EPA unit risk ( $4.2 \times 10^{-3}$  per  $mcg/m^3$ ) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for cadmium. The cadmium risk specific air concentration calculated from this toxicity value is  $2.4 \times 10^{-4}$   $mcg/m^3$ .

### 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. Office of Environmental Health Hazard Assessment. Air Toxics Hot Spot Program Risk Assessment Guideline. Part II. Technical Support Documentation for Describing Available Cancer Potency Factors.  
[http://www.oehha.ca.gov/air/cancer\\_guide/TSD2.html](http://www.oehha.ca.gov/air/cancer_guide/TSD2.html).

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

NYSDOH (New York State Department of Health). 1990. Ambient Air Criteria Document: Cadmium. Albany, NY: Bureau of Toxic Substance Assessment.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 11/12/1986. Last revised: 06/01/1992.  
<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 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

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**Chemical Name: Carbon Tetrachloride**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for Carbon Tetrachloride (CAS Number 56-23-5)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"><li>♦ US EPA Region 3 (2003)</li><li>♦ US EPA EPA ODW (2004)</li><li>♦ US EPA OPP (1997)</li></ul>	$7 \times 10^{-4}$	0.71	NOEL	1000	Based on liver lesions in rats exposed by corn oil gavage 5 days per week for 12 weeks. Study LOEL = 7.1 mg/kg/day.
RIVM (2000)	$4 \times 10^{-3}$	1	NOEL	250	Based on same study as US EPA IRIS.
WHO (1999)	$1.4 \times 10^{-3}$	0.71	NOEL	500	Based on same study as US EPA IRIS.

<sup>1</sup>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 carbon tetrachloride is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (1.0 mg/kg/day, 5 days per week). The RIVM value does not time-weight the NOEL dose for the 5 days per week dosing scheme and reduces the uncertainty factor for a sub-chronic study from 10 to 2.5 without clearly documenting a justification for that choice. The WHO and US EPA values were almost identically derived, except WHO chose to reduce the total uncertainty factor applied to the NOEL by a factor of 2 due to the use of bolus gavage dosing. The WHO did not provide sufficient justification for reduction of the uncertainty factor, and the US EPA derivation is more consistent with generally accepted risk assessment practices by applying 10-fold uncertainty factors to account for inter- and intra-species variability and the use of a sub-chronic study. Therefore, the US EPA reference dose ( $7 \times 10^{-4}$

mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for carbon tetrachloride.

### 3. Review Dates

Summary table completion: May, 2004

Toxicity value recommendation: June, 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/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: 5/20/85. Last revised: 6/01/91. <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 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). 2003. Guidelines for drinking water quality, 3<sup>rd</sup> Ed. World Health Organization, Geneva.

[http://www.who.int/docstore/water\\_sanitation\\_health/GDWQ/draftchemicals/carbontetrachloride2003.pdf](http://www.who.int/docstore/water_sanitation_health/GDWQ/draftchemicals/carbontetrachloride2003.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

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**Chemical Name: Carbon Tetrachloride**

**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 Carbon Tetrachloride (CAS Number 56-23-5)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	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)	7.7 x 10 <sup>-6</sup>	0.13	linearized multistage model, extra risk	body surface area <sup>2</sup>	Based on the geometric mean of potency factors from four studies. The studies reported hepatocellular carcinomas and hepatomas in hamsters, rats and mice exposed by gavage.
Health Canada (1986)	2.7 x 10 <sup>-5</sup> to 8.7 x 10 <sup>-5</sup>	-- <sup>3</sup>	linearized multistage model	body surface area <sup>2</sup>	Based on hepatocellular carcinomas in male mice exposed for 78 weeks by gavage, and on hepatic neoplastic nodules and hepatocellular carcinomas in male rats exposed for 78 weeks by gavage.
CA EPA (2004) CA EPA (2002)	6.7 x 10 <sup>-6</sup>	0.15	linearized multistage model, extra risk	body surface area <sup>2</sup>	Based on three of the same studies and reviews as US EPA IRIS (2004) (rat data were excluded). The CA EPA Toxicity Criteria Database cites the oral cancer slope factor as equal to the inhalation slope factor. The inhalation slope factor was derived based on route extrapolation

					from oral gavage data and includes a 50% absorption fraction by inhalation.
CA EPA (2000)	$5.6 \times 10^{-6}$	0.18	linearized multistage model, extra risk	--	Based on one of the studies used by US EPA

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>No cancer potency factor was derived. The range of risk specific doses was obtained from the drinking water unit risk range of  $3.3 \times 10^{-7}$  to  $1.04 \times 10^{-6}$  per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day. It is not clear whether these estimates represent maximum likelihood or upper-bound risk values.

## 2. Recommendation and Rationale

The US EPA IRIS, Health Canada and CA EPA potency estimates are based on liver tumors in animals, and are derived using similar methods, with the difference being the specific animal dose response data sets chosen for the derivations. Health Canada reports drinking water unit risk values (cancer risk per unit concentration in drinking water) and does not specify whether the values are maximum likelihood or upper-bound risk estimates. CA EPA reports in their Toxicity Criteria Database (TCDB; CA EPA, 2004) an oral cancer slope factor (equivalent to a cancer potency factor) that is the same value as an inhalation cancer slope factor based on route-extrapolation from several of the oral liver-tumor data sets used by US EPA to derive their cancer potency factor. The inhalation slope factor is reported to reflect an assumption of 50% absorption via inhalation. Since the oral and inhalation slope factors on the TCDB are equal, this suggests that the oral slope factor is derived from the inhalation slope factor rather than directly from the oral tumor data. In the documentation of the CA EPA drinking water Public Health Goal for carbon tetrachloride, they report a slightly different oral cancer slope factor based on mouse liver tumors in one of the four oral studies used by US EPA. This is reported to be the same tumor data used to derive the point estimate for the inhalation slope factor, but the values do not differ by the factor of 2 that would be expected based on the 50% absorption assumption. The complete basis for the two somewhat conflicting oral cancer potency values from CA EPA is unclear from the available documentation. The US EPA IRIS derivation is more transparent and better reflects the weight of evidence from for liver tumor potency since it is the geometric mean of estimates from 4 sets of liver tumor data. Therefore the US EPA IRIS cancer potency factor (0.13 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for carbon tetrachloride. The carbon tetrachloride risk specific dose calculated from this toxicity value is  $7.7 \times 10^{-6}$  mg/kg/day.

## 3. Review Dates

Summary table completion: May, 2004

Toxicity value recommendation: November, 2004

#### 4. References for Summary Table

CA EPA(California Environmental Protection Agency). 2000. Public health goals for chemicals in drinking water. Carbon tetrachloride. Office of Environmental Health Hazard Assessment. Sacramento, CA. <http://www.oehha.ca.gov/water/phg/allphgs.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. Sacramento, CA. [http://www.oehha.ca.gov/air/cancer\\_guide/TSD2.html](http://www.oehha.ca.gov/air/cancer_guide/TSD2.html)

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

Health Canada. 1986. 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>

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: 12/04/86. Last revised: 6/01/91. <http://www.epa.gov/iris/subst/0408.htm>.

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: Carbon Tetrachloride**

**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 Carbon Tetrachloride  
(CAS Number 56-23-5)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA Region 3 (2004a, b)	2	6.5 x 10 <sup>3</sup>	LOEL	3000	Based on increased relative liver weight in female guinea pigs exposed via inhalation for 7 hours/day, 5 days/week for 6 months. No effects were observed in males. Provisional value with limited documentation.
ATSDR (2003)	180 (0.03 ppm)	5.6 x 10 <sup>3</sup> (0.9 ppm)	NOEL	30	Based on liver toxicity in male and female rats exposed via inhalation for 6 hours/day, 5 days/week for 104-weeks. Study LOEL = 2.8 x 10 <sup>4</sup> mcg/m <sup>3</sup> (4.5 ppm).
CA EPA (2003)	40	1.1 x 10 <sup>4</sup> (1.7 ppm)	LOEL	300	Based on the same study used by US EPA.
RIVM (2001)	60	6.4 x 10 <sup>3</sup>	NOEL	100	Based on liver toxicity in male and female rats in a 200-day inhalation study. Study LOEL = 1.3 x 10 <sup>4</sup> mcg/m <sup>3</sup> .

<sup>1</sup>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 carbon tetrachloride derived by authoritative bodies from the list in item 5 (below) are all based on liver toxicity observed in rats or guinea pigs exposed via inhalation. A LOEL was observed in the subchronic guinea pig study that, on a time-weighted continuous basis, was below the rat LOELs and was very close to the rat NOELs (one of which was from a chronic study), suggesting that guinea pigs may be a more sensitive species than rats for carbon tetrachloride liver toxicity. The US EPA considered the response observed in guinea pigs a minimal LOEL, since effects were only seen in one sex (females, not males) and the increase in relative liver weight, although statistically significant, was only about 10%. The US EPA used a 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. CA EPA used an adjustment of 1.7-fold to increase the HEC LOEL based on the ratio of blood:air partitioning coefficients in guinea pigs and humans. The US EPA applied a total uncertainty factor of 3000, including 10-fold to account for intraspecies variability, 3-fold for interspecies variability, 30-fold for use of a subchronic minimal LOEL and an additional 3-fold for database deficiencies including lack of adequate respiratory, reproductive and developmental data. The CA EPA applied a total uncertainty factor of 300, including 10-fold for intraspecies variability, 3-fold for interspecies variability and 10-fold for the use of a subchronic minimal LOEL. Although reducing the uncertainty factor for use of a LOEL to 3 could be justified based on the minimal response observed in guinea pigs at the LOEL dose, the CA EPA does not adequately justify the reduction of the subchronic study uncertainty factor from 10 to 3. Also, the US EPA pharmacokinetic adjustment was more consistent with currently accepted risk assessment practice than CA EPA's, since the default value of 1 is to be used if blood:air partitioning data are unavailable or if the animal:human partitioning ratio is greater than 1. Therefore the US EPA reference concentration (2 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for carbon tetrachloride.

### 3. Review Dates

Summary table completion: July, 2004

Toxicity value recommendation: October, 2004

### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological Profile for carbon tetrachloride. 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 Carbon Tetrachloride. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency. [http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](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 Region 3 (United States Environmental Protection Agency Region 3). 2004a. Risk-based Concentration Table. Superfund Technical Support Section. <http://www.epa.gov/reg3hwmd/risk/human/index.htm>

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004b. Risk assessment issue paper for: Derivation of a provisional subchronic RfC for carbon tetrachloride (CASRN 56-23-5). 96-023/06-20-96

## 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: Carbon Tetrachloride**

**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 Carbon Tetrachloride (CAS Number 56-23-5)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	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)	0.07	$1.5 \times 10^{-5}$	linearized multistage model, extra risk	body surface area <sup>2</sup>	Unit risks were estimated based on route-to-route extrapolation of data from four studies where increased incidence of liver tumors was observed in mice, rats, and hamsters exposed via gavage. Extrapolation assumed 70 kg adult body weight, 20 m <sup>3</sup> /day continuous inhalation and 40% human absorption via inhalation. The unit risk value is the geometric mean of the results from the four studies.
CA EPA (2002)	0.024	$4.2 \times 10^{-5}$	linearized multistage model, extra risk	body surface area <sup>2</sup>	Based on three of the same studies and reviews as US EPA IRIS (2004) (rat data were excluded). Route-to-route extrapolation assumed 60 kg adult body weight, 18 m <sup>3</sup> /day continuous inhalation and 50% human absorption via inhalation. The unit risk value is the middle estimate of the results from the three studies.

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

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

**2. Recommendation and Rationale**

The inhalation unit risks derived by authoritative bodies are both based on route-to-route extrapolation of data showing increased liver tumor incidence in rats, mice and hamsters exposed via gavage. The mode of action of carbon tetrachloride carcinogenicity is thought to involve the action of oxidative metabolites in the liver rather than the parent compound. The enzyme system involved in the production of this metabolite is present in many tissues including lung, but its activity is much greater in the liver than elsewhere. Because there is a substantial first pass effect through the liver with oral exposure, liver tumors associated with oral exposure could be considered similar to a direct site-of-contact effect that would not be appropriately extrapolated to a different exposure route. The relative potency by the two routes would depend on relative rates of appearance of the metabolite in the liver, which would in turn depend on several pharmacokinetic factors including relative rates of absorption and excretion, the rate of systemic distribution from the lung to distant tissues including the liver and relative enzyme activities (affinity and saturability) in the different tissues. These factors introduce additional uncertainty to an analysis based on a route extrapolation. However, in the absence of inhalation-specific carcinogenicity data a value based on the assumption of equivalent potency by the two routes will be used. The US EPA used conventional body weight and inhalation rate values and 40% inhalation absorption of carbon tetrachloride in humans to extrapolate the inhalation unit risks from oral cancer potency values, and then took the geometric mean of four unit risks to derive their value. The CA EPA used values for body weight and inhalation rate that are somewhat less consistent with accepted risk assessment practice in their route conversion. They also assumed a somewhat higher inhalation absorption fraction and eliminated the rat data set from their unit risk calculations based on the lack of statistically significant increased tumor incidence after correcting for excess mortality. The rat data set gives the lowest unit risk of the four estimates. The CA EPA does not provide a clear basis for deviating from accepted default values in their route extrapolation procedure or for choosing the middle unit risk value of the three they derived from the mouse and hamster data. The US EPA derivation is based on assumptions more consistent with currently-accepted risk assessment practices and is somewhat more transparent in its derivation of a single estimate from the four data sets. Therefore, the US EPA unit risk ( $1.5 \times 10^{-5}$  per mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for carbon tetrachloride. The carbon tetrachloride risk specific air concentration calculated from this toxicity value is 0.07 mcg/m<sup>3</sup>.

### 3. Review Dates

Summary table completion: July 2004

Toxicity value recommendation: November, 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](http://www.oehha.ca.gov/air/cancer_guide/TSD2.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. Agency consensus date: 12/04/1986. Last revised: 06/01/1991. <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 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: Chlordane (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 Chlordane (CAS Number 12789-03-6)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"><li>◆ US EPA Region 3 (2004)</li><li>◆ US EPA ODW (2004)</li></ul>	$5 \times 10^{-4}$	0.15	NOEL	300	Based on hepatic necrosis in mice exposed in their diets for 104 weeks
US EPA OPP (1997) Also used by: <ul style="list-style-type: none"><li>◆ US HEAST (1997)</li><li>◆ NYS DEC (1997)</li></ul>	$6 \times 10^{-5}$	0.055	NOEL	1000	Based on liver hypertrophy in female rats exposed in diet for 130 weeks.
ATSDR (2004)	$6 \times 10^{-4}$	0.055	NOEL	100	Based on same study as US EPA OPP (1997).
WHO (1993)	$5 \times 10^{-4}$	0.05	NOEL	100	Based on same study as US EPA OPP (1997).

<sup>1</sup>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 chlordane reference dose is liver necrosis in mice chronically exposed to chlordane via the diet. The basis for the other reference doses for chlordane is liver hypertrophy in female rats chronically exposed to chlordane via the diet in a parallel experiment by the same investigators as the US EPA IRIS mouse study. Although US EPA (OPP and HEAST) previously based a reference dose derivation on the female rat data, the IRIS derivation discusses a re-evaluation of those data and notes that interpretation of the liver lesions is confounded by leukemia-related liver effects in some animals. The older EPA analysis also included a 10-fold uncertainty factor to account for lack of an adequate reproductive toxicity study and an adequate chronic toxicity study in a second

species and the generally insensitive endpoints studied. The latter two points are questionable, given the two rodent studies used as the critical studies in the two different assessments, and the large database of supporting studies indicating the liver as the primary target organ for chlordane toxicity. An extra uncertainty factor of 3 was applied in the more recent US EPA IRIS derivation to account for the lack of an adequate reproductive study, and is more consistent with the quality of the database and accepted practice. Given the confounding of the female rat liver non-neoplastic effects by the leukemia-related effects and the database uncertainty factor used in the US EPA IRIS assessment, the US EPA IRIS reference dose ( $5 \times 10^{-4}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for chlordane.

As described in the Technical Support Document, the information in this fact sheet is applicable to alpha-chlordane, gamma-chlordane or mixtures of alpha- and gamma-chlordane.

### 3. Review Dates

Summary table completion: June, 2004

Toxicity value recommendation: June, 2004

### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological profile for chlordane. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

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

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

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Last revised: 2/07/1998. Agency consensus date: 11/03/1997. <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 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>

WHO (World Health Organization). 2003. Guidelines for drinking water quality, 3<sup>rd</sup> Ed. World Health Organization, Geneva [http://www.who.int/docstore/water\\_sanitation\\_health/GDWQ/Chemicals/chlordanesum.htm](http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/chlordanesum.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: Chlordane (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 Chlordane (CAS Number 12789-03-6)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA HEAST (1997) ♦ US EPA Region 3 (2004)	2.9 x 10 <sup>-6</sup>	0.35	linearized multistage model, extra risk	BW <sup>3/4</sup> <sup>2</sup>	Based on the geometric mean of 5 sets of dose-response data for liver tumors in mice exposed via the diet.
CA EPA (1997)	7 x 10 <sup>-7</sup>	1.3	Linear extrapolation from LED <sub>10</sub> <sup>3</sup> point of departure	BW <sup>3/4</sup> <sup>2</sup>	Based on the geometric mean of 4 sets of dose-response data for liver tumors in mice exposed via the diet.
NYS DEC (1997)	1.5 x 10 <sup>-6</sup>	0.68	linearized multistage model, extra risk	BW <sup>3/4</sup> <sup>2</sup>	Based on the geometric mean of 4 sets of dose-response data for liver tumors in mice exposed via the diet.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.25</sup>.

<sup>3</sup>LED<sub>10</sub> = The 95% lower confidence limit on the dose that causes a 10% increase in tumor incidence.

**2. Recommendation and Rationale**

The basis of the cancer potency factors for chlordane derived by authoritative bodies is an increased incidence of liver tumors in male and female mice chronically exposed to chlordane in the diet. In each case, the derived cancer potency factor is a geometric mean of cancer potency factors from several individual tumor-data sets. Four data sets are common to all three derivations, while the US EPA value includes data from a fifth study not represented by the other two values. All values are based on body weight interspecies dose scaling. CA EPA derived their value based on a point-of-departure low-dose extrapolation methodology, while the NYS DEC and US EPA values are derived using the linearized multistage model extrapolation procedure. Although the CA EPA point-of-departure method derivation is more consistent with current accepted risk assessment practices, the US EPA value reflects more

extensive and more recent dose-response data. Therefore, the US EPA cancer potency factor (0.35 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for chlordane. The chlordane risk specific dose calculated from this toxicity value is  $2.9 \times 10^{-6}$  mg/kg/day.

As described in the Technical Support Document, the information in this fact sheet is applicable to alpha-chlordane, gamma-chlordane or mixtures of alpha- and gamma-chlordane.

### 3. Review Dates

Summary table completion: June, 2004

Toxicity value recommendation: June, 2004

### 4. References for Summary Table

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

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

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

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Agency consensus review date: 11/03/1997. Last revised: 2/07/1998. <http://www.epa.gov/iris/subst/0408.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

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**Chemical Name: Chlordane (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 Chlordane (CAS Number 57-74-9)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2004)	0.7	650	NOEL	1000	Based on increased liver weights in rats exposed by inhalation 8 hours per day, 5 days per week, for 13 weeks. Study LOEL = 6500 mcg/m <sup>3</sup> .
ATSDR (1994)	0.02	24	NOEL	1000	Based on hepatocellular hypertrophy in the same study used by US EPA IRIS (2004). Study LOEL = 240 mcg/m <sup>3</sup> .

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

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

**2. Recommendation and Rationale**

The available reference concentrations for chlordane derived by authoritative bodies from the list in item 5 (below) are based on the same subchronic inhalation study in rats. The ATSDR considered the lowest exposure level from this study a NOEL and the next level (the middle exposure level) a LOEL for mild liver effects (hepatocellular enlargement or vacuolization and slight changes in serum chemistry). The ATSDR applied a total uncertainty factor of 1000 to the NOEL, including 10-fold each for intraspecies variability, interspecies variability, and use of a subchronic study. The US EPA did not consider the mild liver lesions at the middle exposure level adverse, and designated this level the NOEL. The LOEL was assigned the highest exposure level for increased liver weights and changes in serum chemistry indicative hepatic functional alteration. The US EPA used dosimetric modeling for a particle extrarespiratory effect to estimate the human equivalent concentration at the NOEL, and applied a total uncertainty factor of 1000, including 3 for inter species extrapolation, 10 for intraspecies variability, 10 for the use of a subchronic study, and an additional 3-fold to account for database limitations, based on the lack of reproductive studies. Although the mild effects seen at the lowest dose in the study progressed to more pronounced effects at higher doses in rats, the same study reported no effects in monkeys at the middle exposure level. This suggests that rats may be more sensitive to the liver effects of chlordane than primates, and supports US EPA's use of the higher LOEL, as response

levels in primates may be more relevant to human effect levels. The US EPA derivation also uses dosimetric modeling to estimate the point of departure, which is more consistent with current risk assessment practices. Therefore, the US EPA reference concentration (0.7 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chlordane.

As described in the Technical Support Document, the information in this fact sheet is applicable to alpha-chlordane, gamma-chlordane or mixtures of alpha- and gamma-chlordane.

### 3. Review Dates

Summary table completion: December, 2004

Toxicity value recommendation: December, 2004

### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1994. Toxicological Profile for Chlordane Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. <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: 11/03/1997. Last revised: 02/07/1998. <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. 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: Chlordane (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 Chlordane (CAS Number 57-74-9)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	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)	0.01	1 x 10 <sup>-4</sup>	linearized multistage model, extra risk	BW <sup>¾</sup> 2	Based on route-to-route extrapolation of an oral cancer potency factor (0.35 per mg/kg/day), which is the geometric mean of five data sets from three dietary studies showing incidences of hepatocellular carcinomas in mice.
CA EPA (2004)	2.9 x 10 <sup>-3</sup>	3.4 x 10 <sup>-4</sup>	not clearly specified	not clearly specified	Based on route-to-route extrapolation of an oral cancer potency factor (1.2 per mg/kg/day). Details of derivation not available.

<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> air concentration), where 1 x 10<sup>-6</sup> concentration = 1 x 10<sup>-6</sup> / inhalation unit risk.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.25</sup>.

**2. Recommendation and Rationale**

The two inhalation unit risks derived by authoritative bodies are based on route-to-route extrapolation of oral cancer potency factors. Details on the CA EPA's documentation are not available. Therefore, the US EPA IRIS unit risk (1 x 10<sup>-4</sup> per mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for chlordane. The chlordane risk specific concentration calculated from this toxicity value is 0.01mcg/m<sup>3</sup>.

As described in the Technical Support Document, the information in this fact sheet is applicable to alpha-chlordane, gamma-chlordane or mixtures of alpha- and gamma-chlordane.

**3. Review Dates**

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

#### 4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2004. Office of Environmental Health Hazard Assessment. Toxicity Criteria Database.  
<http://www.oehha.ca.gov/risk/ChemicalDB/cancerpotency.asp?name=Chlordane&number=57749>.

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: 11/03/1997. Last revised: 02/07/1998. <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>

#### 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: Chlorobenzene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for Chlorobenzene (CAS Number 108-90-7)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: <ul style="list-style-type: none"><li>◆ US EPA Region 3 (2003)</li><li>◆ US EPA HEAST (1997)</li><li>◆ NYS DEC (1997)</li></ul>	0.02	19	NOEL	1000	Based on histopathologic changes in the liver of male and female dogs given chlorobenzene in capsules for 13 weeks. Study LOEL = 39 mg/kg/day
RIVM (2000)	0.2	19.5	NOEL	100	Based on the same data as the US EPA IRIS derivation.
Health Canada (1992)	0.086	43	NOEL	500	Based on histopathologic changes in liver of male rats and mice given chlorobenzene by gavage for 103 weeks.
WHO (1996)	0.086	43	NOEL	500	Based on same data as Health Canada (1991).

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

**2. Recommendation and Rationale**

The basis for the US EPA IRIS and RIVM chlorobenzene reference doses is liver histopathology effects in dogs exposed orally for 13 weeks. The basis for the Health Canada and WHO reference doses for chlorobenzene is liver neoplastic nodules in male rats chronically exposed to chlorobenzene via gavage. Although the rodent study would generally be chosen as the basis for a reference dose because animals were exposed for their entire lifetimes (rather than only sub-chronically as in the dog study), the dog study identified a LOEL dose essentially the same as the NOEL dose in the rat study, suggesting dogs may be a more sensitive species. RIVM only applied a total uncertainty factor of 100 to the dog NOEL, suggesting that an additional uncertainty factor to account for the use of sub-chronic value was unnecessary because a higher NOEL dose existed (i.e., the rat NOEL). This rationale does not account for the LOEL dose in the dog study and is not consistent with generally accepted risk assessment practice. Therefore, the US EPA reference dose (0.02 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for chlorobenzene.

### 3. Review Dates

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

### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1990. Toxicological Profile for Chlorobenzene. U.S. Department of Health and Human Services, Public Health Service. December. <http://www.atsdr.cdc.gov/toxprofiles/tp131.html>.

Health Canada. 1992. Priority substances list assessment report No. 3: Chlorobenzene. Ottawa. Ministry of Public Works and Government Services. <http://www.hc-sc.gc.ca/hecs-sesc/exsd/pdf/chlorobenzene.pdf>.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 193-216. <http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf>

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

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

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 01/19/89. 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>.

WHO. (World Health Organization). 1996. Monochlorobenzene. [http://www.who.int/docstore/water\\_sanitation\\_health/GDWQ/draftchemicals/monochlorobenzene2003.pdf](http://www.who.int/docstore/water_sanitation_health/GDWQ/draftchemicals/monochlorobenzene2003.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  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

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**Chemical Name: Chlorobenzene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for Chlorobenzene (CAS Number 108-90-7)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
ATSDR (1990) Health Canada (1991) RIVM (2000) US EPA IRIS (2004)	--	--	--	--	One chronic animal bioassay showed a positive trend for carcinogenicity but had serious methodological flaws. Data are inadequate to evaluate carcinogenic potential.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for chlorobenzene is not available.\*

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

**3. Review Dates**

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

**4. References for Summary Table**

ATSDR (Agency for Toxic Substances and Disease Registry). 1990. Toxicological Profile for Chlorobenzene. U.S. Department of Health and Human Services, Public Health Service. December. <http://www.atsdr.cdc.gov/toxprofiles/tp131.html>.

Health Canada. 1992. Priority substances list assessment report: Chlorobenzene. Ottawa. 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, p 193-216. <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: 04/04/1990. Last revised: 03/01/1991. <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  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

**Chemical Name: Chlorobenzene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for Chlorobenzene  
(CAS Number 108-90-7)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA Region 3 (2004a, b)	60	$5.8 \times 10^4$	NOEL	1000	Based on liver toxicity in parental and offspring rats exposed by inhalation for 6 hours/day and 7 days/week in a multigenerational study. Study LOEL = $1.73 \times 10^5$ mcg/m <sup>3</sup> .
Health Canada (1996a, b) as cited by TERA, 2004	10	$5 \times 10^4$	LOEL	5000	Based on increased absolute and relative liver weights in rats exposed by inhalation for 7 hours/day, 5 days/week for up to 24 weeks.
RIVM (2000)	500	--	--	--	Based on same study as Health Canada. Value was adopted from a third-party risk assessment without supporting documentation.
CA EPA (2003)	$1 \times 10^3$	$1.2 \times 10^5$	NOEL	100	Based on same study as US EPA Region 3.

<sup>1</sup>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 chlorobenzene derived by authoritative bodies from the list in item 5 (below) are all based on liver toxicity in rats exposed via inhalation. The Health Canada and RIVM derivations are based on a subchronic LOEL for liver toxicity in rats exposed via inhalation. RIVM concluded no adequate data were available to derive a reference concentration, but chose to adopt a value derived by another organization without any supporting documentation. The Health Canada derivation is a modification of the value they derived in 1992 (Health Canada, 1993) under the priority substances program and complete details of the newer derivation were not available. TERA (2004) reports that Health Canada indirectly scaled the exposure concentration in rats to an exposure concentration in a human child (age 5 –11) by estimating per unit body weight intake in rats and then back-calculating a human exposure concentration based on assumed inhalation rates and body weights. Despite that adjustment, Health Canada applied a 10-fold uncertainty factor for interspecies variability, along with 10-fold factors for intraspecies variability and use of a subchronic value. They also used a 5-fold uncertainty factor for use of a minimal LOEL, for a total uncertainty factor of 5000. The US EPA and CA EPA values are derived from a NOEL in a multigenerational reproductive study where increased liver weights were observed in both parental and offspring male rats. The US EPA applied a total uncertainty factor of 1000, including 10-fold to account for intraspecies variability, 3-fold with a default pharmacokinetic adjustment (equal to 1) to account for interspecies variability and 10-fold for use of a subchronic NOEL and an additional 3-fold to account for database uncertainties including lack of data on neurotoxicity and toxicity of the entire respiratory system. The CA EPA applied the same 10-fold and 3-fold uncertainty factors to account for intra- and interspecies variability, respectively, and included a 3-fold uncertainty factor for use of a subchronic NOEL. CA EPA used a pharmacokinetic adjustment of 2-fold to increase the human equivalent NOEL, based on the ratio of blood:air partitioning coefficients in rats and humans. Current guidance is to use a default pharmacokinetic adjustment of 1 if partitioning coefficient data are unavailable or if the animal:human ratio is greater than 1. Overall, the US EPA derivation is most consistent with currently-accepted risk assessment practice. Therefore the US EPA reference concentration (60 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chlorobenzene.

## 3. Review Dates

Summary table completion: May, 2004

Toxicity value recommendation: October, 2004

## 4. References for Summary Table

CA EPA(California Environmental Protection Agency). 2003. Chronic toxicity summary: chlorobenzene. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacramento, CA.

[http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html)

Health Canada, Environment Canada. 1993. Priority Substances List Assessment Report: chlorobenzene. 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. H46-2/96-194E.

Health Canada. 1996b. Canadian Environmental Protection Act. Priority Substances List. Supporting Documentation: Health-Based Tolerable Daily Intakes/Concentrations and Tumourigenic Doses/Concentrations for Priority Substances. (unpublished). (as cited by TERA, 2004)

RIVM (National Institute of Public Health & Environmental Protection). 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 Region 3 (United States Environmental Protection Agency Region 3). 2004a. Risk-based Concentration Table. Superfund Technical Support Section.  
<http://www.epa.gov/reg3hwmd/risk/human/index.htm>

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004b. Risk assessment issue paper for: derivation of a provisional chronic RfC for chlorobenzene (CASRN 108-90-7). 98-020/09-18-98.

## 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: Chlorobenzene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Chlorobenzene (CAS Number 108-90-7)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	No human data, inadequate animal data and predominantly negative genetic toxicity data in bacterial, yeast, and mouse lymphoma cells.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An inhalation unit risk for chlorobenzene is not available.\*

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

**3. Review Dates**

Summary table completion: May, 2004

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: 04/04/1990. Last revised: 03/01/1991. <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  
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed  
Toxicity Values)  
Region 3 Risk-Based Concentrations  
Office of Pesticides  
Office of Drinking Water  
Health Effects Assessment Summary Tables  
New York State Department of Health  
New York State Department of Environmental Conservation  
Agency for Toxic Substances and Disease 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: Chloroform**  
**Exposure Route: Oral**  
**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for Chloroform (CAS Number 67-66-3)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA Region 3 (2003)</li> <li>◆ US EPA OPP (1997)</li> <li>◆ US EPA ODW (2002)</li> <li>◆ US EPA HEAST (1997)</li> </ul>	0.01	12.9	LOEL	1000	Based on moderate to marked fatty cyst formation in the liver and elevated SGPT (serum glutamate-pyruvate transaminase) in male and female dogs in a 7.5-year feeding (gelatin capsule) study. The study LOEL of 15 mg/kg/day was time-weighted based on exposure for 6 days per week.
ATSDR (1997)	0.01	12.9	LOEL	1000	Based on the same study and review as US EPA IRIS (2004).
RIVM (2001)	0.03	30	LOEL	1000	Based on liver toxicity in male and female mice in a chronic drinking water study (limited information available.)

<sup>1</sup>Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. LOEL: lowest observed effect level; UF: uncertainty factor.

**2. Recommendation and Rationale**

The basis for the US EPA IRIS and ATSDR reference dose is liver toxicity in dogs chronically exposed to chloroform in gelatin capsules. The basis for the RIVM reference dose for chloroform is liver toxicity mice chronically exposed to chloroform in drinking water. A NOEL was not observed in either study. The lower LOEL in the dog study was dismissed in the RIVM derivation without a clear rationale provided in the limited documentation for that value. The dog study suggests that effects may occur at lower doses than the LOEL identified in the mouse study. Therefore, the US EPA IRIS and ATSDR reference dose (0.01 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for chloroform.

### 3. Review Dates

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

### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1997. Toxicological profile for chloroform. 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.

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: 07/27/01. Last revised: 10/19/01.  
<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.

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

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Agency for Toxic Substances and Disease Registry  
California Environmental Protection Agency  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

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**Chemical Name: Chloroform**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Cancer Potency Values for Chloroform (CAS Number 67-66-3)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	The US EPA states there is sufficient evidence to conclude that a non-genotoxic mode of action for carcinogenicity applies to chloroform. Based on a margin of exposure analysis, the chloroform RfD is considered protective for oral cancer risk.
Health Canada (1993)	$7.8 \times 10^{-4}$	-- <sup>2</sup>	linearized multistage model	body weight <sup>3</sup>	Based on increased renal tubular cell adenomas or adenocarcinomas (combined) observed in male rats exposed via drinking water for two years.
CA EPA (1990)	$3.2 \times 10^{-5}$	0.031	linearized multistage model, extra risk	body surface area <sup>4</sup>	Based on the geometric mean of 11 slope factors from several studies of the incidence of liver and kidney tumors in male and female mice and rats.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>No cancer potency factor was derived. The risk specific dose was obtained from the drinking water unit risk of  $3.64 \times 10^{-8}$  per microgram per liter, assuming a 70 kg person drinks 2 liters of water per

<sup>3</sup>Factor for dose adjustment from animal to humans is 1.

<sup>4</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

**2. Recommendation and Rationale**

The basis of the Health Canada cancer potency estimate is an increase in renal tubular cell adenomas or adenocarcinomas in rats exposed in drinking water for two years, while the CA EPA

cancer potency estimate is based on seven studies showing an increased incidence of liver and kidney tumors in rats and mice. The Health Canada potency estimate is based on a single data set, while CA EPA potency factor is based on the geometric mean of 11 data sets from seven studies, which may be a more robust and representative evaluation of the available dose response information. The Health Canada derivation also does not scale the experimental doses in going from animal to humans, while the CA EPA potency is based on body surface area scaling, which is more consistent with current risk assessment practices. The US EPA no longer recommends an oral cancer potency factor for chloroform because of evidence that suggests that chloroform-induced kidney and liver cancers in laboratory animals are the result of repeated cytotoxicity and regenerative cell proliferation in these target organs, and that these events occur only after high chloroform doses. Although sustained or repeated cytotoxicity with regenerative hyperplasia is probably a causal factor in animal cancers caused by chloroform, other modes of action (e.g., genotoxicity) could also contribute at lower doses, and these have not been rigorously investigated. Therefore, the CA EPA cancer potency factor (0.031 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for chloroform. The chloroform risk specific dose calculated from this toxicity value is  $3.2 \times 10^{-5}$  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). 1990. Proposed Identification of Chloroform as a Toxic Air Contaminant: Part B Health Assessment. Sacramento, CA: California Air Resources Board, California Environmental Protection Agency.  
<http://www.oehha.ca.gov/risk/pdf/Chlorofchp8.pdf>

Health Canada. 1993. 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>

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: 7/27/2001. Last revised: 10/19/01.  
<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

New York State Department of Health  
New York State Department of Environmental Conservation  
Agency for Toxic Substances and Disease 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: Chloroform**  
**Exposure Route: Inhalation**  
**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for Chloroform (CAS Number 67-66-3)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA Region 3 (2004a, b)	50	4.5 x 10 <sup>3</sup>	NOEL	100	Based on liver and kidney toxicity in mice exposed by inhalation for 6 hours/day, 5 days/week for up to 13 weeks. Study LOEL = 2.9 x 10 <sup>4</sup> mcg/m <sup>3</sup> .
ATSDR (1997)	100 (0.02 ppm)	9.8 x 10 <sup>3</sup> (2 ppm)	LOEL	100	Based on liver effects in 68 workers occupationally exposed to chloroform over one to four years.
CA EPA (2003)	300	7.8 x 10 <sup>4</sup> (16 ppm)	LOEL	300	Based on liver and kidney toxicity in rats exposed by inhalation for 7 hours/day, 5 days/week for 6 months.
RIVM (2001) TERA (2004)	100	1.1 x 10 <sup>5</sup>	NOEL	1000	Based on the same study as CA EPA; limited documentation.

<sup>1</sup>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 chloroform derived by authoritative bodies from the list in item 5 (below) are based on liver toxicity observed in workers exposed to chloroform in workplace air, and liver and kidney toxicity observed in mice and rats exposed to chloroform via inhalation. The CA EPA and RIVM based their derivations on a 6-month rat inhalation study. The CA EPA considered the lowest exposure level in that study a LOEL and converted that exposure level to a human equivalent air concentration by adjusting to a time-weighted continuous exposure that was then increased by a pharmacokinetic adjustment of 3-fold representing the ratio of rat:human blood:air partitioning coefficients. RIVM cites an earlier chloroform assessment without full documentation that identified the same exposure level in the rat study as a NOEL. The CA EPA conclusion that the lowest

exposure level represented a LOEL is confirmed by the review presented in US EPA Region 3 (2004b). Therefore, the RIVM analysis appears to be in error in this respect. RIVM equated the rat exposure level to an equivalent human exposure level with any adjustment for non-continuous exposure or pharmacokinetic variability. The CA EPA applied a total uncertainty factor of 300, including 10-fold to account for intraspecies variability, 3-fold to account for interspecies variability and 10-fold for use of a LOEL. RIVM applied a total uncertainty factor of 1000 that, as cited by TERA (2004), included 10-fold factors for intra- and interspecies variability and another 10-fold factor accounting for the adjustment from discontinuous to continuous exposure. Neither the CA EPA nor RIVM provided any justification for not including an uncertainty factor accounting for the use of a subchronic point of departure. In terms of estimating the human equivalent concentration and in terms of applying uncertainty factors, neither the CA EPA nor the RIVM derivations are entirely consistent with currently accepted risk assessment practice.

The ATSDR based their value on a human occupational study where workers were exposed to chloroform vapors for one to four years at concentrations that varied by approximately 100-fold. They considered the lower end of this range a LOEL for liver effects and applied a total uncertainty factor of 100 to that LOEL to account for intraspecies variability and the use of a LOEL.

The US EPA derivation is based on liver and kidney toxicity in a subchronic mouse inhalation study. The human equivalent NOEL was estimated from the mouse NOEL adjusted for continuous exposure and for pharmacokinetic variability by using the recommended default adjustment (equal to 1) for a systemic gas when the blood:air partitioning coefficient in animals is greater than the partitioning coefficient in humans. The US EPA applied a total uncertainty factor of 100, including 10-fold to account for intraspecies variability and 3-fold each to account for interspecies variability and database deficiencies including uncertainty regarding the potential for neurotoxicity as a sensitive effect in humans. An additional factor to account for use of a subchronic NOEL was considered unnecessary based on data indicating that effects following inhalation exposure are not strongly duration dependent.

The ATSDR and US EPA derivations are generally more consistent with currently-accepted risk assessment practice than the CA EPA and RIVM derivations. The animal data used by US EPA identified and accounts for effects on an additional tissue (kidney) not addressed by the occupational studies. Therefore the US EPA reference concentration (50 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chloroform.

### **3. Review Dates**

Summary table completion: July, 2004

Toxicity value recommendation: October, 2004

### **4. References for Summary Table**

ATSDR (Agency for Toxic Substances and Disease Registry). 1997. Toxicological Profile for chloroform. 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: Chloroform. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacramento, CA. [http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](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>

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

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

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004b. Risk assessment issue paper for: Derivation of provisional subchronic and chronic RfCs for chloroform (CASRN 67-66-3). SRC TR 02-085/1-22-03.

## **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: Chloroform**  
**Exposure Route: Inhalation**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Chloroform (CAS Number 67-66-3)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2004)	0.04	2.3 x 10 <sup>-5</sup>	linearized multistage model, extra risk	body surface area <sup>2</sup>	Based on route-to-route extrapolation from a single data set of hepatocellular carcinoma in female mice in a two-year oral gavage study.
CA EPA (2002)	0.2	5.3 x 10 <sup>-6</sup>	linearized multistage model, extra risk	PBPK estimate of internal dose metric or body surface area <sup>2</sup> depending on data set and study analysis	Based on route-to-route extrapolation of several oral cancer potency estimates from chronic oral studies in mice and rats, specifically incorporating the arithmetic average of unit risks for renal tumors in male rats from two different analyses of two different studies (four total unit risks) and the geometric mean for two different analyses of supporting data sets of renal tumors in male mice and liver tumors in female rats (an additional four total unit risks).

Health Canada (2004) and as detailed by TERA (2004)	7.4 x 10 <sup>5</sup> reported as lower bound on TC <sub>05</sub> <sup>3</sup> ; linear equivalent risk specific concentration = 14.8	-- <sup>4</sup>	--	PBPK estimate of internal dose metric	Based on the relationship between internal dose metrics derived via PBPK modeling and kidney tumor incidence in rats exposed for their lifetimes via drinking water. Benchmark dose modeling was used to derive the equivalent rate of metabolite formation in humans associated with a 5% increase in lifetime cancer risk and then a continuous inhalation exposure associated with the benchmark rate of metabolite formation was derived as the risk-specific concentration.
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<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> air concentration = 1 x 10<sup>-6</sup> / unit risk.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>TC<sub>05</sub> = The concentration in air (expressed in mcg/m<sup>3</sup>) associated with a 5% increase in incidence or mortality due to tumors.

<sup>4</sup>The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported, but would be equal to 1 x 10<sup>-6</sup> divided by the 10<sup>-6</sup> risk-specific concentration.

## 2. Recommendation and Rationale

The inhalation unit risks derived by authoritative bodies are all based on route-to-route extrapolation from studies of rats or mice orally exposed to chloroform. Increased incidence of liver tumors in mice and kidney tumors in rats was observed in these studies. The US EPA IRIS value is derived from liver tumor data in mice exposed by gavage while the CA EPA and Health Canada values are based on the incidence of kidney tumors in rats exposed by gavage or drinking water. The US EPA IRIS notes that their assessment, originally done in 1987, does not incorporate new data or more recent cancer risk-assessment guidelines and is currently being revised. The oral cancer risk assessment on IRIS reflects the conclusion that chloroform carcinogenicity results from a non-genotoxic mode of action involving regenerative hyperplasia following tissue necrosis. Therefore, an oral cancer potency factor is not derived and a margin of exposure analysis is presented supporting the oral reference dose (RfD) as being protective of increased cancer risk from chloroform exposure. The CA EPA value was derived from two combined analyses of four separate data sets. One analysis followed older default practices for animal to human dose scaling, while the other used PBPK-based scaling to develop human doses equivalent to rodent exposures in terms of an internal dose metric. Of the four data sets, two were considered as the primary dose-response data by CA EPA and two others were considered to be supporting data. No basis is provided for this distinction, and no basis is provided for the method used to combine the data sets, which entailed taking a geometric mean of the four derivations based on the supporting data sets and then combining, via an arithmetic mean, that geometric mean with the four derivations based on the primary data sets. The Health Canada derivation is based on one of the data sets considered as primary data by CA EPA and used PBPK modeling and a benchmark dose approach to estimate the lower bound on the air concentration associated with a 5% increased excess tumor

incidence. This derivation follows currently accepted risk assessment practice, but Health Canada did not explicitly report a unit risk or a  $10^{-6}$  risk-specific concentration based on their derivation. However, since the 95% lower bound on the  $TC_{05}$  is reported, a linear extrapolation to the  $10^{-6}$  risk-specific concentration is implied following currently accepted risk assessment practice by dividing the lower bound on the  $TC_{05}$  by 50,000. Dividing  $10^{-6}$  by the  $10^{-6}$  risk-specific concentration implied by the lower bound on the  $TC_{05}$  would yield the equivalent unit risk. Therefore, the Health Canada unit risk ( $6.8 \times 10^{-8}$  per  $mcg/m^3$ ) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for chloroform. The chloroform risk specific air concentration calculated from this toxicity value is  $14.8 mcg/m^3$ .

### 3. Review Dates

Summary table completion: July, 2004

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](http://www.oehha.ca.gov/air/cancer_guide/TSD2.html)

Health Canada, Environment Canada. 2004. Health Bases Guidance Values for Substances on the Second Priority Substances List. Health Canada. <http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl2.htm>

TERA (Toxicology Excellence for Risk Assessment). 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. Verification Date: 08/26/1987. Last revised: 10/19/2001. <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

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**Chemical Name: Chromium (III)**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for Inorganic Chromium (III)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA HEAST (1997)	1.5	1468	NOEL	1000	Based on the absence of toxic effects in male and female rats fed 5% Cr <sub>2</sub> O <sub>3</sub> baked in bread for 600 feedings (840 days) for an average total dose of 1800 g/kg. A LOEL was not identified. The NOEL was adjusted for continuous exposure and the molar fraction contribution of chromium (III) to Cr <sub>2</sub> O <sub>3</sub> . This RfD is limited to metallic chromium (III) of insoluble salts.
RIVM (2001)	5 x 10 <sup>-3</sup> (water soluble chromium compounds)	2.5 0.46	NOEL	500 100	Based on two chronic feeding study in rats with chromium compounds of varying water solubility (limited information available).
	5 (insoluble chromium compounds)	--	--	--	Based on RIVM's assertion that chronic NOELs for water insoluble chromium compounds are approximately 1,000 times higher than for soluble chromium compounds.

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

**2. Recommendation and Rationale**

Both chromium (III) reference doses are based on NOELs from chronic feeding studies in rats. There is a large degree of variation in NOEL (and therefore reference dose) estimates between the US EPA and RIVM because the toxicity in rodent feeding studies apparently varies substantially with the water solubility of the particular chromium compound being tested. The US EPA reference dose is only intended for assessment of exposure to insoluble chromium (III) salts. RIVM derived a value



specifically from a soluble form of chromium (III), and then extrapolated that result to a second reference dose for insoluble chromium compounds, based on an inference from available chronic rodent NOELs that insoluble forms were approximately 1000-fold less toxic than soluble forms. If chromium (III) is present in the form of soluble salts, or if the form of chromium (III) (and, therefore, its solubility) is unknown, then the RIVM reference dose for water-soluble compounds ( $5 \times 10^{-3}$  mg/kg/day) is the toxicity value recommended for use in the derivation of a non-cancer-based soil cleanup objective for chromium (III). If it is known that chromium (III) is present as insoluble salts, then the US EPA reference dose (1.5 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for insoluble chromium (III) salts.

### 3. Review Dates

Summary table completion: May, 2004

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, p 249-257.

<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: 04/28/98. Last revised: 09/03/98.

<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

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**Chemical Name: Chromium (III)**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for Inorganic Chromium (III)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (2000)	--	--	--	--	Human data are not available. Negative results for rats and mice have been reported in oral, inhalation, intrapleural injection, or intrabronchial implantation laboratory studies.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for chromium (III) is not available.\*

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

**3. Review Dates**

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

**4. References for Summary Table**

ATSDR (Agency for Toxic Substances and Disease Registry). 2000. Toxicological profile for chromium. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System).  
2004. Office of Research and Development, National Center for Environmental Assessment.  
Verification date: 04/28/98. Last revised: 09/03/98.  
<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

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**Chemical Name: Chromium (III)**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for Inorganic Chromium (III)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA IRIS (2004)	--	--	--	--	Data are considered to be inadequate for development of an RfC due to the lack of a relevant toxicity study addressing respiratory effects of chromium (III).
RIVM (2001)	60	600	NOEL	10	Based on kidney effects in workers occupationally exposed to metallic chromium. The reference concentration is intended only for metallic chromium and insoluble Cr(III) salts.

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

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

**2. Recommendation and Rationale**

The RIVM value is the only available reference concentration for chromium (III) derived by an authoritative body from the list in item 5 (below). Therefore the RIVM reference concentration (60 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chromium(III).

**3. Review Dates**

Summary table completion: September, 2004

Toxicity value recommendation: October, 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/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. Last revised: 09/03/1998. <http://www.epa.gov/iris/index.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

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**Chemical Name: Chromium (III)**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Inorganic Chromium (III)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	The data from inhalation exposures of animals to trivalent chromium do not support determination of the carcinogenicity of trivalent chromium.

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

**2. Recommendation and Rationale**

An inhalation unit risk for chromium (III) is not available.\*

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

**3. Review Dates**

Summary table completion: September, 2004

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: 09/03/1998  
<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: Chromium (VI)**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for Inorganic Chromium (VI)**

Agency	Reference Dose <sup>1</sup> (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)	$3 \times 10^{-3}$	2.5	NOEL	900 <sup>2</sup>	Based on a lack of adverse effects in male and female rats given chromium as K <sub>2</sub> CrO <sub>4</sub> in a 1-year drinking water study. A LOEL was not observed. This reference dose is limited to soluble salts of chromium (VI).
RIVM (2001)	$5 \times 10^{-3}$	2.5	NOEL	500	Based on the same study as US EPA IRIS (2004).

<sup>1</sup>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.

<sup>2</sup>Includes modifying factor (see Recommendation and Rationale, below).

**2. Recommendation and Rationale**

The basis for the two reference doses for chromium (VI) are essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (2.5 mg/kg/day). Both derivations include 100-fold uncertainty factors accounting for interspecies and intraspecies variability. RIVM applied an additional 5-fold uncertainty factor to account for the less-than-lifetime exposure (1 year vs. 2 years), while the US EPA used a 3-fold factor to account for the uncertainty associated with less-than-lifetime dosing. The US EPA also included a modifying factor of 3 to account for uncertainty raised by an epidemiologic study in China suggesting chronic exposure to chromium (VI) in drinking water could be associated with gastrointestinal effects in humans. The additional modifying factor in the US EPA derivation is consistent with current risk assessment practice. Therefore, the US EPA reference dose ( $3 \times 10^{-3}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for chromium (VI).

### 3. Review Dates

Summary table completion: May, 2004

Toxicity value recommendation: June, 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/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: 04/28/98. Last revised: 09/03/98. <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: Chromium (VI)**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for Inorganic Chromium (VI)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	No data were located in the available literature that suggests chromium (VI) is carcinogenic by the oral route of exposure.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for chromium (VI) for oral exposure 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**

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: 04/28/98. Last revised: 09/03/98. <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

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**Chemical Name: Chromium (VI)**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for Inorganic Chromium (VI)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA IRIS (2004)	8.0 x 10 <sup>-3</sup>	0.714	LOEL	90	Based on nasal septum atrophy in workers exposed in chrome plating plants. The reference concentration applies to chromic acid mists and dissolved chromium (VI) aerosols.
	0.1	34	BMCL <sub>10</sub> <sup>2</sup>	300	Based on increased lung and spleen weight and several indicators of toxic effects on the lower respiratory system in bronchioalveolar lavage fluid in rats from two studies exposed to sodium dichromate particulate aerosols for 90 days. The reference concentration applies to chromium (VI) particulates.
CA EPA (2003)	0.2	24.5	BMCL <sub>05</sub> <sup>2</sup>	100	Based on the same rat studies as the US EPA IRIS reference concentration for chromium (VI) particulates. This reference concentration is intended to apply to soluble hexavalent chromium compounds other than chromic acid.

	$2 \times 10^{-3}$	0.68	LOEL	300	Based on the same human study as the US EPA IRIS reference concentration for chromium (VI) chromic acid mists and dissolved aerosols. This reference concentration is intended to apply to chromium trioxide as chromic acid mist.
TERA (2004)	0.3	80	BMCL <sup>2,3</sup>	300	Based on the same rat studies as the US EPA IRIS reference concentration for chromium (VI) particulates. This reference concentration is intended to apply to chromium particulates.

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

<sup>2</sup>BMCL<sub>x</sub>: benchmark concentration – the lower 95% confidence limit on the dose corresponding to a x% relative change in the endpoint compared to the control.

<sup>3</sup>Whether TERA’s BMCL represents a level associated with a 5 or 10% incremental increase in the modeled effect is not clearly presented in their documentation, but the range of BMCL values is the same as the range presented by US EPA IRIS for their BMCL<sub>10</sub> estimates, suggesting TERA’s estimates are also BMCL<sub>10s</sub>.

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

## 2. Recommendation and Rationale

The reference concentrations for chromium (VI) derived by authoritative bodies from the list in item 5 (below) are based on data from occupational studies and inhalation studies in rats. The US EPA has derived separate reference concentrations for particulate chromium (VI) aerosols and for chromic acid mists and other soluble chromium (VI) aerosols. TERA’s reference concentration is specifically for hexavalent chromium particulates. The CA EPA derived two reference concentrations, based on the same rat and human studies used for the two US EPA IRIS derivations, but one is specified for chromic acid mists and the other is for other hexavalent chromium soluble compounds. Thus, the CA EPA has not presented a reference concentration specifically for evaluation of chromium (VI) particulates, although their derivation of the value for dissolved hexavalent chromium compounds other than chromic acid is very similar to the US EPA and TERA derivations for particulate hexavalent chromium and includes a pharmacokinetic adjustment based on relative particulate deposition in the respiratory tract of rats and humans. The particulate reference concentrations are the only values relevant to exposure scenarios involving contaminated soil, so the US EPA and CA EPA chromic acid values are not considered further. The three values based on lower respiratory tract and immune system toxicity and increased spleen weight in rats exposed via inhalation for 90 days all are based on benchmark concentration estimates for a large number of quantitative endpoints measured in two related studies. The US EPA used the lowest BMCL<sub>10</sub> estimate from the various endpoints as their point of departure, and the CA EPA used a single BMCL<sub>05</sub> estimate for their point of departure, although whether or not this was the lowest value is unclear from their documentation. TERA based their value on the arithmetic average of all the BMCLs they estimated. TERA’s documentation does not specify whether their estimates are BMCL<sub>05s</sub> or BMCL<sub>10s</sub>, but the reported range of BMCLs is the same as the range reported by US EPA, suggesting the TERA value is an arithmetic mean of BMCL<sub>10s</sub>. All three derivations used the same pharmacokinetic adjustment to account for relative particulate deposition in

the lower respiratory tract of rats versus humans. The US EPA and TERA both applied a total uncertainty factor of 300, including 10-fold to account for intraspecies variability, 10-fold to account for use of a subchronic study and 3-fold to account for interspecies variability. The CA EPA derivation included a total uncertainty factor of 100, which differed from the other derivations only in the use of a 3-fold factor accounting for use of a subchronic study. The US EPA noted that data from one of the 90-day rat studies indicated that particles were still accumulating in the lung at the end of the study, suggesting that longer exposure duration could result in reaching a critical concentration in the lung. They also suggest that subchronic studies may not adequately predict inflammatory effects in the lung associated with chronic exposure. Therefore, the use of a 10-fold factor to account for uncertainties associated with a subchronic point of departure appears justified. The US EPA chose to use the lowest BMCL as their point of departure, while TERA used the arithmetic mean of all the BMCL estimates. The BMCL estimates range by more than 3-fold from lowest to highest, and so, based on US EPA benchmark dose default guidance, the BMCL shows some model dependence that should be accounted for by using the lowest BMCL estimate as the point of departure. Therefore the US EPA reference concentration (0.1 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chromium (VI).

### **3. Review Dates**

Summary table completion: September, 2004

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 Hexavalent Chromium (Soluble Compounds). Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency.

[http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html)

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: 04/28/1998. Last revised: 09/03/1998. <http://www.epa.gov/iris/index.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

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**Chemical Name: Chromium (VI)**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Inorganic Chromium (VI)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	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)	8 x 10 <sup>-5</sup>	0.012	multistage model, extra risk	--	Based on the incidence of lung cancer in a combined cohort of 332 workers. The original study assumed cancer mortality was due to chromium (VI), which was further assumed to be no less than one-seventh of total chromium. However, the unit risk derivation is based on total chromium exposure.
CA EPA (2002)	6.7 x 10 <sup>-6</sup>	0.15	linearized multistage model, extra risk	--	Based on the same study as US EPA IRIS (2004). CA EPA reports that their unit risk estimate is an upper bound from a multistage linearized “crude” procedure, whereas the US EPA derivation is a maximum likelihood estimated from a multistage “competing risks” analysis.
Health Canada (1993)	0.66 reported as a TC <sub>05</sub> <sup>2</sup> ; linear equivalent risk specific concentration = 1.3 x 10 <sup>-5</sup>	-- <sup>3</sup>	--	--	Based on the same study as US EPA IRIS (2004). The TC <sub>05</sub> is derived for chromium (VI) assuming that is 1/7 <sup>th</sup> of total chromium and assumes no competing causes of

					death.
NYS DOH (1990)	$2 \times 10^{-5}$	0.05	linear average relative risk model	--	Based on the same study as US EPA IRIS (2004). The unit risk is based on analytical data indicating that 21% of the total chromium in facility air was chromium (VI).
WHO (2000)	$2.5 \times 10^{-5}$	0.04	--	--	Based on several occupational cohort studies of chromate workers not including the study cohort used by US EPA. The unit risk is the geometric mean of four estimates that span about 1 order of magnitude.
RIVM (2001)	$2.5 \times 10^{-5}$	0.04	--	--	Based on the same derivation used by WHO.

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

<sup>2</sup>TC<sub>05</sub> = The concentration in air (expressed in mcg/m<sup>3</sup>) associated with a 5% increase in incidence or mortality due to tumors. The TC<sub>05</sub> represents a maximum likelihood estimate rather than a lower-bound estimate.

<sup>3</sup>The risk estimate was only reported as a risk-specific concentration; a unit risk was not explicitly reported, but would be equal to  $1 \times 10^{-6}$  divided by the  $10^{-6}$  risk-specific concentration.

## 2. Recommendation and Rationale

The inhalation unit risks derived by authoritative bodies are all based on increased incidence of lung cancer in cohort studies of chromium industry workers. The US EPA, CA EPA, NYS DOH and Health Canada derivations are all based on the same cohort analysis but use differing procedures to derive their unit risk or risk-specific concentration values. The WHO (and RIVM) value is derived from analyses of four other occupational cohort data sets. The US EPA considered some of the studies used by the WHO as possible sources of dose-response data and concluded that there were significant deficiencies with the exposure data available from those studies, which precluded their use in deriving a unit risk. The Health Canada value is a modeled maximum likelihood estimate of the exposure level associated with a 5% increased tumor incidence and so does not represent a lower-bound exposure estimate, but could be used as the basis of a linear extrapolation to a maximum likelihood  $10^{-6}$  risk-specific air concentration. The CA EPA (2002) and the US EPA analyses differ in that the US EPA unit risk is a maximum likelihood estimate rather than an upper-bound and the US EPA analysis takes competing causes of mortality into account while the CA EPA “crude” analysis assumes no competing causes of mortality. Both differences contribute to a more conservative CA EPA unit risk estimate, although US EPA showed that the difference between the crude and competing mortality derivations was small. The NYS DOH derivation makes use of chromium (VI) analytical data for the same chromium facility and

cohort considered in the US EPA, CA EPA and Health Canada derivations. The result is a unit risk based specifically on the species of interest (chromium (VI)). Therefore, the NYS DOH unit risk (0.05 per mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for chromium (VI). The chromium (VI) risk specific airconcentration calculated from this toxicity value is  $2 \times 10^{-5}$  mcg/m<sup>3</sup>.

### 3. Review Dates

Summary table completion: September, 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](http://www.oehha.ca.gov/air/cancer_guide/TSD2.html)

Health Canada. 1993. Priority Substances List Assessment Report: Chromium and its compounds. 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). 1990. Ambient Air Criteria Document for Chromium. Bureau of Toxic Substance Assessment. Albany, NY: New York State Department of Health.

RIVM. 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: 04/28/1998. Last revised: 09/03/1998. <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.), Chapter 6.4, Chromium. World Health Organization, Copenhagen, Denmark. [http://www.euro.who.int/air/Activities/20020620\\_1](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

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**Chemical Name: Chrysene**  
**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 Chrysene (CAS Number 218-01-9)**

Agency	Reference Dose <sup>1</sup> (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.

<sup>1</sup>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 chrysene 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 chrysene with respect to noncancer endpoints. The basis for choosing pyrene as a chemical surrogate for chrysene 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 chrysene (see Oral Non-Cancer Toxicity Value Documentation for pyrene).

**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). 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

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**Chemical Name: Chrysene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Cancer Potency Values for Chrysene (CAS Number 218-01-9)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	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 carcinogenicity was observed in several inadequate studies in animals exposed dermally or by intraperitoneal injection.
US EPA OSRTI (2004) US EPA Region 3 (2003)	$1.37 \times 10^{-4}$	0.0073	--	--	Based on a relative potency factor of 0.001 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.
CA EPA (2002)	$8.33 \times 10^{-6}$	0.12	--	--	Based on a potency equivalency factor of 0.01 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)	$5.0 \times 10^{-4}$	-- <sup>2</sup>	--	--	Based on a potency equivalency factor of 0.01 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).
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<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>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 chrysene 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 (0.01) yields a cancer potency factor 0.0903 per mg/kg/day, which is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for chrysene (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The chrysene risk specific dose calculated from this toxicity value is  $1.1 \times 10^{-5}$  mg/kg/day.

## 3. Review Dates

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

NCEA (National Center for Environmental Assessment). 2004. Provisional Peer-Reviewed Toxicity Values (PPRTVs) Database, Office of Superfund Remediation and Technology Innovation. <http://hhpprtv.ornl.gov>.



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/subst/0408.htm>.

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

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**Chemical Name: Chrysene**  
**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 Chrysene (CAS Number 218-01-9)**

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

<sup>1</sup>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 chrysene is not available from the authoritative bodies listed in item number 5 (below). Chrysene 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<sup>3</sup> 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<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for chrysene.

**3. Review Dates**

Summary table completion: February, 2005  
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: Chrysene**  
**Exposure Route: Inhalation**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Chrysene (CAS Number 218-01-9)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2002)	9.1 x 10 <sup>-2</sup>	1.1 x 10 <sup>-5</sup>	--	--	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 0.01. The PEF for chrysene is based on its ability (relative to benzo[a]pyrene) to induce skin cancer in mice on dermal application.
--	9.1 x 10 <sup>-2</sup>	1.1 x 10 <sup>-5</sup>	--	--	Based on the CA EPA unit risk for benzo[a]pyrene and application of the recommended relative potency factor of 0.01.

<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> air concentration), where 1 x 10<sup>-6</sup> concentration = 1 x 10<sup>-6</sup> / inhalation unit risk.

**2. Recommendation and Rationale**

The unit risk values for chrysene are based on benzo(a)pyrene and the application of relative potency factors. The recommended unit risk value for benzo(a)pyrene is 1.1 x 10<sup>-3</sup> per mcg/m<sup>3</sup> (see Inhalation Cancer Toxicity Value Documentation for benzo(a)pyrene). Application of the recommended relative potency factor (0.01) yields a unit risk of 1.1 x 10<sup>-5</sup> per mcg/m<sup>3</sup>, which is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for chrysene (see Chapter 5.1.5 of technical support document for discussion of recommended relative

potency factors). The chrysene risk specific air concentration calculated from this toxicity value is  $9.1 \times 10^{-2}$  mcg/m<sup>3</sup>.

### 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](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

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

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

**1. Summary of Available Oral Reference Doses for Inorganic Copper**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA HEAST (1997)  Also used by: ♦ US EPA Region 3 (2003)	0.04	0.08	LOEL	2	Based on current US EPA action level for copper in drinking water of 1.3 mg/L, which was derived from a LOEL of 5.3 mg/person (0.08 mg/kg/day for a 70-kg person) from a single dose oral study reporting gastrointestinal irritation. The allocation of all the dose to water, and the assumption of water consumption rate of 2 L/day
RIVM (2001)	0.14	--	--	--	Equal to the RIVM derived maximum daily copper intake of the (Dutch) population.
IOM (2001)	0.14	0.14	NOEL	1	Based on absence of liver effects in 7 adults (assumed weight of 70 kg) who ingested 10 mg copper daily (as copper gluconate) during a 12-week study

<sup>1</sup>Agencies use different terms for the reference dose, including acceptable daily intake and chronic minimal risk level. LOEL: lowest observed effect level; UF: uncertainty factor.

**2. Recommendation and Rationale**

The basis for the US EPA and RIVM reference dose values are not well documented. The US EPA drinking water action level (and the HEAST reference dose) are based on a report (Wyllie, 1975) of

gastrointestinal irritation in women who consumed a copper-contaminated beverage (a cocktail containing alcohol). A review of the report, however, reveals potential confounding factors and significant uncertainties in dose estimates that seriously weaken confidence in the derived reference dose. The RIVM value appears to be an exposure-based, rather than health-effect-based reference dose.

The IOM (2001) considered a large uncertainty factor unnecessary given the large international database in humans indicating no adverse effects from daily consumption of 10 to 20 mg/day of copper in foods and the rarity of observed liver damage from copper exposure in human populations with normal homeostatic mechanisms for regulation the uptake and excretion of copper. Moreover, copper is an essential element, and the routine application of traditional uncertainty factor leads to reference doses that are below those doses needed for nutritional needs (NRC, 2000). Therefore, the IOM (2001) reference dose (0.14 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for copper.

### **3. Review Dates**

Summary table completion: February, 2005

Toxicity value recommendation: February, 2005

### **4. References for Summary Table**

IOM (Institute of Medicine). 2001. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington, DC: National Academy Press.

NRC (National Research Council). 2000. Copper in Drinking Water. Washington, DC: National Academy Press.

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

US EPA HEAST (United States Environmental Protection Agency Health Effects Assessment Summary Tables). 1997. FY 1997 Update. Document No. 9200.6-303 997-1. Washington, DC: Office of Research and Development, Office of Emergency and Remedial Response.

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

Wyllie, J. 1957. Copper poisoning at a cocktail party. *Am. J. Public Health.* 47:617.

### **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: Copper**  
**Exposure Route: Oral**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for Inorganic Copper**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	There are no human data and inadequate animal data on the potential carcinogenicity of copper compounds.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for copper is not available.\*

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

**3. Review Dates**

Summary table completion: May, 2004  
 Toxicity value recommendation: June, 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: 9/15/87. Last revised: 8/1/91. <http://www.epa.gov/iris/index.html>.

United States Environmental Protection Agency  
Integrated Risk Information System  
National Center for Environmental Assessment  
Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed  
Toxicity Values)  
Region 3 Risk-Based Concentrations  
Office of Pesticides  
Office of Drinking Water  
Health Effects Assessment Summary Tables  
New York State Department of Health  
New York State Department of Environmental Conservation  
Agency for Toxic Substances and Disease 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: Copper**  
**Exposure Route: Inhalation**  
**Toxicity: Non-cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for Inorganic Copper**

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

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

**2. Recommendation and Rationale**

An inhalation reference concentration for copper is not available from the authoritative bodies listed in item number 5 (below). Copper is a toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for copper is 0.14 mg/kg/day. Therefore, a reference concentration of 490 mcg/m<sup>3</sup> based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for copper.

**3. Review Dates**

Summary table completion: February, 2005  
 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  
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Toxicity Values)  
Region 3 Risk-Based Concentrations  
Office of Pesticides  
Office of Drinking Water  
Health Effects Assessment Summary Tables  
New York State Department of Health  
New York State Department of Environmental Conservation  
Agency for Toxic Substances and Disease 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: Copper**  
**Exposure Route: Inhalation**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Inorganic Copper**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for copper is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005  
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: Cyanide**  
**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 Free Cyanide (CAS Number 57-12-5)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA Region 3 (2003)</li> <li>◆ US EPA HEAST (1997)</li> <li>◆ CA EPA (1997)</li> <li>◆ NYS DEC (1997)</li> </ul>	0.02 (as CN <sup>-</sup> )	10.8	NOEL	500	The NOEL is the highest dose tested in a 2-year dietary study in male and female rats.  A later subchronic to chronic oral exposure study observed weight loss, thyroid effects, and myelin degeneration in rats with a LOEL = 30 mg/kg/day.
RIVM (2001)	0.05 (as CN <sup>-</sup> )	5	NOEL	100	Based on the same study as US EPA IRIS, except that the NOEL was determined to be 5 mg/kg/day.
WHO (1996)	0.012 (as CN <sup>-</sup> )	1.2	LOEL	100	Based on behavioral changes and reduced serum thyroid hormone levels in pigs exposed via gavage for 6 months

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

**2. Recommendation and Rationale**

The basis for the US EPA IRIS and RIVM reference doses for cyanide is identical with respect to choice of study and species, but the presence or absence of effects at the two non-zero doses in the study has been interpreted differently. There were no toxic effects observed in the study, and the US EPA and NYS DEC considered the higher dose a NOEL. However RIVM (based on an earlier WHO analysis) noted that increased cyanide metabolites were observed in blood at the higher dose and considered the lower dose the NOEL. The limited RIVM documentation does not fully support this decision, as the appearance of increased cyanide metabolites in the blood is a reflection of detoxification of the increased cyanide dose and would not necessarily suggest an increased risk for toxicity below exposure levels where the metabolic pathway is saturated. No other effects were observed at the higher dose. The WHO reference dose is based on a more recent analysis of a six-month study in pigs where the only effects observed were decreased serum thyroid hormone levels at

all non-zero doses and behavioral changes (increasing ambivalence and slower response times to stimuli) at the highest dose, which was identified as the LOEL. Although WHO based their derivation on this study, they raised questions about the biological significance of the observed effects and only applied a total uncertainty factor of 100 to account for interspecies and intraspecies variability, in effect treating the highest dose tested equivalent to a chronic NOEL. The study is limited for use in deriving a chronic oral exposure reference dose as the animals were starved and were exposed by gavage. Bolus dosing greatly increases the potential for detoxification enzymes to be overwhelmed resulting in higher systemic doses of free cyanide than would occur with drinking water or dietary exposure at the same daily dose rate. The US EPA included a modifying factor of 5 in their derivation to account for the reduced effect of cyanide exposure in food compared to drinking water. Based on the US EPA interpretation of the NOEL and the additional accounting of uncertainty in the US EPA derivation, 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 cyanide.

### 3. Review Dates

Summary table completion: May, 2004

Toxicity value recommendation: September, 2004

### 4. References for Summary Table

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

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for Cyanide. 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 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: 08/05/85. Last revised: 02/01/93. <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>

WHO (World Health Organization). 1996. Guidelines for drinking water quality, 3<sup>rd</sup> Ed. World Health Organization, Geneva. [http://www.who.int/docstore/water\\_sanitation\\_health/GDWQ/Chemicals/chemicalsindex.htm](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

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

**New York State Department of Health**  
**Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for Free Cyanide (CAS Number 57-12-5)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
	--	--	--	--	No values or reviews were found in any of the listed sources.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for cyanide is not available.\*

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

**3. Review Dates**

Summary table completion: May, 2004  
 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

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**Chemical Name: Cyanide**  
**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 Cyanide (CAS Number 57-12-5)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
RIVM (2001)	25	2.5 x 10 <sup>3</sup>	LOEL	100	Based on CNS and thyroid effects in workers exposed by inhalation. The LOEL (7 x 10 <sup>3</sup> mcg/m <sup>3</sup> ) was adjusted to account for occupational ventilation rates and continuous exposure.

<sup>1</sup>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 RIVM value is the only available reference concentration for cyanide from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore the RIVM reference concentration (25 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for cyanide.

**3. Review Dates**

Summary table completion: September, 2004

Toxicity value recommendation: October, 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

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

**New York State Department of Health**  
**Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Inorganic Cyanide**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
--	--	--	--	--	Cancer potency values for inhalation were not available.

<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  concentration =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An inhalation unit risk for cyanide is not available.\*

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

**3. Review Dates**

Summary table completion: September, 2004

Toxicity value recommendation: October, 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  
Division of Drinking Water and Environmental Management  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

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**Chemical Name: p,p'-Dichlorodiphenyldichloroethane (4,4'-DDD)**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for p,p'-Dichlorodiphenyldichloroethane (DDD)  
(CAS Number 72-54-8)**

Agency	Reference Value <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
RIVM (2000)	$5 \times 10^{-4}$	0.05	NOEL	100	Based on liver lesions in rats fed commercial grade DDT in corn oil mixed with powdered food for 27 weeks. DDD is structurally similar to and is a metabolite of DDT. Study LOEL = 0.25 mg/kg/day.

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

**2. Recommendation and Rationale**

The RIVM value is the only available reference dose for p,p'-DDD from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore the RIVM reference dose ( $5 \times 10^{-4}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for p,p'-DDD.

**3. Review Dates**

Summary table completion: March, 2004  
Toxicity value recommendation: June, 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, p 249-257. <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  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

**Chemical Name: p,p'-Dichlorodiphenyldichloroethane (4,4'-DDD)**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for p,p'-Dichlorodiphenyldichloroethane (DDD)  
(CAS Number 72-54-8)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) Also used by: ♦ CA EPA (2004)	4.2 x 10 <sup>-5</sup>	0.24	Linearized multistage model, extra risk	body surface area <sup>2</sup>	Cancer potency factor based on increased incidence of liver tumors in male mice exposed to DDD in their diets for 130 weeks.
NYS DEC (1997)	8.0 x 10 <sup>-6</sup>	0.125	Linearized multistage model, extra risk	BW <sup>3/4</sup> <sup>3</sup>	Based on the same tumor incidence data as the US EPA IRIS cancer potency factor.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.25</sup>.

**2. Recommendation and Rationale**

The basis of the cancer potency factors derived by authoritative bodies is identical with respect to study, species, critical effect and tumor incidence data. The only difference between the values is the use of body surface area scaling for interspecies extrapolation by the US EPA and BW<sup>3/4</sup> scaling by the NYS DEC. The latter method is more consistent with currently accepted risk assessment practice. Therefore, the NYS DEC cancer potency factor (0.125 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for p,p'-DDD. The p,p'-DDD risk specific dose calculated from this toxicity value is 8.0 x 10<sup>-6</sup> mg/kg/day.

**3. Review Dates**

Summary table completion: February, 2004

Toxicity value recommendation: June, 2004

#### 4. References for Summary Table

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>

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

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 06/24/87. Last revised: 08/22/88. <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  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

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**Chemical Name: p,p'-Dichlorodiphenyldichloroethane (4,4'-DDD)**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for p,p'-Dichlorodiphenyldichloroethane (DDD) (CAS Number 72-54-8)**

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

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

**2. Recommendation and Rationale**

An inhalation reference concentration for p,p'-DDD is not available from the authoritative bodies listed in item number 5 (below). DDD is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for p,p'-DDD is 5 x 10<sup>-4</sup> mg/kg/day. Therefore, a reference concentration of 1.8 mcg/m<sup>3</sup> based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for p,p'-DDD.

**3. Review Dates**

Summary table completion: February, 2005  
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: p,p'Dichlorodiphenyldichloroethane (4,4'-DDD)**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for p,p'Dichlorodiphenyldichloroethane (DDD)  
(CAS Number 72-54-8)**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for p,p'-DDD is not available from the authoritative bodies listed in item number 5 (below). DDD is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral cancer potency factor based on cancer effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a unit risk from the cancer potency factor. The recommended oral cancer potency factor for p,p'-DDD is 0.125 per mg/kg/day. Therefore, a unit risk of  $3.6 \times 10^{-5}$  per mcg/m<sup>3</sup> based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for p,p'-DDD. The risk specific air concentration calculated from this toxicity value is 0.028 mcg/m<sup>3</sup>.

**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: p,p'-Dichlorodiphenyldichloroethylene (4,4'-DDE)**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for p,p'-Dichlorodiphenyldichloroethylene (DDE)  
(CAS Number 72-55-9)**

Agency	Reference Value <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
RIVM (2000)	5 x 10 <sup>-4</sup>	0.05	NOEL	100	Based on liver lesions in rats fed commercial grade DDT in corn oil mixed with powdered food for 27 weeks. DDE is structurally similar to and is a metabolite of DDT. Study LOEL = 0.25 mg/kg/day.
NYS DEC (1997)	0.012	12	LOEL	1000	Based on liver effects (centrilobular necrosis) in rats in a 78-week dietary study.
ATSDR (2002)	--	--	--	--	Toxicity studies reviewed, but a chronic reference value was not derived.

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

**2. Recommendation and Rationale**

The basis of the NYS DEC reference dose for p,p'-DDE is liver toxicity in a chronic rat feeding study. The RIVM value is derived based on structural similarity of p,p'-DDE to p,p'-DDT, the presumption that structurally similar chemicals have similar toxic effects, and DDE's relationship as a metabolite of DDT. The NYS DEC value is based on chemical specific information. In addition, the study used by the NYS DEC (NCI, 1978) exposed the animals for a larger portion of their lifetimes than the study used by RIVM. Therefore, the NYS DEC reference dose (0.012 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for p,p'-DDE.

**3. Review Dates**

Summary table completion: April, 2005

Toxicity value recommendation: September, 2004



#### 4. References for Summary Table

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

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

NCI (National Cancer Institute). 1978. Bioassays of DDT, TDE and p,p'-DDE for possible carcinogenicity. US Department of Health Education and Welfare, Public Health Service, National Institutes of Health. NCI-CG-TR-131.

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

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

<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

Health Canada

World Health Organization

National Institute of Public Health & Environmental Protection, Netherlands

**Chemical Name: p,p'-Dichlorodiphenyldichloroethylene (4,4'-DDE)**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for p,p'-Dichlorodiphenyldichloroethylene (DDE) (CAS Number 72-55-9)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2003) ♦ CA EPA (2004)	2.9 x 10 <sup>-6</sup>	0.34	Linearized multistage model, extra risk	body surface area <sup>2</sup>	The cancer slope factor is the geometric mean of six slope factors from three different dietary studies. The studies observed hepatocellular carcinomas and hepatomas in both sexes of mice after 78 and 130 weeks of DDE dietary exposure, respectively, and an increase in liver neoplastic nodules in both sexes of hamsters after 128 weeks dietary exposure to DDE.
NYS DEC (1997)	5.4 x 10 <sup>-6</sup>	0.185	Linearized multistage model, extra risk	BW <sup>3/4</sup> <sup>3</sup>	Slope factor based on same studies as US EPA.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.25</sup>.

**2. Recommendation and Rationale**

The basis of the cancer potency factors derived by authoritative bodies is identical with respect to study, species, critical effect and tumor incidence data. The only difference between the values is the use of body surface area scaling for interspecies extrapolation by the US EPA and BW<sup>3/4</sup> scaling by the NYS DEC. The latter method is more consistent with currently accepted risk assessment practice. Therefore, the NYS DEC cancer potency factor (0.185 per mg/kg/day) is the toxicity value

recommended for use in the derivation of an oral cancer-based soil cleanup objective for p,p'-DDE. The p,p'-DDE risk specific dose calculated from this toxicity value is  $5.4 \times 10^{-6}$  mg/kg/day.

### 3. Review Dates

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

### 4. References for Summary Table

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>

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

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 06/24/87. Last revised: 08/22/88. <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  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

**Chemical Name: p,p'-Dichlorodiphenyldichloroethylene (4,4'-DDE)**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for  
p,p'-Dichlorodiphenyldichloroethylene (DDE) (CAS Number 72-55-9)**

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

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

**2. Recommendation and Rationale**

An inhalation reference concentration for p,p'-DDE is not available from the authoritative bodies listed in item number 5 (below). DDE is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for p,p'-DDE is 0.012 mg/kg/day. Therefore, a reference concentration of 42 mcg/m<sup>3</sup> based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for p,p'-DDE.

**3. Review Dates**

Summary table completion: February, 2005  
Toxicity value recommendation: April, 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: p,p'-Dichlorodiphenyldichloroethylene (4,4'-DDE)**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for p,p'-Dichlorodiphenyldichloroethylene (DDE)  
(CAS Number 72-55-9)**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for p,p'-DDE is not available from the authoritative bodies listed in item number 5 (below). DDE is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral cancer potency factor based on cancer effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a unit risk from the cancer potency factor. The recommended oral cancer potency factor for p,p'-DDE is 0.185 per mg/kg/day. Therefore, a unit risk of  $5.3 \times 10^{-5}$  per mcg/m<sup>3</sup> based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for p,p'-DDE. The risk specific air concentration calculated from this toxicity value is 0.019 mcg/m<sup>3</sup>.

**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: p,p'-Dichlorodiphenyltrichloroethane (4,4'-DDT)**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for p,p'-Dichlorodiphenyltrichloroethane (DDT)  
(CAS Number 50-29-3)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: ♦ US EPA HEAST (1997) ♦ US EPA Region 3 (2003)	$5 \times 10^{-4}$	0.05	NOEL	100	Based on liver lesions in rats fed commercial grade DDT in corn oil mixed with powdered food for 27 weeks. Study LOEL = 0.25 mg/kg/day.
NYS DEC (1997)	$5 \times 10^{-4}$	0.05	NOEL	100	Based on same data used to derive US EPA IRIS value
ATSDR (2002)	$5 \times 10^{-4}$	0.05	NOEL	100	Based on same data used to derive US EPA IRIS value
RIVM (2001)	$5 \times 10^{-4}$	0.05	NOEL	100	Based on same data used to derive US EPA IRIS value

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

**2. Recommendation and Rationale**

The basis for the various reference doses for DDT (and the reference doses themselves) are identical with respect to choice of study, species, adverse effect and identification of the point of departure (0.05 mg/kg/day). Therefore, the US EPA reference dose ( $5 \times 10^{-4}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for DDT.

**3. Review Dates**

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



#### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2002. Toxicological Profile for DDT, DDE, DDD. U.S. Department of Health and Human Services, Public Health Service. <http://www.atsdr.cdc.gov/toxprofiles/tp35.html>

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

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001. <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. Agency verification date: 12/18/1985. Last revised: 02/01/1996. <http://www.epa.gov/iris/subst/0147.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 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: p,p'-Dichlorodiphenyltrichloroethane (4,4'-DDT)**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for p,p'-Dichlorodiphenyltrichloroethane (DDT)  
(CAS Number 50-29-3)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ EPA Region 3 (2004) ♦ CA EPA (2004)	2.9 x 10 <sup>-6</sup>	0.34	linearized multistage model, extra risk	body surface area <sup>2</sup>	Based on hepatocellular adenomas and carcinomas and malignant lung tumors in two rat and four mouse studies where animals were exposed in their diet for their lifetime or for multiple generations (two of the mouse studies). The potency factor is the geometric mean of 10 individual values.
NYS DEC (1997)	5.3 x 10 <sup>-6</sup>	0.189	linearized multistage model, extra risk	BW <sup>3/4</sup> <sup>3</sup>	Value was based on same studies used by EPA IRIS.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.25</sup>.

**2. Recommendation and Rationale**

All the cancer potency factors derived by authoritative bodies are based on the same set of 10 cancer potency factors derived from six feeding studies in mice and rats showing an increased incidence of liver and lung tumors. The US EPA IRIS value is a geometric mean of the 10 individual values. The NYS DEC value differs only in applying BW<sup>3/4</sup> scaling rather than body surface area scaling to convert the rodent potency factor to a human potency factor. Since that methodology is more

consistent with currently accepted risk assessment practice, the NYS DEC cancer potency factor (0.189 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for DDT. The DDT risk specific dose calculated from this toxicity value is  $5.3 \times 10^{-6}$  mg/kg/day.

### 3. Review Dates

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

### 4. References for Summary Table

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>

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

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment.  
<http://www.epa.gov/iris/subst/0147.htm>

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Agency verification date: 06/24/1987. Last revised: 05/01/1991. <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: p,p'-Dichlorodiphenyltrichloroethane (4,4'-DDT)**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for  
p,p'-Dichlorodiphenyltrichloroethane (DDT) (CAS Number 50-29-3)**

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

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

**2. Recommendation and Rationale**

An inhalation reference concentration for p,p'-DDT is not available from the authoritative bodies listed in item number 5 (below). DDT is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for p,p'-DDT is 5 x 10<sup>-4</sup> mg/kg/day. Therefore, a reference concentration of 1.8 mcg/m<sup>3</sup> based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for p,p'-DDT.

**3. Review Dates**

Summary table completion: February, 2005

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: p,p'-Dichlorodiphenyltrichloroethane (4,4'-DDT)**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for p,p'-Dichlorodiphenyltrichloroethane (DDT)  
CAS Number 50-29-3)**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for p,p'-DDT is not available from the authoritative bodies listed in item number 5 (below). DDT is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral cancer potency factor based on cancer effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a unit risk from the cancer potency factor. The recommended oral cancer potency factor for p,p'-DDT is 0.189 per mg/kg/day. Therefore, a unit risk of  $5.4 \times 10^{-5}$  per mcg/m<sup>3</sup> based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for p,p'-DDT. The risk specific air concentration calculated from this toxicity value is 0.018 mcg/m<sup>3</sup>.

**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: Dibenz[a,h]anthracene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for Dibenz[a,h]anthracene (CAS Number 53-70-3)**

Agency	Reference Dose <sup>1</sup> (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.

<sup>1</sup>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 dibenz[a,h]anthracene 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 dibenz[a,h]anthracene with respect to noncancer endpoints. The basis for choosing pyrene as a chemical surrogate for dibenz[a,h]anthracene 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 dibenz[a,h]anthracene (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: Dibenz[a,h]anthracene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Cancer Potency Values for Dibenz[a,h]anthracene (CAS Number 53-70-3)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1995)	--	--	--	--	Human data are not available. Dibenz [a,h]anthracene produced carcinomas in mice following oral or dermal exposure and injection site tumors in several species following sub-cutaneous or intramuscular administration.
US EPA OSRTI (2004) US EPA Region 3 (2003)	$1.37 \times 10^{-7}$	7.3	--	--	Based on a relative potency factor of 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.
RIVM (2001)	$5.0 \times 10^{-6}$	-- <sup>2</sup>	--	--	Based on a potency equivalency factor of 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).
CA EPA (1992)	$2.44 \times 10^{-7}$	4.1	linearized multistage model, extra risk	body surface area <sup>3</sup>	Based on increased incidence of lung carcinomas in mice exposed in aqueous olive oil emulsion.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>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.

<sup>3</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

## 2. Recommendation and Rationale

The CA EPA cancer potency factor for dibenz[a,h]anthracene is based on a less than lifetime study in mice that used a single exposure level. The primary limitation of the study is the use of one exposure level (at which 100% of the animals tested developed lung tumors) which consequently provides no information on dose response. The CA EPA oral study is therefore not chosen for deriving a quantitative estimate of cancer potency. The remaining cancer potency values for dibenz[a,h]anthracene 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 (1) yields a cancer potency factor 9.03 per mg/kg/day, which is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for dibenz[a,h]anthracene (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The dibenz[a,h]anthracene risk specific dose calculated from this toxicity value is  $1.1 \times 10^{-7}$  mg/kg/day.

## 3. Review Dates

Summary table completion: April, 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 Environmental Protection Agency). 1992. Expedited Cancer Potency Values and Proposed Regulatory Levels for Certain Proposition 65 Chemicals. Office of Environmental Health Hazard Assessment, Reproductive and Cancer Hazard Assessment Section, California Environmental Protection Agency. <http://www.oehha.ca.gov/risk/ChemicalDB/OEHHA1992.html>.

NCEA (National Center for Environmental Assessment). 2004. Provisional Peer-Reviewed Toxicity Values (PPRTVs) Database, Office of Superfund Remediation and Technology Innovation. <http://hhpprtv.ornl.gov>.

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/subst/0408.htm>.

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

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**Chemical Name: Dibenz[a,h]anthracene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for Dibenz[a,h]anthracene  
(CAS Number 53-70-3)**

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

<sup>1</sup>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 dibenz[a,h]anthracene is not available from the authoritative bodies listed in item number 5 (below). Dibenz[a,h]anthracene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure and for which an oral reference dose 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<sup>3</sup> 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<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for dibenz[a,h]anthracene.

**3. Review Dates**

Summary table completion: February, 2005  
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: Dibenz[a,h]anthracene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Dibenz[a,h]anthracene (CAS Number 53-70-3)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2002)	8.3 x 10 <sup>-4</sup>	1.2 x 10 <sup>-3</sup>	linearized multistage model, extra risk	not clearly specified	Estimated from route-to-route extrapolation of an oral cancer potency factor of 4.1 per mg/kg/day, which was based on the increased incidence of lung carcinomas in mice exposed in aqueous olive oil emulsion.
--	9.1 x 10 <sup>-4</sup>	1.1 x 10 <sup>-3</sup>	--	--	Based on the CA EPA unit risk for benzo[a]pyrene and application of the recommended relative potency factor of 1.

<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> air concentration), where 1 x 10<sup>-6</sup> concentration = 1 x 10<sup>-6</sup> / inhalation unit risk.

**2. Recommendation and Rationale**

The CA EPA inhalation unit risk for dibenz[a,h]anthracene is based on a less than lifetime oral study in mice that used a single exposure level. The primary limitations of the study include the use of one exposure level (at which 100% of the animals tested developed lung tumors) which consequently provides no information on dose response, and the relevance of the administration in an aqueous olive oil emulsion to exposure by inhalation. The CA EPA oral study is therefore not chosen for deriving a quantitative estimate of the inhalation unit risk. The unit risk value for dibenz[a,h]anthracene is based on benzo(a)pyrene and the application of a relative potency factor. The recommended unit risk value for benzo(a)pyrene is 1.1 x 10<sup>-3</sup> per mcg/m<sup>3</sup> (see Inhalation Cancer Toxicity Value Documentation for benzo(a)pyrene). Application of the recommended relative potency factor (1) yields a unit risk of 1.1 x 10<sup>-3</sup> per mcg/m<sup>3</sup>, which is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for dibenz[a,h]anthracene (see Chapter 5.1.5 of technical support document for discussion of recommended relative potency factors). The dibenz[a,h]anthracene risk specific air concentration calculated from this toxicity value is 9.1 x 10<sup>-4</sup> mcg/m<sup>3</sup>.

### 3. Review Dates

Summary table completion: November, 2004

Toxicity value recommendation: February, 2005

### 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/hot\\_spots/pdf/TSDNov2002.pdf](http://www.oehha.ca.gov/air/hot_spots/pdf/TSDNov2002.pdf)

### 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: Dibenzofuran**

**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 Dibenzofuran (CAS Number 132-64-9)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA Region 3 (2003)	$2 \times 10^{-3}$	25	LOEL	10,000	Based on kidney toxicity (histopathological changes) in female albino rats in a 200-day dietary study.

<sup>1</sup>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 dibenzofuran derived by an authoritative body from the list in item 5 (below). Confidence in the US EPA value is low because the study, published in 1940, used only five female animals per exposure group, did not test male animals for the same 200-day exposure period, and did not include a histopathological examination of kidneys from animals in the lowest exposure group (12.5 mg/kg/day). Thus it is unknown if the histopathological changes in the kidney occurred at the lowest exposure level. In addition, an uncertainty factor of 10,000 was applied to the next highest dose (25 mg/kg/day), which was considered the LOEL. Use of an excessively large uncertainty factor is not consistent with current risk assessment practice. In the absence of any other values from authoritative bodies, the US EPA reference dose ( $2 \times 10^{-3}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for dibenzofuran.

**3. Review Dates**

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

**4. References for Summary Table**

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

## **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: Dibenzofuran**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for Dibenzofuran (CAS Number 132-64-9)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	No human or animals data available.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for dibenzofuran is not available.\*

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

**3. Review Dates**

Summary table completion: April, 2004  
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: 10/05/1989. Last revised: 10/01/1990.  
<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  
A-299

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

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

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

**1. Summary of Available Inhalation Reference Concentrations for Dibenzofuran**  
**(CAS Number 132-64-9)**

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

<sup>1</sup>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 dibenzofuran is not available from the authoritative bodies listed in item number 5 (below). Dibenzofuran 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<sup>3</sup> of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for dibenzofuran is  $2 \times 10^{-3}$  mg/kg/day. Therefore, a reference concentration of 7.0 mcg/m<sup>3</sup> 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 dibenzofuran.

**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: Dibenzofuran**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for Dibenzofuran (CAS Number 132-64-9)**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for dibenzofuran is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005

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: 1,2-Dichlorobenzene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for 1,2-Dichlorobenzene (CAS Number 95-50-1)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004) Also used by: <ul style="list-style-type: none"><li>US EPA Region 3 (2003)</li><li>US EPA HEAST (1997)</li><li>US EPA ODW (2004)</li><li>NYS DEC (1997)</li></ul>	0.09	85.7	NOEL	1000	Based on the absence of treatment related effects in rats and mice exposed by corn oil gavage for 103 weeks.
WHO (1993)	0.429	42.9	NOEL	100	Based on tubular degeneration ( <i>sic</i> ) in the kidneys of the most highly exposed male mice exposed by corn oil gavage for 103 weeks.
RIVM (2000)	0.43	43	NOEL	100	Based on tubular regeneration in the kidneys of the most highly exposed male mice exposed by corn oil gavage for 103 weeks.
ATSDR (2004)	0.4	43	NOEL	100	Based on tubular regeneration in the kidneys of the most highly exposed male mice exposed by corn oil gavage for 103 weeks.
Health Canada (1987)	0.021	21	LOEL	1000	Based on increases in serum cholesterol (males), total serum protein (females) and serum glucose levels (females) in rats exposed by gavage 5 days per week for 13 weeks.
Health Canada (1993)	0.43	43	NOEL	100	Based on tubular regeneration in the kidneys of the most highly exposed male mice exposed by corn oil gavage for 103 weeks.

<sup>1</sup>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 reference doses for 1,2-dichlorobenzene derived by the US EPA, WHO, RIVM, ATSDR and Health Canada (1993) is identical with respect to choice of study and species, but the interpretation of the critical effect or lack of effect in the study varies among the authoritative bodies. The US EPA concluded that the renal tubule regeneration observed in the high-dose male mice was of questionable significance the effect was not observed in female mice or rats of either sex, and because the male mouse control incidence was significantly lower than those of three other approximately concurrent control groups. The US EPA therefore considered the highest dose tested a NOEL. The WHO, RIVM, ATSDR and Health Canada (1993) considered the increasing trend in the renal tubule effect in male mice treatment related, and so chose the low dose as a NOEL. The US EPA included an additional uncertainty factor of 10 to account for database deficiencies (including lack of a supporting reproductive study and inadequate chronic toxicity in a second species) that the WHO, RIVM, ATSDR and Health Canada (1993) did not include, presumably because they considered the available chronic toxicity studies in rats and mice to be of sufficient quality. For its Water Quality and Health program, Health Canada (1987) derived a reference dose based on changes in blood parameters in a subchronic rat gavage study. Health Canada (1987) used uncertainty factors of 10 for use of a LOEL, 10 for use of a subchronic study and 10 for interspecies extrapolation to derive its reference dose. An uncertainty factor for intraspecies extrapolation was not used on the basis of the LOEL being for a sensitive effect and at an exposure level below the NOELs in the chronic study. Since the subchronic LOEL is lower than the chronic NOEL and thereby may represent a more sensitive toxic endpoint, the Health Canada (1987) reference dose (0.021 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-dichlorobenzene.

## 3. Review Dates

Summary table completion: April, 2004

Toxicity value recommendation: October, 2004

## 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2004. Toxicological Profile for Dichlorobenzenes. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. <http://www.atsdr.cdc.gov/toxpro2.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>

Health Canada. 1993. Priority Substances List Assessment Report: 1,2-Dichlorobenzene. 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 1,2-Dichlorobenzene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 193-203. <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: 02/16/1989. Last revised: 3/1/1991. <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). 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. [http://www.who.int/docstore/water\\_sanitation\\_health/GDWQ/Chemicals/Dichlorobenzenessum.htm](http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/Dichlorobenzenessum.htm)

## 5. Authoritative Bodies Checked for Reference Values

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

**Chemical Name: 1,2-Dichlorobenzene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for 1,2-Dichlorobenzene (CAS Number 95-50-1)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) RIVM (2000) Health Canada (1991) NYSDEC (1997)	--	--	--	--	Human data are not available. Available animal studies show both positive and negative trends for carcinogenicity

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for 1,2-dichlorobenzene is not available.\*

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

**3. Review Dates**

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

**4. References for Summary Table**

Health Canada. 1993. Priority substances list assessment report: 1,2-dichlorobenzene. 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 1,2-Dichlorobenzene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 193-203. <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: 02/16/89. Last revised: 1/1/1991. <http://www.epa.gov/iris/subst/0408.htm>.

## **5. Authoritative Bodies Checked for Cancer Potency Values:**

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

**Chemical Name: 1,2-Dichlorobenzene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for 1,2-Dichlorobenzene  
(CAS Number 95-50-1)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA HEAST (1997)  Also used by: ♦ US EPA Region 3 (2003)	200	2 x 10 <sup>5</sup>	NOEL	1000	Based on decreased weight gain in rats exposed by inhalation for 7 months.
RIVM (2000)	600	6 x 10 <sup>4</sup>	NOEL	100	Based on decreased spleen weight in guinea pigs exposed via inhalation for 7 hours/day, 5 days/week for up to 7 months. LOEL = 5.6 x 10 <sup>5</sup> mcg/m <sup>3</sup> .

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

**2. Recommendation and Rationale**

The reference concentrations for 1,2-dichlorobenzene derived by authoritative bodies from the list in item 5 (below) are both based on subchronic inhalation studies. The US EPA reference concentration is based on decreased weight gain in rats, while the RIVM value is based on decreased spleen weight in guinea pigs. Both values are derived using default reference concentration methods, including application of 10-fold uncertainty factors to account for inter- and intraspecies variability. The US EPA derivation includes an additional 10-fold uncertainty factor for use of a subchronic study. Study durations were very similar in both cases and the additional 10-fold uncertainty factor is consistent with current risk assessment practices. Therefore, the US EPA reference concentration (200 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,2-dichlorobenzene.

**3. Review Dates**

Summary table completion: May, 2004

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/rapporten/711701025.pdf>

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

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Risk-based Concentration Table. Superfund Technical Support Section.  
<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

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**Chemical Name: 1,2-Dichlorobenzene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for 1,2-Dichlorobenzene (CAS Number 95-50-1)**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for 1,2-dichlorobenzene is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005

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  
A-312



Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed  
Toxicity Values)

Region 3 Risk-Based Concentrations

Office of Pesticides

Office of Drinking Water

Health Effects Assessment Summary Tables

New York State Department of Health

New York State Department of Environmental Conservation

Agency for Toxic Substances and Disease 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: 1,3-Dichlorobenzene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for 1,3-Dichlorobenzene (CAS Number 541-73-1)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
NYS DEC (1997)	$9 \times 10^{-3}$	9	LOEL	1000	Based on biochemical indicators of liver dysfunction in male rats exposed by corn oil gavage for 90 days
US EPA Region 3 (2003 <sup>2</sup> ; 2004; Draft)	$3 \times 10^{-3}$	9	LOEL	3000	Based on same study and same effects as NYS DEC reference dose.
US EPA OW (2004)	0.09	--	--	--	Information on the basis of the reference dose is unavailable.

<sup>1</sup>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.

<sup>2</sup> Value in online table is in error; correct value obtained via personal communication (US EPA Region 3, 2004)

**2. Recommendation and Rationale**

The basis of the US EPA Region 3 and NYS DEC reference doses is identical with respect to study, species and critical effect. The basis of the US EPA Office of Water value is unclear based on available documentation. NYS DEC applied an uncertainty factor of 1000 to the subchronic LOEL. They cited US EPA IRIS documentation noting that in a study of chronic oral exposure to a related chemical (1,4-dichlorobenzene) in rats, liver lesions in rats did not progress in severity with increasing duration of exposure, and so used a less than 10-fold uncertainty factor (unspecified, but would be UF = 1 if other conventional UF's are assumed) to account for the use of a subchronic study. The US EPA Region 3 value is based on application of a total uncertainty factor of 3000, accounting for interspecies and intraspecies variability, the use of a LOEL, the use of a subchronic study and database deficiencies. In citing the lack of progression of the rat liver lesions with chronic 1,4-dichlorobenzene exposure, the US EPA IRIS documentation for the 1,4-dichlorobenzene reference concentration reduces the sub-chronic uncertainty factor from 10 to 3, rather than 1. Therefore, the US EPA Region 3 reference dose ( $3 \times 10^{-3}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,3-dichlorobenzene.

### 3. Review Dates

Summary table completion: April, 2004  
Toxicity value recommendation: June, 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 1,3-Dichlorobenzene. Albany, NY: Division of Water.

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Risk-based Concentration Table. Superfund Technical Support Section. Cited as an NCEA provisional value (not peer reviewed). <http://www.epa.gov/reg3hwmd/risk/human/index.htm>

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2004. Personal communication from Region 3 staff correcting error in risk-based concentration table.

US EPA Region 3 (United States Environmental Protection Agency Region 3). Draft. Risk assessment issue paper for: derivation of a provisional RfD for 1,3-dichlorobenzene (CASRN 541-73-1).

US EPA OW (United States Environmental Protection Agency Office of Water). 2004. 2004 Edition of the Drinking Water Standards and Health Advisories. EPA 822-R-04-005. <http://www.epa.gov/waterscience/drinking/standards/dwstandards.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: 1,3-Dichlorobenzene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for 1,3-Dichlorobenzene (CAS Number 541-73-1)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Human data and chronic animal bioassays are not available. Limited genotoxicity studies do not suggest carcinogenic potential.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for 1,3-dichlorobenzene is not available.\*

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

**3. Review Dates**

Summary table completion: March, 2004  
Toxicity value recommendation: June, 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: 09/01/90. Verification date: 12/06/89.  
<http://www.epa.gov/iris/index.html>.

## 5. Authoritative Bodies Checked for Cancer Potency Values:

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

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**Chemical Name: 1,3-Dichlorobenzene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for 1,3-Dichlorobenzene  
(CAS Number 541-73-1)**

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

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

**2. Recommendation and Rationale**

An inhalation reference concentration for 1,3-dichlorobenzene is not available from the authoritative bodies listed in item number 5 (below). 1,3-Dichlorobenzene is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for 1,3-dichlorobenzene is 3 x 10<sup>-3</sup> mg/kg/day. Therefore, a reference concentration of 10 mcg/m<sup>3</sup> based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,3-dichlorobenzene.

**3. Review Dates**

Summary table completion: February, 2005  
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: 1,3-Dichlorobenzene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for 1,3-Dichlorobenzene (CAS Number 541-73-1)**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for 1,3-dichlorobenzene is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005

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  
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Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed  
Toxicity Values)

Region 3 Risk-Based Concentrations

Office of Pesticides

Office of Drinking Water

Health Effects Assessment Summary Tables

New York State Department of Health

New York State Department of Environmental Conservation

Agency for Toxic Substances and Disease 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: 1,4-Dichlorobenzene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for 1,4-Dichlorobenzene (CAS Number 106-46-7)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
RIVM (2000)	0.1	10 110	NOEL LOEL	100 1000	Equivalent values based on NOEL for multiple effects seen in dogs exposed to 1,4-dichlorobenzene for one year and LOEL for kidney and parathyroid toxicity in male rats exposed via gavage for 2 years.
NYS DEC (1997)	0.1	107 107	NOEL LOEL	1000 1000	Based on a sub-chronic NOEL for kidney toxicity in male rats exposed by gavage for 13 weeks and a chronic LOEL for kidney toxicity in male rats exposed by gavage for 2 years
US EPA Region 3 (2003, draft)	0.03	30	NOEL	1000	Based on developmental effects (damage to pups) in rats exposed by olive oil gavage in a two generation fertility study. Study LOEL = 90 mg/kg/day
WHO (1993)	0.107	107	LOEL	1000	Based on kidney and parathyroid toxicity in male rats exposed by corn oil gavage for 2 years.
Health Canada (1993)	0.078	39	NOEL	500	Based on route to route extrapolation in rats exposed by inhalation for 76 weeks.

<sup>1</sup>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 WHO reference dose and one of the RIVM reference dose derivations for 1,4-

dichlorobenzene is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (rat LOEL; 110 mg/kg/day when rounded to 2 significant digits). The RIVM reference dose is also supported by a chronic dog NOEL that is 10-fold lower than the rat LOEL, resulting in the same reference dose value. The basis for the NYS DEC reference dose includes the same chronic LOEL as used by RIVM and WHO, as well as a subchronic NOEL that is essentially equal to the chronic LOEL. The Health Canada value is based on an inhalation exposure study and is not chosen for derivation of an oral reference dose, given the availability of good quality oral data. The basis of the US EPA Region 3 value is a 2-generation reproductive and developmental study where a NOEL was identified for various developmental abnormalities, increased relative liver weights and reduced growth rates in pups and reduced fetal and pup survival. A total uncertainty factor of 1000 was applied to account for interspecies and intraspecies variability and extrapolation of a subchronic NOEL. This value is currently only documented in a draft support document. However, a lower LOEL was identified in the 2-generation study than in the 2-year study used as the basis of the reference doses derived by RIVM, WHO or NYSDEC. Therefore, the US EPA Region 3 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 1,4-dichlorobenzene.

### 3. Review Dates

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

### 4. References for Summary Table

Health Canada. 1993. Priority substances list assessment report: 1,4-dichlorobenzene. 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 1,4-Dichlorobenzene. Albany, NY: Division of Water.

RIVM. 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 192-216. <http://www.rivm.nl/bibliotheek/rapporten/711701025.pdf>

US EPA Region 3 (United States Environmental Protection Agency Region 3). 2003. Draft. Risk assessment issue paper for derivation of a provisional oral RfD for 1,4-dichlorobenzene (CASRN 106-46-7).

WHO (World Health Organization). 1993. Guidelines for drinking-water quality, 2nd ed. Vol. 1. Recommendations. Geneva, World Health Organization.  
[http://www.who.int/docstore/water\\_sanitation\\_health/GDWQ/Chemicals/Dichlorobenzenessum.htm](http://www.who.int/docstore/water_sanitation_health/GDWQ/Chemicals/Dichlorobenzenessum.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

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**Chemical Name: 1,4-Dichlorobenzene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for 1,4-Dichlorobenzene (CAS Number 106-46-7)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA HEAST (1997)  Also used by: ♦ US EPA Region 3 (2003)	4.2 x 10 <sup>-5</sup>	0.024	linearized multistage model	body surface area <sup>2</sup>	Based on the combined incidence of liver adenomas and carcinomas in male mice exposed by gavage for two years
Health Canada (1987)	6.6 x 10 <sup>-5</sup> to 2.4 x 10 <sup>-4</sup>	-- <sup>3</sup>	linearized multistage model	body surface area <sup>2</sup>	Range based on hepatocellular adenomas in male mice and adrenal gland pheochromocytomas in male mice exposed by gavage for two years.
CA EPA (1997)	1.9 x 10 <sup>-4</sup>	5.4 x 10 <sup>-3</sup>	linearized multistage model	BW <sup>3/4</sup> <sup>4</sup>	Based on the same tumor data as the US EPA value
NYS DEC (1997)	9.1 x 10 <sup>-5</sup>	0.011	linearized multistage model (extra risk)	BW <sup>3/4</sup> <sup>4</sup>	Based on the same tumor data as the US EPA value

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>No cancer potency factor was derived. The risk specific dose was obtained from the drinking water unit risk range of 1.2 x 10<sup>-7</sup> to 4.3 x 10<sup>-7</sup> per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day.

<sup>4</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.25</sup>.

**2. Recommendation and Rationale**

The basis for the various cancer potency values for are essentially identical with respect to choice of study, species and tumor data, and all three values were derived using a linearized multistage approach to model the dose-response data. Health Canada also used an additional data set for adrenal gland tumors in male mice exposed by gavage to get a range of risk-specific water concentrations for their Water Quality and Health program. The NYS DEC and CA EPA both used BW <sup>3</sup>/<sub>4</sub> scaling for interspecies extrapolation, while the US EPA (HEAST and Region 3 RBC) and Health Canada used body surface area scaling. CA EPA also used an adjustment for intercurrent mortality that reduced their cancer potency factor by about 2-fold compared to the NYS DEC value. Survival did not differ significantly between control and dosed animals in the critical study, and a clear technical rationale was not provided for the adjustment used by CA EPA. Therefore, the NYS DEC cancer potency factor (0.011 per mg/kg/day) is the toxicity value recommended for use in the derivation of a cancer-based soil cleanup objective for 1,4-dichlorobenzene. The 1,4-dichlorobenzene risk specific dose calculated from this toxicity value is  $9.1 \times 10^{-5}$  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). 1997. Public Health Goal for 1,4-Dichlorobenzene in Drinking Water. Office of Environmental Health Hazard Assessment. [http://www.oehha.ca.gov/water/phg/pdf/14dcb\\_c.pdf](http://www.oehha.ca.gov/water/phg/pdf/14dcb_c.pdf)

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>

NYS DEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for 1,4-Dichlorobenzene. Albany, NY: Division of Water.

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

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

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**Chemical Name: 1,4-Dichlorobenzene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for 1,4-Dichlorobenzene  
(CAS Number 106-46-7)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2003) ♦ US EPA HEAST (1997) ♦ CA EPA (2003)	800	7.5 x 10 <sup>4</sup>	NOEL	100	Based on increased liver weights in male rats exposed by inhalation for 6 hours/day and 7 days/week in a multigenerational study. Study LOEL = 2.25 x 10 <sup>5</sup> mcg/m <sup>3</sup> .
ATSDR (2004)	120	3.4 x 10 <sup>3</sup>	NOEL	30	Based on nasal olfactory lesions in female rats exposed by inhalation for 6 hours/day, 5 days/week for 104 weeks. Study LOEL = 1.3 x 10 <sup>4</sup> mcg/m <sup>3</sup> .
Health Canada (1993)	270 <sup>2</sup>	6.7 x 10 <sup>4</sup>	NOEL	500	Based on increased liver and kidney weights and urinary protein in rats exposed by inhalation 5 hours/day, 5 days/week for 76 weeks. Study LOEL = 4.5 x 10 <sup>5</sup> mcg/m <sup>3</sup> . A tolerable daily intake of 0.078 mg/kg/d was derived based on default assumptions for rat body weight and respiration rate.
RIVM (2000)	670	6.7 x 10 <sup>4</sup>	NOEL	100	Based on the same study used by Health Canada (1998).

<sup>1</sup>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.

<sup>2</sup>Derived from a per-unit-body-weight tolerable daily intake based on default assumptions of 70 kg adult body weight and 20 m<sup>3</sup> per day respiration rate.

## 2. Recommendation and Rationale

The available reference concentrations for 1,4-dichlorobenzene derived by authoritative bodies from the list in item 5 (below) are based on two different rat studies that reported similar effects and similar NOEL points of departure, and on a third rat study that reported effects on the respiratory tract following chronic exposure. The ATSDR value is based on nasal lesions in rats exposed to 1,4-dichlorobenzene by inhalation for 104-weeks. The point of departure was derived using the EPA's inhalation dosimetric adjustment methodology (US EPA, 1994) and calculation of the regional gas deposition ratio between rats and humans, treating 1,4-dichlorobenzene as a Category 1 gas. However, 1,4-dichlorobenzene does not have some of the characteristics of a Category 1 gas as defined by EPA's guidance (US EPA, 1994), which include water solubility and lack of significant accumulation in the blood. Also, no evidence is provided suggesting the nasal lesions are the result of local absorption and metabolism, which is another defining characteristic of a Category 1 gas. The ATSDR does not provide a justification for this categorization, and therefore the value is derived in a manner not entirely consistent with EPA's guidance. The US EPA IRIS value is based on increased liver weights in rats exposed via inhalation in a 2-generation study, while the Health Canada and RIVM values are based on increased liver and kidney weights and urinary protein levels in rats exposed via inhalation for 76 weeks, with an additional 36 weeks of observation. The US EPA derivation includes a total uncertainty factor of 100, including a factor of 10 accounting for intraspecies variability, a factor of 3 combined with a pharmacokinetic adjustment (equal to 1) to account for interspecies variability and a factor of 3 to account for the use of a subchronic study. The latter uncertainty factor was reduced from 10 based on other data suggesting that rodent liver lesions generally did not progress with longer duration of exposure to 1,4-dichlorobenzene. RIVM applied 100-fold uncertainty factors to account for interspecies and intraspecies variability, while Health Canada applied a total uncertainty factor of 500. Health Canada derivation included a 10-fold factors to account for intraspecies and interspecies variability, but also included a factor of 5 to account for uncertainties regarding carcinogenicity. They also included an indirect adjustment for inhalation intake in rats compared to inhalation intake in humans by deriving a dose per unit body weight tolerable daily intake from the inhalation point of departure, using default assumptions for rat respiration rate and body weight. The additional factor regarding carcinogenic uncertainty is inappropriate in the current context, since non-cancer and cancer effects are being assessed separately. The indirect pharmacokinetic adjustment based on default body weights and breathing rates is also not consistent with currently-accepted risk assessment practice. The US EPA IRIS derivation is most consistent with currently accepted risk assessment practice since it explicitly employs a pharmacokinetic adjustment for a gas that causes systemic effects, and adjusts the interspecies uncertainty factor accordingly. Therefore the US EPA reference concentration (800 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,4-dichlorobenzene.

## 3. Review Dates

Summary table completion: May, 2004

Toxicity value recommendation: October, 2004

## 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2004. Toxicological Profile for Dichlorobenzenes. 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). 2003. Chronic toxicity summary: 1,4-dichlorobenzene. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacramento, CA. [http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](http://www.oehha.ca.gov/air/chronic_rels/AllChrels.html)

Health Canada. 2000. Priority Substances List Assessment Report: 1,4-dichlorobenzene. 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 (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 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: 06/25/1992. Last revised: 11/01/1996. <http://www.epa.gov/iris/subst/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

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**Chemical Name: 1,4-Dichlorobenzene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for 1,4-Dichlorobenzene (CAS Number 106-46-7)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA Region 3 (2004)	0.16	$6.3 \times 10^{-6}$ <sup>2</sup>	linear multistage	body surface area <sup>3</sup>	Estimated from route-to-route extrapolation of an oral cancer potency factor of 0.022 per mg/kg/day, which was based on the incidence of combined hepatocellular adenomas and carcinomas in male mice exposed by gavage for two years.
CA EPA (2002)	0.091	$1.1 \times 10^{-5}$	linear multistage	body surface area <sup>3</sup>	Based on same study as US EPA Region 3. Estimated from route-to-route extrapolation of an oral cancer potency factor of 0.04 per mg/kg/day.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>The value was originally reported as an inhalation cancer slope factor (per mg/kg/day) and was converted to a unit risk by assuming a 70 kg adult breathes 20 m<sup>3</sup> of air per day.

<sup>3</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

**2. Recommendation and Rationale**

Both the US EPA Region 3 and CA EPA unit risks are based on an increased incidence of liver tumors in mice exposed by gavage to 1,4-dichlorobenzene for two years. However, these values are derived via oral-to-inhalation route extrapolation from oral cancer potency factors that were not recommended as the oral cancer toxicity value for 1,4-dichlorobenzene. Since no toxicity values from the authoritative bodies listed in item 5 (below) are based on inhalation data, and at least one authoritative body derived a unit risk using exposure route extrapolation, a default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a unit

risk from the recommended cancer potency factor. The recommended oral cancer potency factor for 1,4-dichlorobenzene is 0.011 per mg/kg/day. Therefore the unit risk of  $3.1 \times 10^{-6}$  per mcg/m<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,4-dichlorobenzene. The 1,4-dichlorobenzene risk specific air concentration calculated from this toxicity value is 0.32 mcg/m<sup>3</sup>.

### 3. Review Dates

Summary table completion: May, 2004

Toxicity value recommendation: December, 2004

### 4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2002. Technical Support Document for Describing Available Cancer Potency Factors, December. Sacramento, CA: Office of Environmental Health Hazard Assessment, Air Toxicology and Epidemiology Section, California Environmental Protection Agency. [http://www.oehha.ca.gov/air/cancer\\_guide/TSD2.html](http://www.oehha.ca.gov/air/cancer_guide/TSD2.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: 1,1-Dichloroethane**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for 1,1-Dichloroethane (CAS Number 75-34-3)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA HEAST (1997)  Also used by: ♦ US EPA Region 3 (2003)	0.1	115	NOEL	1000	Based on route to route extrapolation from a 13-week rat inhalation study where no effect was observed.

<sup>1</sup>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 HEAST value is the only available reference dose for 1,1-dichloroethane derived by an authoritative body from the list in item 5 (below). The US EPA HEAST reference dose is based on route to route extrapolation from a subchronic inhalation study in rats that used two exposure levels which did not result in adverse effects. The inhaled dose at the lower of the two exposure levels was calculated and used as the point of departure. However, the highest NOEL is more typically used as the point of departure. Since the database for 1,1-dichloroethane is very limited, and the derivation of the reference dose is not consistent with current risk assessment practice, a reference dose for use in derivation of an oral non-cancer-based soil cleanup objective for 1,1-dichloroethane is not recommended. The development of the oral-based soil cleanup objective will use the recommended cancer toxicity value.

**3. Review Dates**

Summary table completion: April, 2004

Toxicity value recommendation: October, 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 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: 1,1-Dichloroethane**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for 1,1-Dichloroethane (CAS Number 75-34-3)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2002)	$1.8 \times 10^{-4}$	$5.7 \times 10^{-3}$	multistage time-to-tumor model	body surface area <sup>2</sup>	Based on mammary gland adenocarcinomas observed in female rats exposed by corn oil gavage in a chronic bioassay.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

**2. Recommendation and Rationale**

The CA EPA cancer potency factor is the only available factor from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. The CA EPA cancer potency factor (0.0057 per mg/kg/day) is therefore the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for 1,1-dichloroethane. The 1,1-dichloroethane risk specific dose calculated from this toxicity value is  $1.8 \times 10^{-4}$  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). 2002. Toxicity Criteria Database. Office of Environmental Health Hazard Assessment. Cancer Potency Values. Technical Support Document for Describing Available Cancer Potency Factors.  
[http://www.oehha.ca.gov/air/hot\\_spots/pdf/TSDNov2002.pdf](http://www.oehha.ca.gov/air/hot_spots/pdf/TSDNov2002.pdf).



## **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-Dichloroethane**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for 1,1-Dichloroethane (CAS Number 75-34-3)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA HEAST (1997)  Also used by: ♦ US EPA Region 3 (2004)	500	5 x 10 <sup>5</sup>	NOEL	1,000	Based on kidney damage in cats exposed by inhalation six hours per day, five days per week for 13 weeks. Study LOEL = 1 x 10 <sup>6</sup> mcg/m <sup>3</sup> .

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

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

**2. Recommendation and Rationale**

The US EPA value is the only available reference concentration for 1,1-dichloroethane derived by an authoritative body from the list in item 5 (below). The US EPA HEAST reference concentration is based on kidney toxicity in a limited subchronic inhalation study in cats that used two exposure levels. The study is weakened by the small number of animals per exposure group (two), and the fact that the same animals were used for both exposure levels, meaning that the exposures to different levels of 1,1-dichloroethane did not happen concurrently, and in fact involved the same animals. Since the database for 1,1-dichloroethane is very limited, and the study used as the basis for the reference concentration has significant methodological limitations, a reference concentration for use in derivation of an inhalation non-cancer-based soil cleanup objective for 1,1-dichloroethane is not recommended. The development of the inhalation-based soil cleanup objective will use the recommended cancer toxicity value.

**3. Review Dates**

Summary table completion: July, 2004

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 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

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**Chemical Name: 1,1-Dichloroethane**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for 1,1-Dichloroethane (CAS Number 75-34-3)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2002)	0.625	$1.6 \times 10^{-6}$	multistage time-to-tumor model	body surface area <sup>2</sup>	Based on route-to-route extrapolation of an oral cancer potency factor of $5.7 \times 10^{-3}$ per mg/kg/day, which is based on mammary gland adenocarcinomas observed in female rats in a 78-week corn oil gavage study.

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

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

**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 ( $1.6 \times 10^{-6}$  per mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for 1,1-dichloroethane. The 1,1-dichloroethane risk specific air concentration calculated from this toxicity value is 0.625 mcg/m<sup>3</sup>.

**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. Technical Support Document for Describing Available Cancer Potency Factors, December. Sacramento, CA: Office of Environmental

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

**Chemical Name: 1,1-Dichloroethene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for 1,1-Dichloroethene (CAS Number 75-35-4)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"><li>♦ US EPA HEAST (1997)</li><li>♦ US EPA Region 3 (2003)</li><li>♦ US EPA ODW (2004)</li></ul>	0.05	4.6	BMDL <sub>10</sub>	100	Based on 2 year drinking water study where liver toxicity (midzonal fatty changes) was observed in female rats. Study NOEL = 9 mg/kg/day. Study LOEL = 14 mg/kg/day
ATSDR (1994)	$9 \times 10^{-3}$	9	LOEL	1000	Based on the same study as US EPA IRIS, but ATSDR considered the minimal hepatocellular swelling observed in female rats at the lowest dose a biologically significant effect
Health Canada (1994)	$3 \times 10^{-3}$	9	LOEL	3000	Based on same study as US EPA IRIS, Health Canada considered the lowest dose a LOEL based on midzonal fatty changes in the livers of females.
WHO (2003)	0.05	4.6	BMDL <sub>10</sub>	100	Based on same study as US EPA IRIS

<sup>1</sup>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<sub>10</sub>: lower bound on benchmark dose at 10% effect

## 2. Recommendation and Rationale

The basis for the four different reference doses for 1,1-dichloroethene is identical with respect to the choice of study and species. The critical effect for the ATSDR reference dose was minimal hepatic swelling at the lowest dose in female rats. In a recent update of the US EPA assessment (which is mirrored by the WHO assessment), the US EPA concluded that the minimal hepatic swelling was not a biologically significant effect because it was not accompanied by other biochemical, histopathological or functional changes. The US EPA, WHO and Health Canada reference dose values are based on midzonal fatty changes in liver. Health Canada considered the lowest dose (9 mg/kg/day) a LOEL, while the US EPA considered the statistically significant fatty changes in the liver at this dose a minimal adverse effect. The US EPA and WHO derived a lower point of departure than the ATSDR and Health Canada LOEL using a benchmark dose approach, but in doing so, reduced the uncertainty factor by 10 and 30-fold, respectively, in their derivation of the reference dose. Health Canada also used an additional uncertainty factor of 3 to account for limited evidence of carcinogenicity, which is not relevant in this context since cancer and non-cancer evaluations are being done separately. Based on the questionable biological significance of the minimal hepatic swelling, and the use of the more robust BMDL approach, the US EPA reference dose (0.05 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,1-dichloroethene.

## 3. Review Dates

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

## 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1994. Toxicological Profile for 1,1-Dichloroethene. U.S. Department of Health and Human Services, Public Health Service. May. <http://www.atsdr.cdc.gov/toxprofiles/tp39.html>.

Health Canada. 1994. 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>

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: 06/07/02. Last revised: 08/13/02. <http://www.epa.gov/iris/subst/0408.htm>.

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: 1,1-Dichloroethene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for 1,1-Dichloroethene (CAS Number 75-35-4)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1994)	--	--	--	--	One limited epidemiological study provided no evidence of carcinogenicity. Data from four oral animal studies in do not suggest carcinogenicity by the oral route of exposure and are inadequate for deriving a cancer potency factor.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for 1,1-dichloroethene is not available.\*

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

**3. Review Dates**

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

#### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 1994. Toxicological Profile for 1,1-Dichloroethene. U.S. Department of Health and Human Services, Public Health Service. May. <http://www.atsdr.cdc.gov/toxprofiles/tp39.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: 06/07/02. Last revised: 08/13/02. <http://www.epa.gov/iris/subst/0408.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  
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Health Effects Assessment Summary Tables  
New York State Department of Health  
New York State Department of Environmental Conservation  
Agency for Toxic Substances and Disease Registry  
California Environmental Protection Agency  
Office of Environmental Health Hazard Assessment  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

**Chemical Name: 1,1-Dichloroethene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for 1,1-Dichloroethene  
(CAS Number 75-35-4)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2003)	200	6.9 x 10 <sup>3</sup>	BMCL <sub>10</sub> <sup>2</sup>	30	Based on liver toxicity (midzonal fatty changes) in female rats exposed by inhalation 6 hours/day, 5 days/week, for 18 months. Study NOEL = 1.77 x 10 <sup>4</sup> mcg/m <sup>3</sup> ; Study LOEL = 5.32 x 10 <sup>4</sup> mcg/m <sup>3</sup> .
CA EPA (2003)	70	2.0 x 10 <sup>4</sup>	NOEL	300	Based on increased mortality and liver toxicity in guinea pigs exposed continuously via inhalation for 90 days. Study LOEL (increased mortality) = 6.1 x 10 <sup>4</sup> mcg/m <sup>3</sup> ; Study LOEL (liver effects) = 1.89 x 10 <sup>5</sup> mcg/m <sup>3</sup> .

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

<sup>2</sup>BMCL<sub>10</sub> = the 95% lower bound on the modeled benchmark concentration associated with 10% incidence of the toxic effect

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

**2. Recommendation and Rationale**

The reference concentrations for 1,1-dichloroethene derived by authoritative bodies from the list in item 5 (below) are based on inhalation studies in rats and guinea pigs. The CA EPA based their derivation on a 90-day continuous exposure guinea pig study where mortality was increased at 6.1 x 10<sup>4</sup> mcg/m<sup>3</sup>, while the US EPA based their reference concentration on an 18-month rat study where liver toxicity was observed at a time-weighted exposure concentration of 5.32 x 10<sup>4</sup> mcg/m<sup>3</sup>. The CA EPA

applied a total uncertainty factor of 300 to the subchronic NOEL and assumed the default dosimetry of equal effects at equal air concentrations for a gas causing systemic toxicity. The total uncertainty of 300 included 10-fold for intraspecies variability, 10-fold for a subchronic study and 3-fold for interspecies variability. The US EPA made the same dosimetric adjustment used by the CA EPA (i.e., equal effects at equal air concentrations based on default systemic gas) and estimated a point of departure based on a BMCL<sub>10</sub>. They applied a total uncertainty factor of 30; 10-fold to account for intraspecies variability and 3-fold to account for interspecies variability. An additional uncertainty factor for a less than lifetime study was not considered necessary because the liver effects observed at interim sacrifices during the study were not progressing, and in fact were decreasing in incidence with study duration. Given that the rat study duration was a large fraction of the lifetime and the lack of progression of the observed effects, this judgement appears consistent with current risk assessment practice, as is the use of a benchmark air concentration approach to estimate the point of departure. Therefore the US EPA reference concentration (200 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,1-dichloroethene.

### 3. Review Dates

Summary table completion: April, 2004

Toxicity value recommendation: October, 2004

### 4. References for Summary Table

CA EPA(California Environmental Protection Agency). 2003. Chronic toxicity summary: 1,1-dichloroethylene. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacramento, CA.

[http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](http://www.oehha.ca.gov/air/chronic_rels/AllChrels.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: 06/07/2002. Last revised: 08/13/2002.

<http://www.epa.gov/iris/subst/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

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**Chemical Name: 1,1-Dichloroethene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for 1,1-Dichloroethene (CAS Number 75-35-4)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	Studies have been reviewed but weight of evidence is not sufficient to justify deriving an inhalation unit risk.

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

**2. Recommendation and Rationale**

An inhalation unit risk for 1,1-dichloroethene is not available.\*

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

**3. Review Dates**

Summary table completion: May, 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: 06/07/2002. Last revised: 08/13/2002.

<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  
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Health Effects Assessment Summary Tables  
New York State Department of Health  
New York State Department of Environmental Conservation  
Agency for Toxic Substances and Disease 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: 1,2-Dichloroethane**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for 1,2-Dichloroethane (CAS Number 107-06-2)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA Region 3 (2003)	0.02	--	--	--	Listed as an NCEA provisional value, but no further information available as to the derivation of the number.
CA EPA (1999)	0.045	45.3	NOEL	1000	Based on renal lesions in female rats in a 13-week drinking water study. Study LOEL = 90.6 mg/kg/day.
NYS DEC (1997)	5.8 x 10 <sup>-3</sup>	58	LOEL	10,000	Based on significant dose-related increases in kidney weight and kidney-to-body-weight ratio in male and female rats in a 13-week drinking water study.

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

**2. Recommendation and Rationale**

The basis of the CA EPA and NYS DEC reference doses is identical with respect to study and species. The basis of the US EPA Region 3 reference dose is not clearly documented. The CA EPA and NYS DEC values are both derived from a 13-week drinking water study in rats. Significant increases in absolute and relative kidney weights were observed at the lowest dose tested, although histopathological kidney lesions were only observed at higher doses. The NYS DEC considered the lowest dose where kidney weight effects occurred a LOEL, while CA EPA did not consider those effects to be of toxicological significance, and identified this dose with only kidney weight changes unaccompanied by any histopathological changes as a NOEL. Although the absolute and relative kidney weight changes observed at the lowest dose in this subchronic study could represent precursors for frank toxic effects at higher doses, the identification of this dose as a LOEL led to default uncertainty factors totaling 10,000 (NYS DEC, 1997). Exposure at the level of the CA EPA reference dose is still over 1000 times lower than the dose level identified as a LOEL by the NYS DEC, and the derivation of the CA EPA reference dose is consistent with currently accepted risk assessment practice. Therefore, the CA EPA reference dose (0.045 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,2-dichloroethane.



### 3. Review Dates

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

### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2001. Toxicological profile for 1,2-dichloroethane. Update. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

CA EPA (California Environmental Protection Agency). 1999. Public Health Goal for 1,2-dichloroethane in Drinking Water. Sacramento, CA. Division of Drinking Water and Environmental Management.

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

Health Canada, Environment Canada. 1994. Priority substances list assessment report: 1,2-dichloroethane. 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 1,2-Dichloroethane. Albany, NY: Division of Water.

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

<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: 1,2-Dichloroethane**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for 1,2-Dichloroethane (CAS Number 107-06-2)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2003) ♦ ATSDR (2001)	1.1 x 10 <sup>-5</sup>	0.091	linearized multistage model (with time-to-death analysis), extra risk	body surface area <sup>2</sup> with time weighting for gavage dosing, less-than-lifetime dosing and % metabolized	Based on the induction of several tumor types in rats and mice treated by corn oil gavage. The cancer potency factor is derived from the data set of hemangiosarcomas in male rats. Dose scaling not clearly specified in IRIS, but see NYS DEC (1997).
Health Canada (1994) (see also TERA, 2004)	1.2 x 10 <sup>-4</sup>	-- <sup>3</sup>	linearized multistage model	body weight <sup>4</sup>	Based on the incidence of several tumor types in male and female rats and mice. A range of risk-specific doses was derived and the lowest value is presented (limited methodology information available)
Health Canada (1987)	1.8 x 10 <sup>-5</sup>	-- <sup>5</sup>	linearized multistage model	body surface area <sup>2</sup>	Based on circulatory system hemangiosarcomas in male rats exposed for 78 weeks by corn oil gavage.

RIVM (2001)	$1.4 \times 10^{-4}$	-- <sup>6</sup>	linear extrapolation	body weight <sup>3</sup>	Based on the incidence of forestomach and mammary gland tumors in an oral study in rats. (Limited methodology information available)
CA EPA (1999)	$2.1 \times 10^{-5}$	0.047	linear extrapolation from LED <sub>10</sub> <sup>7</sup>	BW <sup>3/4</sup> <sup>8</sup>	Based on the same study and data set as US EPA IRIS.
NYS DEC (1997)	$1.7 \times 10^{-5}$	0.06	linearized multistage model	BW <sup>3/4</sup> <sup>8</sup>	Based on the same study and review as US EPA IRIS.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>No cancer potency factor was derived. The risk specific dose was obtained by linear extrapolation from the modeled TD05 (6.2 mg/kg/day), the dose associated with a 5% increase in mean tumor incidence (not a lower-bound estimate; TERA, 2004)

<sup>4</sup>Factor for dose adjustment from animal to humans is 1.

<sup>5</sup>No cancer potency factor was derived. The risk specific dose was obtained from the drinking water unit risk of  $1.6 \times 10^{-6}$  per microgram per liter, assuming a 70 kg person drinks 2 liters of water per day.

<sup>6</sup>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)

<sup>7</sup>LED<sub>10</sub> = lower bound on the dose associated with 10% tumor incidence above background.

<sup>8</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.25</sup>.

## 2. Recommendation and Rationale

The basis of the cancer potency factors appears to be identical with respect to the critical study. The basis of the US EPA, CA EPA, Health Canada (1987) and NYS DEC cancer potency factors is increased liver hemangiosarcoma tumor incidence in male rats. The US EPA fit a quantal model with a time-to-death analysis and used body surface area scaling with time weighting for gavage dosing and less-than-lifetime exposure and adjustments for percent of administered dose metabolized. CA EPA estimated an LED<sub>10</sub> based on BW<sup>3/4</sup> scaling, making the same time-weighting adjustments as US EPA, but not adjusting for percent metabolized at the different doses. They then used a linear extrapolation from the LED<sub>10</sub> to estimate the cancer potency factor. The NYS DEC adjusted the US EPA value to reflect BW<sup>3/4</sup> scaling, rather than body surface area scaling, which was also used by Health Canada (1987). It is unclear which tumor data were used by RIVM and Health Canada (1994) to derive their potency estimates, and both values represent linear extrapolations from a dose associated with an observed tumor incidence or a modeled mean tumor incidence (respectively) and therefore do not reflect lower-bound estimates on the  $10^{-6}$  lifetime risk specific dose. The CA EPA derivation is most consistent with currently-accepted risk assessment practice in terms of method used for inter-species dose scaling and high-to-low dose extrapolation, and the effect of not adjusting for percent of administered dose metabolized is small compared to the effect of the different extrapolation procedures. Therefore, the CA EPA cancer potency factor (0.047 per mg/kg/day) is the toxicity value recommended

for use in the derivation of an oral cancer-based soil cleanup objective for 1,2-dichloroethane. The 1,2-dichloroethane risk specific dose calculated from this toxicity value is  $2.1 \times 10^{-5}$  mg/kg/day.

### 3. Review Dates

Summary table completion: April, 2004

Toxicity value recommendation: November, 2004

### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2001. Toxicological profile for 1,2-dichloroethane. Update. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. <http://www.atsdr.cdc.gov/toxprofiles/tp38.html>

CA EPA (California Environmental Protection Agency). 1999. Public health goal for 1,2-dichloroethane in drinking water. Office of Environmental Health Hazard Assessment. <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>

Health Canada, Environment Canada. 1994. Priority Substances List Assessment Report: 1,2-Dichloroethane. Ottawa, Ministry of Public Works and Government Services. <http://www.hc-sc.gc.ca/hecs-sesc/exsd/psl1.htm>. Cancer potency value calculation available on 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 1,2-Dichloroethane. Albany, NY: Division of Water.

RIVM. 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 249-257. <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. Verification date: 12/04/86. Last revised: 01/01/91. <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

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**Chemical Name: 1,2-Dichloroethane**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for 1,2-Dichloroethane  
(CAS Number 107-06-2)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
US EPA Region 3 (2004)	5	$1.4 \times 10^4$	LOEL	3000	Based on gastrointestinal, liver and gallbladder effects in exposed workers. Information on duration of exposure not available.
ATSDR (2001)	$2.4 \times 10^3$ (0.6 ppm)	$2.02 \times 10^5$ (50 ppm)	NOEL	90	Based on lack of any observed gross or histopathological effects in rats exposed by inhalation for two years. Only a single exposure level was tested in this study, therefore a LOEL was not established.
CA EPA (2003)	400	$8.5 \times 10^3$	NOEL	30	Based on significant elevation of liver enzymes in rats exposed via inhalation for 12 months. Study LOEL = $4.2 \times 10^4$ mcg/m <sup>3</sup> . A pharmacokinetic adjustment of 1.5-fold was applied to the animal NOEL to obtain a human equivalent concentration.

<sup>1</sup>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 1,2-dichloroethane derived by authoritative bodies from the list in item 5 (below) are based on lack of any observed effect in a single-dose rat study, effects on liver enzymes in another rat study and liver, gallbladder and gastrointestinal effects in aircraft industry workers. The US EPA value is based on an occupational study that lacks information on duration of employment or exposure, did not control A-359 for confounding exposures such as other solvents or

alcohol consumption, and failed to include medical evaluation of control (unexposed) workers or any statistical analysis of the observed health endpoints. Given these deficiencies, adequate justification was not provided for selection of this study over available animal data as the basis of a reference concentration. The ATSDR point of departure was not corrected for intermittent exposure (7 hours/day, 5 days per week). They applied a total uncertainty factor of 90, including 10-fold to account for intraspecies variability, 3-fold to account for interspecies variability after making a pharmacokinetic adjustment (equal to 1) based on a systemic effects caused by a gas, and 3-fold as a modifying factor for database deficiencies. The CA EPA based their derivation on liver enzyme changes in rats exposed for 12 months. They corrected for intermittent exposure and used a value of 1.5 to adjust for pharmacokinetic variability based on the relative absorption of 1,2-dichloroethane as a systemic gas in rats and humans. This adjustment is not consistent with currently-accepted guidance which recommends a default adjustment of 1 if partitioning coefficient data are unavailable or if the animal:human partitioning coefficient ratio is greater than 1. The CA EPA applied a total uncertainty factor of 30 to account for intra- and interspecies variability, with no additional factor to account for the subchronic study duration. Both the ATSDR and CA EPA derivations deviate somewhat from currently-accepted risk assessment practice. The two-year study used by ATSDR employed only one experimental air concentration, which was considered a NOEL. However, the air concentration at the LOEL identified in the 12-month study used by the CA EPA in their derivation is considerably lower than the two-year NOEL. Therefore the CA EPA reference concentration (400 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,2-dichloroethane.

### 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). 2001. Toxicological profile for 1,2-dichloroethane. Update. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

CA EPA(California Environmental Protection Agency). 2000. Chronic toxicity summary: ethylene dichloride. Chronic reference exposure levels. Office of Environmental Health Hazard Assessment. Sacramento, CA. [http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](http://www.oehha.ca.gov/air/chronic_rels/AllChrels.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

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**Chemical Name: 1,2-Dichloroethane**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for 1,2-Dichloroethane (CAS Number 107-06-2)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA Region 3 (2004)	0.04	2.6 x 10 <sup>-5</sup>	linearized multistage model, extra risk	not clearly specified	Estimated by route to route extrapolation of a oral cancer potency factor of 0.091 per mg/kg/day which was based on the incidence of hemangiosarcomas in male rats in a two-year gavage study.
CA EPA (2002)	0.05	2.1 x 10 <sup>-5</sup>	multistage time-to-tumor model, extra risk	body surface area <sup>2</sup>	Based on route-to-route extrapolation from an oral cancer potency factor of 0.072 per mg/kg/day, which is based on the same data set reviewed in US EPA IRIS (2004).
RIVM (2001)	0.48	-- <sup>3</sup>	linear extrapol.	--	Based on route-to-route extrapolation of an oral risk-specific dose of 0.014 mg/kg/day at a lifetime risk of 1 in 10,000, which was derived from tumor data in rats chronically exposed via gavage (possibly the same study as used by US EPA IRIS, but limited review information available).

<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> concentration), where 1 x 10<sup>-6</sup> air concentration = 1 x 10<sup>-6</sup> / unit risk.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>Cancer risk is only expressed as a risk-specific air concentration; a unit risk is not directly reported.

## 2. Recommendation and Rationale

The basis of the two well-documented inhalation unit risks derived by authoritative bodies is circulatory system hemangiosarcomas in male rats exposed via gavage. However, these values are derived via oral-to-inhalation route extrapolation from oral cancer potency factors that were not recommended as the oral cancer toxicity value for 1,2-dichloroethane. Since exposure route extrapolation is the basis of the unit risks from authoritative bodies, and in the absence of route-specific data, a default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a unit risk from the recommended oral cancer potency factor. The recommended oral cancer potency factor for 1,2-dichloroethane is 0.047 per mg/kg/day. Therefore the unit risk of  $1.3 \times 10^{-5}$  per mcg/m<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,2-dichloroethane. The 1,2-dichloroethane risk specific air concentration calculated from this toxicity value is 0.074 mcg/m<sup>3</sup>.

## 3. Review Dates

Summary table completion: July, 2004

Toxicity value recommendation: November, 2004

## 4. References for Summary Table

CA EPA (California Environmental Protection Agency). 2002. Technical Support Document for Describing Available Cancer Potency Factors. Sacramento, CA.  
[http://www.oehha.ca.gov/air/cancer\\_guide/TSD2.html](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 IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 12/04/1986. Last revised: 01/01/1991. <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 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: *cis*-1,2-Dichloroethene**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for *cis*-1,2-Dichloroethene (CAS Number 156-59-2)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA OSRTI (2004)  Also used by: <ul style="list-style-type: none"><li>♦ US EPA Region 3 (2003)</li><li>♦ US EPA HEAST (1997)</li><li>♦ US EPA ODW (2004)</li></ul>	0.01	32	NOEL	3000	Based on effects in blood (decreased hematocrit and hemoglobin) of rats exposed for 90 days by corn oil gavage. Study LOEL = 97 mg/kg/day.
NYS DEC (1997)	0.03	32	NOEL	1000	Based on same study and NOEL as US EPA OSRTI.
RIVM (2001)	$6 \times 10^{-3}$	32	NOEL	5000	Based on same study and NOEL as US EPA OSRTI.

<sup>1</sup>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 *cis*-1,2-dichloroethene is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (32 mg/kg/day). All of the derivations include a 1000-fold uncertainty factor accounting for interspecies and intraspecies variability, and the uncertainty introduced by the lack of a chronic study. The US EPA included an additional factor of 3 and RIVM added a factor of 5 to account for database limitations including the lack of reproductive and developmental studies and the low quality of the existing less-than-lifetime studies. An additional uncertainty factor for database limitations appears justified in light of the limited available toxicological information for *cis*-1,2-dichloroethene. An uncertainty factor of 3 to account for database limitations is most consistent with currently-accepted risk assessment practices. Therefore, the US EPA 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 *cis*-1,2-dichloroethene.

### 3. Review Dates

Summary table completion: April, 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 1,2-Dichloroethene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 249-257.  
<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 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 OSRTI (Office of Superfund Remediation and Technology Innovation). 2004. Provisional Toxicity Value Summary (PPRTV) for Bromomethane. 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). 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



**Chemical Name: *cis*-1,2-Dichloroethene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for *cis*-1,2-Dichloroethene (CAS Number 156-59-2)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1996) RIVM (2001) NYS DEC (1997)	--	--	--	--	No human or animal data available, generally nonpositive results in mutagenicity assays.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for *cis*-1,2-dichloroethene is not available.\*

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

**3. Review Dates**

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

**4. References for Summary Table**

ATSDR (Agency for Toxic Substances and Disease Registry). 1996. Toxicological profile for 1,2-Dichloroethene. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

NYSDEC (New York State Department of Environmental Conservation). 1997. Combined Regulatory Impact and Draft Environmental Impact Statement; Human Health Fact Sheet for *cis*-1,2-dichloroethene. Albany, NY: Division of Water.



RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM report no. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001, p 249-257.  
<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: 9/07/89. Last revised: 2/01/95.  
<http://www.epa.gov/iris/subst/0408.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: *cis*-1,2-Dichloroethene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for *cis*-1,2-Dichloroethene  
(CAS Number 156-59-2)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
RIVM (2001)	30	32 mg/kg/d and direct oral – inhalation route extrapolation	NOEL	5000	Based on decreased body weight and effects on blood parameters in a sub-chronic rat gavage study. NOEL = 32 mg/kg/day; Study LOEL = 97 mg/kg/day. Route-to-route extrapolation was applied to derive a reference concentration.

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

**2. Recommendation and Rationale**

The RIVM value is the only available reference concentration for *cis*-1,2-dichloroethene 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 reference dose that was not recommended as the oral non-cancer toxicity value for *cis*-1,2-dichloroethene. Since no toxicity values from the authoritative bodies listed in item 5 (below) are based on inhalation data, and at least one authoritative body derived a reference concentration using exposure route extrapolation, a default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a reference concentration from the recommended reference dose. The recommended oral reference dose for *cis*-1,2-dichloroethene is 0.01 mg/kg/day. Therefore the reference concentration of 35 mcg/m<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *cis*-1,2-dichloroethene.

**3. Review Dates**

Summary table completion: July, 2004

Toxicity value recommendation: December, 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  
Office of Environmental Health Hazard Assessment  
Health Canada  
World Health Organization  
National Institute of Public Health & Environmental Protection, Netherlands

**Chemical Name: *cis*-1,2-Dichloroethene**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for *cis*-1,2-Dichloroethene (CAS Number 156-59-2)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)	--	--	--	--	No data in humans or animals and generally negative results in mutagenicity assays.

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

**2. Recommendation and Rationale**

An inhalation unit risk for *cis*-1,2-dichloroethene is not available.\*

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

**3. Review Dates**

Summary table completion: July, 2004

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: 09/07/1989. Last revised: 02/01/1995.  
<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:** *trans*-1,2-Dichloroethene

**Exposure Route:** Oral

**Toxicity:** Non-Cancer

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

**1. Summary of Available Oral Reference Doses for *trans*-1,2-Dichloroethene (CAS Number 156-60-5)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"><li>◆ US EPA Region 3 (2003)</li><li>◆ US EPA HEAST (1997)</li><li>◆ US EPA ODW (2004)</li><li>◆ NYS DEC (1997)</li></ul>	0.02	17	NOEL	1000	Based on increased serum alkaline phosphatase in male mice exposed via drinking water for 90 days. Study LOEL = 175 mg/kg/day
RIVM (2001)	0.017	17	NOEL	1000	Based on same data as US EPA IRIS.

<sup>1</sup>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 *trans*-1,2-dichloroethene is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure (17 mg/kg/day), although the US EPA identified the increase in serum alkaline phosphatase as the key effect, while RIVM noted other effects at the same LOEL dose including decreased antibody-producing cells in the spleen and increased relative liver weight. The two values differ only because of differences in the precision with which they are reported. The US EPA reference dose (0.02 mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for *trans*-1,2-dichloroethene.

**3. Review Dates**

Summary table completion: April, 2004

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 *trans*-1,2-Dichloroethene. Albany, NY: Division of Water.

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001.  
<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.  
<http://www.epa.gov/iris/subst/0314.htm>

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: *trans*-1,2-Dichloroethene**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for *trans*-1,2-Dichloroethene (CAS Number 156-60-5)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004) ATSDR (1996) RIVM (2001)	--	--	--	--	No human or animal data available.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e.,  $1 \times 10^{-6}$  dose), where  $1 \times 10^{-6}$  dose =  $1 \times 10^{-6}$  / cancer potency factor.

**2. Recommendation and Rationale**

An oral cancer potency factor for *trans*-1,2-dichloroethene is not available.\*

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

**3. Review Dates**

Summary table completion: April, 2004

Toxicity value recommendation: July, 2004

**4. References for Summary Table**

ATSDR (Agency for Toxic Substances and Disease Registry). 1996. Toxicological Profile for 1,2-Dichloroethene. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. <http://www.atsdr.cdc.gov/toxprofiles/tp87.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 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/0314.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: *trans*-1,2-Dichloroethene**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for *trans*-1,2-Dichloroethene (CAS Number 156-60-5)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
RIVM (2001)	60	1.85 x 10 <sup>5</sup>	LOEL	3000	Based on lung and liver effects in rats exposed via inhalation for 8 or 16 weeks.

<sup>1</sup>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 RIVM value is the only available reference concentration for *trans*-1,2-dichloroethene from an authoritative body listed in item 5 (below), and is derived using methods that reflect general consistency with current risk assessment practice. Therefore the RIVM reference concentration (60 mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for *trans*-1,2-dichloroethene.

**3. Review Dates**

Summary table completion: July, 2004

Toxicity value recommendation: October, 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  
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:** *trans*-1,2-Dichloroethene

**Exposure Route:** Inhalation

**Toxicity:** Cancer

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for *trans*-1,2-Dichloroethene (CAS Number 156-60-5)**

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

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

**2. Recommendation and Rationale**

An inhalation unit risk for *trans*-1,2-dichloroethene is not available.\*

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

**3. Review Dates**

Summary table completion: February, 2005

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  
A-380

Office of Superfund Remediation and Technology Innovation (Provisional Peer Reviewed  
Toxicity Values)

Region 3 Risk-Based Concentrations

Office of Pesticides

Office of Drinking Water

Health Effects Assessment Summary Tables

New York State Department of Health

New York State Department of Environmental Conservation

Agency for Toxic Substances and Disease 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: Dieldrin**  
**Exposure Route: Oral**  
**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for Dieldrin (CAS Number 60-57-1)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA HEAST (1997)</li> <li>◆ US EPA ODW (2004)</li> <li>◆ US EPA OPP (1997)</li> <li>◆ US EPA Region 3 (2004)</li> <li>◆ NYS DEC (1997)</li> <li>◆ ATSDR (2004)</li> </ul>	$5 \times 10^{-5}$	$5 \times 10^{-3}$	NOEL	100	Based on liver lesions in rats exposed by diet for 2 years. Study LOEL = 0.05 mg/kg/day.
WHO (2003)  Also used by: <ul style="list-style-type: none"> <li>◆ Health Canada (1994)</li> </ul>	$1 \times 10^{-4}$	0.025	NOEL	250	Based on NOELs of 1 mg/kg in diet of dogs and 0.5 mg/kg in diet of rats, equivalent to 0.025 mg/kg/day in both species. Limited information is available on the precise studies and points of departure used to obtain the reference dose.
RIVM (2000)	$1 \times 10^{-4}$	0.025	LOEL	250	Based on liver changes in both rats and dogs exposed by diet for a lifetime.

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

**2. Recommendation and Rationale**

The basis for all reference doses for dieldrin, except the RIVM and WHO values, is essentially identical with respect to choice of study, species, adverse effect and identification of the point of departure ( $5 \times 10^{-3}$  mg/kg/day). The exact study forming the basis of the WHO value is not specified, and the

documentation states that the uncertainty factor applied to the LOEL is 250 to take into account cancer effects observed in the mouse. The use of uncertainty factors to account for carcinogenic effects is not relevant in this context since cancer and non-cancer evaluations are being done separately. The RIVM reference dose is based on a chronic feeding study that also reported liver effects in rats and dogs, but the point of departure was a LOEL and was 5-fold higher. The US EPA derivation included a total uncertainty factor of 100 to account for interspecies and intraspecies variability. The RIVM used an additional uncertainty factor of 2.5 to account for the use of a LOEL rather than the conventional factor of 10, which was suggested to be sufficient for the marginal effects observed at the LOEL. However, frank histopathological liver lesions were observed in rats in the study used by US EPA at a dose only 2-fold greater than the RIVM LOEL, suggesting that a deviation from accepted risk assessment practice is not supported in this case. Therefore, the US EPA reference dose ( $5 \times 10^{-5}$  mg/kg/day) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for dieldrin.

### 3. Review Dates

Summary table completion: June, 2004

Toxicity value recommendation: August, 2004

### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological profile for Chlordane. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

Health Canada. 1994. 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>

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

RIVM (National Institute of Public Health & Environmental Protection). 2001. Re-evaluation of human-toxicological maximum permissible risk levels. RIVM Report No. 711701025, National Institute of Public Health and the Environment, Bilthoven, The Netherlands, March 2001.  
<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: 04/16/1987. Last revised: 09/01/1990.  
<http://www.epa.gov/iris>

US EPA ODW (United States Environmental Protection Agency Office of Drinking Water). 2004. EPA 822-R-04-005. Office of Drinking Water, Drinking Water Standards and Health Advisories. Washington, DC.

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

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

WHO (World Health Organization). 2003. Guidelines for drinking water quality, 3<sup>rd</sup> Ed. World Health Organization, Geneva.  
[http://www.who.int/docstore/water\\_sanitation\\_health/GDWQ/draftchemicals/aldrindieldrin2003.pdf](http://www.who.int/docstore/water_sanitation_health/GDWQ/draftchemicals/aldrindieldrin2003.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: Dieldrin**  
**Exposure Route: Oral**  
**Toxicity: Cancer**

**New York State Department of Health**  
**Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for Dieldrin (CAS Number 60-57-1)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: <ul style="list-style-type: none"> <li>◆ US EPA Region 3 (2004)</li> <li>◆ US EPA OPP (1997)</li> <li>◆ US EPA HEAST (1997)</li> <li>◆ CA EPA (1993)</li> </ul>	6.25 x 10 <sup>-8</sup>	16	linearized multistage model, extra risk	body surface area <sup>2</sup>	Geometric mean of 13 potency factors based on increased incidence of liver carcinomas in several strains of mice exposed by diet.
NYS DEC (1997)	1.2 x 10 <sup>-7</sup>	8.32	linearized multistage model, extra risk	BW <sup>¾</sup> <sup>3</sup>	Based on the same liver tumor data as used by US EPA

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

<sup>3</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.25</sup>.

**2. Recommendation and Rationale**

The cancer potency factors derived by the US EPA and the NYS DEC are based on 13 male and female mouse data sets showing increased incidence of liver tumors in animals exposed to dieldrin in the diet. Both cancer potency estimates are based on the geometric mean of the potency estimates derived from the 13 individual data sets. The US EPA used body surface area scaling to extrapolate from rodent to human cancer potency, while the NYSDEC used BW<sup>¾</sup> scaling. The latter method is more consistent with currently accepted risk assessment practice. Therefore, the NYS DEC cancer potency factor (8.32 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for dieldrin. The dieldrin risk specific dose calculated from this toxicity value is 1.2 x 10<sup>-7</sup> 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), 1993. Office of Environmental Health Hazard Assessment. Toxicity Criteria Database.  
<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 Dieldrin. Albany, NY: Division of Water.

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

US EPA IRIS (United States Environmental Protection Agency Integrated Risk Information System). 2004. Office of Research and Development, National Center for Environmental Assessment. Verification date: 4/16/1987. Last revised: 9/01/1990.  
<http://www.epa.gov/iris/subst/0408.htm>.

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: Dieldrin**  
**Exposure Route: Inhalation**  
**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for Dieldrin (CAS Number 60-57-1)**

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

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

**2. Recommendation and Rationale**

An inhalation reference concentration for dieldrin is not available from the authoritative bodies listed in item number 5 (below). Dieldrin is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral reference dose based on effects distant from the site of contact (i.e., the gastrointestinal lining) exists. A default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a reference concentration from the reference dose. The recommended oral reference dose for dieldrin is 5 x 10<sup>-5</sup> mg/kg/day. Therefore, a reference concentration of 0.18 mcg/m<sup>3</sup> based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for dieldrin.

**3. Review Dates**

Summary table completion: February, 2005  
 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: Dieldrin**  
**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 Dieldrin (CAS Number 60-57-1)**

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

<sup>1</sup>The air concentration associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> air concentration = 1 x 10<sup>-6</sup> / unit risk.

**2. Recommendation and Rationale**

An inhalation unit risk for dieldrin is not available from the authoritative bodies listed in item number 5 (below). Dieldrin is a systemic toxicant that is expected to be absorbed into the body following both oral and inhalation exposure, and for which an oral 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<sup>3</sup> of air per day is used to derive a unit risk from the cancer potency factor. The recommended oral cancer potency factor for dieldrin is 8.32 per mg/kg/day. Therefore, a unit risk of 2.4 x 10<sup>-3</sup> per mcg/m<sup>3</sup> based on exposure route extrapolation is the toxicity value recommended for use in the derivation of an inhalation cancer-based soil cleanup objective for dieldrin. The risk specific air concentration calculated from this toxicity value is 4.2 x 10<sup>-4</sup> mcg/m<sup>3</sup>.

**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: 1,4-Dioxane**

**Exposure Route: Oral**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Oral Reference Doses for 1,4-Dioxane (CAS Number 123-91-1)**

Agency	Reference Dose <sup>1</sup> (mg/kg/day)	Point of Departure		UF	Summary
		Dose (mg/kg/day)	Basis		
WHO (2003)	0.096	9.6	NOEL	100	Based on two-year drinking water study with rats experiencing renal tubular epithelial and hepatocellular degeneration and necrosis. Study LOEL = 96 mg/kg/day.
ATSDR (2004)	0.1	9.6	NOEL	100	Based on same study as WHO (2003)

<sup>1</sup>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**

Draft WHO and ATSDR values are the only available reference doses for 1,4-dioxane derived by authoritative body from the list in item 5 (below), and are identical with respect to choice of study, species, identification of critical effect, and point of departure. Therefore the WHO and ATSDR reference doses (0.1 mg/kg/day, rounded to one significant figure) is the toxicity value recommended for use in the derivation of an oral non-cancer-based soil cleanup objective for 1,4-dioxane.

**3. Review Dates**

Summary table completion: April, 2004

Toxicity value recommendation: January, 2005



#### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2004. Toxicological Profile for 1,4-Dioxane. Draft for public comment. Atlanta GA: Department of Health and Human Services.

WHO (World Health Organization). 2003. Guidelines for drinking water quality, 3<sup>rd</sup> Ed. World Health Organization, Geneva.

[http://www.who.int/docstore/water\\_sanitation\\_health/GDWQ/draftchemicals/dioxane2003.pdf](http://www.who.int/docstore/water_sanitation_health/GDWQ/draftchemicals/dioxane2003.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: 1,4-Dioxane**

**Exposure Route: Oral**

**Toxicity: Cancer**

**New York State Department of Health  
Oral Cancer Toxicity Value Documentation**

**1. Summary of Available Oral Cancer Potency Values for 1,4-Dioxane (CAS Number 123-91-1)**

Agency	Risk Specific Dose <sup>1</sup> (mg/kg/day)	Cancer Potency Factor (mg/kg/day) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
US EPA IRIS (2004)  Also used by: ♦ US EPA HEAST (1997) ♦ US EPA Region 3 (2003)	9.1 x 10 <sup>-5</sup>	0.011	linearized multistage model, extra risk	body surface area <sup>2</sup>	Based on squamous cell carcinoma of nasal turbinates in male rats exposed via drinking water for 110 weeks.
CA EPA (2002)	3.7 x 10 <sup>-5</sup>	0.027	linearized multistage model	body surface area <sup>2</sup>	Based on the combined incidence of hepatocarcinomas and adenomas in female mice exposed via drinking water for 90 weeks.

<sup>1</sup>The dose associated with an increased lifetime cancer risk of one-in-one million (i.e., 1 x 10<sup>-6</sup> dose), where 1 x 10<sup>-6</sup> dose = 1 x 10<sup>-6</sup> / cancer potency factor.

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

**2. Recommendation and Rationale**

The basis of the US EPA and CA EPA cancer potency factors is identical with respect to the study used, but the two values are based on tumor data from different species, dosing durations and different tumor sites reported in that study. The animal potency estimate derived from the US EPA data is slightly higher than the animal potency estimate based on the tumor data CA EPA used, although adjustments for exposure duration and interspecies scaling result in a higher human potency estimate derived by CA EPA. A clear technical rationale was not provided for the method CA EPA employed to adjust their potency estimate for the somewhat shorter exposure duration in mice compared to rats in the same study. Therefore, the US EPA cancer potency factor (0.011 per mg/kg/day) is the toxicity value recommended for use in the derivation of an oral cancer-based soil cleanup objective for 1,4-dioxane. The 1,4-dioxane risk specific dose calculated from this toxicity value is 9.1 x 10<sup>-5</sup> mg/kg/day.

**3. Review Dates**

Summary table completion: April, 2004

#### 4. References for Summary Table

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

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. Last Revised 9/01/1990, Verification Date 2/03/1988.  
<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>

#### 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: 1,4-Dioxane**

**Exposure Route: Inhalation**

**Toxicity: Non-Cancer**

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

**1. Summary of Available Inhalation Reference Concentrations for 1,4-Dioxane (CAS Number 123-91-1)**

Agency	Reference Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Point of Departure		UF	Summary
		Air Concentration (mcg/m <sup>3</sup> )	Basis		
ATSDR (2004)	$3.6 \times 10^3$	$1.3 \times 10^5$ (35.5 ppm)	NOEL (PBPK-derived)	30	Based on no effects on liver, kidney, or hematologic function in rats exposed by inhalation 7 hours/day, 5 days/week for 2 years.
CA EPA (2003)	$3 \times 10^3$	$8.3 \times 10^4$ (23 ppm)	NOEL	30	Based on same study as ATSDR (2004).

<sup>1</sup>Agencies use different terms for the reference concentration, including chronic reference exposure level, tolerable concentration and chronic minimal risk level.

NOEL: no observed effect level; UF: uncertainty factor; PBPK: physiologically based pharmacokinetic.

**2. Recommendation and Rationale**

The reference concentrations for 1,4-dioxane derived by authoritative bodies from the list in item 5 (below) are both based on the same chronic inhalation study in rats that used a single exposure level and reported no non-cancer toxic effects. The ATSDR derived a point of departure using pharmacokinetic modeling to obtain the human equivalent air concentration at the NOEL, and applied uncertainty factors of 10 for intraspecies extrapolation and 3 for interspecies extrapolation to obtain their reference concentration. The CA EPA point of departure is the time-weighted air concentration at the NOEL, and assumes a 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. CA EPA also applied uncertainty factors of 10 for intraspecies extrapolation and 3 for interspecies extrapolation to obtain the reference concentration. The use of physiologically-based pharmacokinetic modeling to estimate human equivalent concentrations is consistent with current risk assessment practice. Therefore, the ATSDR reference concentration ( $3.6 \times 10^3$  mcg/m<sup>3</sup>) is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,4-dioxane.

### 3. Review Dates

Summary table completion: July, 2004

Toxicity value recommendation: January, 2005

### 4. References for Summary Table

ATSDR (Agency for Toxic Substances and Disease Registry). 2004. Toxicological Profile for 1,4-Dioxane. Draft for public comment. Atlanta GA: Department of Health and Human Services.

CA EPA (California Environmental Protection Agency). 2004. Chronic Reference Exposure Levels: Chronic Toxicity Summary for 1,4-Dioxane. Sacramento, CA: Office of Environmental Health Assessment, California Environmental Protection Agency.

[http://www.oehha.ca.gov/air/chronic\\_rels/AllChrels.html](http://www.oehha.ca.gov/air/chronic_rels/AllChrels.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

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**Chemical Name: 1,4-Dioxane**

**Exposure Route: Inhalation**

**Toxicity: Cancer**

**New York State Department of Health  
Inhalation Cancer Toxicity Value Documentation**

**1. Summary of Available Inhalation Unit Risk Values for 1,4-Dioxane (CAS Number 123-91-1)**

Agency	Risk Specific Air Concentration <sup>1</sup> (mcg/m <sup>3</sup> )	Unit Risk (mcg/m <sup>3</sup> ) <sup>-1</sup>	Extrapolation Methods		Summary
			High to Low Dose	Animal to Human	
CA EPA (2002)	0.13	$7.7 \times 10^{-6}$	linearized multistage model, extra risk	body surface area <sup>2</sup>	Calculated from the oral cancer potency factor (0.027 per mg/kg/day), which was derived from a single data set of combined incidence of hepatocarcinomas and adenomas in female mice exposed in drinking water for 90 weeks.

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

<sup>2</sup>Factor for dose adjustment from animal to humans is (animal body weight/human body weight)<sup>0.33</sup>.

**2. Recommendation and Rationale**

The CA EPA unit risk ( $7.7 \times 10^{-6}$  per mcg/m<sup>3</sup>) 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 1,4-dioxane. Since no toxicity values from the authoritative bodies listed in item 5 (below) are based on inhalation data, and at least one authoritative body derived a unit risk using exposure route extrapolation, a default oral-to-inhalation extrapolation assuming a 70 kg adult continuously exposed and breathing 20 m<sup>3</sup> of air per day is used to derive a unit risk from the recommended cancer potency factor. The recommended oral cancer potency factor for 1,4-dioxane is 0.011 per mg/kg/day. Therefore the unit risk of  $3.1 \times 10^{-6}$  per mcg/m<sup>3</sup> is the toxicity value recommended for use in the derivation of an inhalation non-cancer-based soil cleanup objective for 1,4-dioxane. The 1,4-dioxane risk specific air concentration calculated from this toxicity value is 0.32 mcg/m<sup>3</sup>.

**3. Review Dates**

Summary table completion: July, 2004

Toxicity value recommendation: December, 2004

#### 4. References for Summary Table

CA EPA (California Environmental Protection Agency) 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.  
[http://www.oehha.ca.gov/air/cancer\\_guide/TSD2.html](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  
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National Institute of Public Health & Environmental Protection, Netherlands