



## CHEMICAL UPDATE WORKSHEET

<b>Chemical Name:</b>	Hexachlorobenzene
<b>CAS #:</b>	118-74-1
<b>Revised By:</b>	RRD Toxicology Unit
<b>Revision Date:</b>	August 18, 2015

### (A) Chemical-Physical Properties

	Part 201 Value	Updated Value	Reference Source	Comments
Molecular Weight (g/mol)	284.78	284.78	EPI	EXP
Physical State at ambient temp	Solid	Solid	MDEQ	
Melting Point (°C)	504	231.80	EPI	EXP
Boiling Point (°C)	325	325.00	EPI	EXP
Solubility (ug/L)	6200	6.2	EPI	EXP
Vapor Pressure (mmHg at 25°C)	0.00001748	1.80E-05	EPI	EXP
HLC (atm-m <sup>3</sup> /mol at 25°C)	1.32E-3	1.70E-03	EPI	EXP
Log Kow (log P; octanol-water)	5.89	5.73	EPI	EXP
Koc (organic carbon; L/Kg)	55300	6195	EPI	EST
Ionizing Koc (L/kg)		NR	NA	NA
Diffusivity in Air (Di; cm <sup>2</sup> /s)	0.0542	2.90E-02	W9	EST
Diffusivity in Water (Dw; cm <sup>2</sup> /s)	5.91E-6	7.85E-06	W9	EST
Soil Water Partition Coefficient (Kd; inorganics)	NR	NR	NA	NA

	Part 201 Value	Updated Value	Reference Source	Comments
Flash Point (°C)	NA	242	PC	EXP
Lower Explosivity Level (LEL; unitless)	NA	NA	NA	NA
Critical Temperature (K)		8.25E+02	EPA2004	EXP
Enthalpy of Vaporization (cal/mol)		1.44E+04	EPA2004	EXP
Density (g/mL, g/cm <sup>3</sup> )		2.044	CRC	EXP
EMSOFT Flux Residential 2 m (mg/day/cm <sup>2</sup> )	2.99E-06	1.34E-05	EMSOFT	EST
EMSOFT Flux Residential 5 m (mg/day/cm <sup>2</sup> )	2.99E-06	1.43E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 2 m (mg/day/cm <sup>2</sup> )	3.57E-06	1.77E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 5 m (mg/day/cm <sup>2</sup> )	3.57E-06	1.81E-05	EMSOFT	EST

**(B) Toxicity Values/Benchmarks**

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
Reference Dose (RfD) (mg/kg/day)	8.0E-4	1.0E-5	PPRTV, 2010	
RfD details	Rat chronic feeding study. NOAEL = 0.08mg/kg; Critical effects = liver effects seen at higher doses; UF = 100 (Arnold et al., 1985). RD calculation date: 5/26/88.	<p><b>Tier 2 Source:</b>  <b>PPRTV:</b>  <b>Basis:</b> The PPRTV p-RfD is selected as it represents a more current evaluation of the available toxicity literature than the IRIS value.  <b>PPRTV</b> sub chronic p-RfD = 1.0E-5 mg/kg-day.  <b>Critical Study:</b> Bourque, AC; Singh, A; Lakhanpal, N; et al. (1995) Ultrastructural changes in ovarian follicles of monkeys administered hexachlorobenzene. Am J Vet Res 56:1673–1677.  <b>Methods:</b> Female Cynomolgus monkeys (4/dose, 6–13 years of age) were administered hexachlorobenzene mixed with glucose in gelatin capsules, daily, at doses of 0, 0.01, 0.1, 1.0, or 10 mg/kg-day for 13 weeks. Controls received only glucose. After the period of treatment, monkeys were given FSH and LH during Days 2 through 7 of the following menstrual period. On the eighth day of the cycle, HCG was given; an ovary from each monkey was subsequently removed 35–38 hours later. Primordial, primary, and growing follicles from controls and each hexachlorobenzene treatment group were examined by TEM.  <b>Critical effects:</b> Ultrastructural (degenerative) changes were noted in the ovarian follicles of all hexachlorobenzene-exposed monkeys.  <b>End point or Point of Departure (POD):</b> The subchronic provisional RfD is lower than the chronic IRIS RfD due to the availability of newer data. The principal study (Bourque, 1995) provided the lowest LOAEL (0.01 mg/kg-day) representing the most sensitive effect in the sub chronic database: degenerative changes in primary ovarian follicles of monkeys. The POD is supported by other studies with an overall LOAEL of 0.1 mg/kg-day (Jarrell et al., 1993; Foster et al., 1992, 1995; Babineau et al., 1991; Sims et al., 1991). The studies provide evidence that hexachlorobenzene is toxic to the mammalian ovary and may interfere with mechanisms regulating ovarian steroidogenesis (ATSDR, 2002; Foster et al., 1992).  <b>Uncertainty Factors:</b> PPRTV had proposed a total uncertainty factor of 1,000 (10 for interspecies variability, 10 for interspecies extrapolation, and 10 for LOAEL to</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		<p>NOAEL extrapolation).  <b>Source:</b> PPRTV, 9/30/2010</p> <p><b>Tier 1 and 2 Sources:</b>  <b>IRIS:</b> The IRIS RfD of 8.0E-4 mg/kg-day is based on a chronic multi-generation feeding study in rats.  <b>Critical Study:</b> Arnold et al., (1985) Long-term toxicity of hexachlorobenzene in the rat and the effect of dietary Vitamin A. Food Chem. Toxic. 23(9): 779-793).  <b>Methods:</b> F0 generation male and female Sprague-Dawley rats were exposed to hexachlorobenzene in diet at doses of 0, 0.32, 1.6, 8.0, or 40 ppm for 90 days prior to mating and until 21 days after parturition. F1 generation males and females (n=50/dose) were then exposed to their respective parents' dose via diet through 130 weeks. The F1 generation was therefore exposed in utero, during nursing and via diet through the remainder of their lifetime.  <b>Critical Effects:</b> hepatic centrilobular basophilic chromogenesis in F1 animals.  <b>NOAEL</b> = 1.6 ppm (0.08 mg/kg/day based on study-based food consumption values). Doses were based on actual food consumption and body weights provided by Arnold at 30 weeks of exposure (US EPA, 1985, 1988).  <b>Uncertainty Factors:</b> = 100 (10 for interspecies extrapolation and 10 for interspecies variability).                      An August, 2003 EPA screening level review did not identify any critical new studies. Last IRIS RfD revision date: 4/1/91.</p> <p><b>MRL 6/2013:</b> The DRAFT chronic oral MRL is 7E-5 mg/kg/day based on hepatic effects observed in F1 male rats in the 0.022 mg/kg/d dose group (see Arnold et al., 1985, study description in IRIS entry above).</p> <p><b>Tier 3 Source:</b>  <b>MDEQ:</b> Per DEQ-CCD, the WRD and RRD adopted the RfD value of 8E-4 mg/kg/d from the IRIS chemical record dated 4/1/1991.</p>		
<b>Oral Cancer Slope Factor (CSF) (mg/kg-day)<sup>-1</sup></b>	1.0E+0	1.6E+0	IRIS, 1996	



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
CSF details	SD rats developed hepatocellular carcinomas after eating HCB in the diet @ 0, 75, & 150 ppm (Erturk et al., 1986); 10E-6 dose = 6.2E-7 mg/kg. Revised species scaling factor of (BWh/BWa) to the 0.25 power used for q* calculation. RD calculation date: 1/25/00.	<p><b>Tier 1 Source:</b>  <b>IRIS:</b>  <b>Basis:</b> IRIS is a Tier 1 source. IRIS oral cancer slope factor value = 1.6E+0 per mg/kg-day  <b>Critical Study:</b> Erturk, E., R.W. Lambrecht, H.A. Peters, D.J. Cripps, A. Gocmen, C.R. Morris and G.T. Bryan. 1986. Oncogenicity of hexachlorobenzene. In: Hexachlorobenzene: Proc. Int. Symp., C.R. Morris and J.R.P. Cabral, Ed. IARC Scientific Publ. No. 77, Oxford University Press, Oxford. p. 417-423.  <b>Methods:</b> Sprague-Dawley rats (n=94/sex/dose) were fed 0, 75, or 150 ppm hexachlorobenzene in their diet for up to 2 years. Interim kills of four rats/group were performed at weeks 0, 1, 2, 3, 4, 8, 16, 32, 48, 64, and 80. The remaining 50 animals/group were observed until natural death or until sacrifice at 2 years.  <b>Critical effects:</b> Hepatocellular carcinomas in treated female rats.  <b>Endpoint:</b> 1.6E+0 per mg/kg-day  <b>Carcinogen Weight-of-Evidence (WOE) Class:</b> B2; probable human carcinogen.  <b>IRIS WOE Basis:</b> HCB, when administered orally, has been shown to induce tumors in the liver, thyroid and kidney in three rodent species.  <b>Source:</b> IRIS, 11/01/1996</p> <p><b>Tier 2 Sources:</b>  <b>PPRTV (09/30/2010):</b> NA – PPRTV reports that a carcinogenicity assessment of hexachlorobenzene was not prepared because IRIS includes a cancer assessment for this compound.  <b>MRL:</b> NA; MRLs are for non-cancer effects only.</p> <p><b>Tier 3 Source:</b>  <b>MDEQ-RRD (1/25/2000):</b> Per DEQ-CCD, the oral cancer slope factor is based on the same study as described in the IRIS entry above, but differs in value (1.0E+0 per mg/kg-day vs 1.6E+0 per mg-day, respectively) due to DEQ-RRD’s application of a revised species scaling factor.</p>		Complete
Reference Concentration (RfC) or Initial	--	3.5E-2	MDEQ, 2015	



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
<b>Threshold Screening Level (ITSL) (<math>\mu\text{g}/\text{m}^3</math>)</b>				
<b>RfC/ITSL details</b>	NA	<p><b>Tier 3 Source:</b>  <b>MDEQ:</b>  <b>Basis:</b> MDEQ is the only available value with a justification. California and New York do not have justifications and RIVM justification is in Dutch. See details below.</p> <p><b>Tier 1 and 2 Sources:</b>  <b>IRIS:</b> Per IRIS, 11/15/1990, no value at this time.  <b>PPRTV (9/30/2010):</b> Per PPRTV, the existing database for hexachlorobenzene does not include studies that can be used to derive inhalation p-RfC values.  <b>MRL (6/2013):</b> Per ATSDR, available data are inadequate for developing inhalation MRL values for hexachlorobenzene.</p> <p><b>Tier 3 Sources:</b>  <b>MDEQ:</b> AQD derived an ITSL of <math>0.035 \mu\text{g}/\text{m}^3</math> based on a 24-hour averaging time (10/28/2015). See Interoffice Communication (IC). The IC includes the derivation of a candidate chronic ITSL of <math>0.25 \mu\text{g}/\text{m}^3</math> based on the ATSDR chronic oral MRL of <math>0.00007 \text{ mg}/\text{kg}/\text{day}</math> and conversion to an inhalation dose. Because the candidate ITSL which was protective of chronic liver effects was not protective for reproductive effects of short-term exposure, it was decided that the candidate ITSL will not be used. Of the three acute benchmarks available, AQD selected the sub chronic RfD from PPRTV to serve as the basis for the ITSL. See the RfD details above and AQD's justification.</p> <p><b>California DTSC:</b> RfC= <math>3.2\text{E}+00 (\text{ug}/\text{kg}\text{-day})^{-1}</math> (needs a justification on study)</p> <p><b>New York DEC:</b> RfC= <math>2.8 \mu\text{g}/\text{m}^3</math> (This is based on extrapolation from the RfD) (needs a justification on study)</p> <p><b>RIVM:</b> RfC= <math>.75 \mu\text{g}/\text{m}^3</math> (MTR Maximum Tolerable Risk Level) (link leads to</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		document in Dutch)		
Inhalation Unit Risk Factor (IURF) (( $\mu\text{g}/\text{m}^3$ ) <sup>-1</sup> )	4.6E-4	4.6E-4	IRIS, 1996	
IURF details		<p><b>Tier 1 Source:</b>  <b>IRIS:</b>  <b>Basis:</b> IRIS is the only available value.  <b>IRIS IURF</b> = 4.6E-4 per <math>\mu\text{g}/\text{m}^3</math>  <b>Critical Study:</b> Erturk, E., R.W. Lambrecht, H.A. Peters, D.J. Cripps, A. Gocmen, C.R. Morris and G.T. Bryan. 1986. Oncogenicity of hexachlorobenzene. In: Hexachlorobenzene: Proc. Int. Symp., C.R. Morris and J.R.P. Cabral, Ed. IARC Scientific Publ. No. 77, Oxford University Press, Oxford. p. 417-423.  <b>Method(s):</b> Sprague-Dawley rats (n=94/sex/dose) were fed 0, 75, or 150 ppm hexachlorobenzene in their diet for up to 2 years. Interim kills of four rats/group were performed at weeks 0, 1, 2, 3, 4, 8, 16, 32, 48, 64, and 80. The remaining 50 animals/group were observed until natural death or until sacrifice at 2 years.  <b>Critical effects:</b> Hepatocellular carcinomas in treated female rats.  <b>Endpoint:</b> 4.6E-4 per <math>\mu\text{g}/\text{m}^3</math>  <b>Carcinogen Weight-of-Evidence (WOE) Class:</b> B2; probable human carcinogen.  <b>IRIS WOE Basis:</b> Hexachlorobenzene, when administered orally, has been shown to induce tumors in the liver, thyroid and kidney in three rodent species.  <b>Source and Date:</b> IRIS, 11/01/1996.</p> <p><b>Tier 2 Sources:</b>  <b>PPRTV (09/30/2010):</b> NA – PPRTV reports that a carcinogenicity assessment of hexachlorobenzene was not prepared because IRIS includes a cancer assessment for this compound.  <b>MRL:</b> NA; MRLs are for non-cancer effects only.</p> <p><b>Tier 3 Source:</b>  <b>MDEQ:</b> Per DEQ-CCD, AQD adopted the IRIS value (4.6E-4 per <math>\mu\text{g}/\text{m}^3</math>) for the IUR. 3/16/1982. AQD conducted a literature review and determined that the IRIS IURF</p>	Complete	



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		is still valid. (10/28/2015)		
<b>Mutagenic Mode of Action (MMOA)? (Y/N)</b>	--	No	USEPA, 2015	
<b>MMOA Details</b>	--	Not listed as a carcinogen with mutagenic MOA in the USEPA OSWER List.		
<b>Developmental or Reproductive Effector? (Y/N)</b>	No	No. The MDEQ does not consider this substance a developmental toxicant at this time. The RfD is based on a reproductive effect.	MDEQ, 2015	
<b>Developmental or Reproductive Toxicity Details</b>	NA	The studies provide evidence that hexachlorobenzene is toxic to the mammalian ovary and may interfere with mechanisms regulating ovarian steroidogenesis See details for the oral RfD.		
<b>State Drinking Water Standard (SDWS) (µg/L)</b>	NA	1	SDWA, 1976	
<b>SDWS details</b>		MI Safe Drinking Water Act (SDWA) 1976 PA 399		
<b>Secondary Maximum Contaminant Level (SMCL) (µg/L)</b>	NA	NO	SDWA, 1976 and USEPA SMCL List	
<b>SMCL details</b>		MI Safe Drinking Water Act (SDWA) 1976 PA 399 and USEPA SMCL List, 2015		
<b>Is there an aesthetic value for drinking water? (Y/N)</b>	No	Not evaluated.	NA	
<b>Aesthetic value details</b>	NA	NA		
<b>Phytotoxicity Value? (Y/N)</b>	No	Not evaluated.	NA	
<b>Phytotoxicity details</b>	NA	NA		
<b>Others:</b>				



**(C) Chemical-specific Absorption Factors**

	Part 201 Value	Update	Source/Reference/ Dates	Comments/Notes /Issues
Gastrointestinal absorption efficiency value (ABS <sub>gi</sub> )	---	1.0	MDEQ, 2015/USEPA RAGS-E, 2004	
ABS <sub>gi</sub> details		RAGS E (USEPA, 2004) Default Value		
Skin absorption efficiency value (AE <sub>d</sub> )	---	0.1	MDEQ, 2015	
AE <sub>d</sub> details				
Ingestion Absorption Efficiency (AE <sub>i</sub> )		0.5	MDEQ, 2015	
AE <sub>i</sub> Details				
Relative Source Contribution for Water (RSC <sub>w</sub> )		0.2	MDEQ, 2015	
Relative Source Contribution for Soil (RSC <sub>s</sub> )		1.0	MDEQ, 2015	
Relative Source Contribution for Air (RSC <sub>A</sub> )		1.0	MDEQ, 2015	
Others				

**(D) Rule 57 Water Quality Values and GSI Criteria**

<b>Current GSI value (µg/L)</b>	0.2 (M); 0.0003
<b>Updated GSI value (µg/L)</b>	0.2 (M); 0.0003
<b>Rule 57 Drinking Water Value (µg/L)</b>	0.2 (M); 0.00045

	<b>Rule 57 Value (µg/L)</b>	<b>Verification Date</b>
<b>Human Non-cancer Values- Drinking water source (HNV-drink)</b>	0.046	7/1997
<b>Human Non-Cancer Values- Non-drinking water sources (HNV-Non-drink)</b>	0.046	7/1997
<b>Wildlife Value (WV)</b>	0.0003	4/1997
<b>Human Cancer Values for Drinking Water Source (HCV-drink)</b>	0.00045	7/1997
<b>Human Cancer values for non-drinking water source (HCV-Non-drink)</b>	0.00045	7/1997
<b>Final Chronic Value (FCV)</b>	ID* (0.0003)	1/1998
<b>Aquatic maximum value (AMV)</b>	ID	1/1998
<b>Final Acute Value (FAV)</b>	ID	1/1998

Sources:

1. MDEQ Surface Water Assessment Section Rule 57 [website](#)
2. MDEQ Rule 57 [table](#)

**(E) Target Detection Limits (TDL)**

	<b>Value</b>	<b>Source</b>
<b>Target Detection Limit – Soil (<math>\mu\text{g}/\text{kg}</math>)</b>	330	MDEQ, 2015
<b>Target Detection Limit – Water (<math>\mu\text{g}/\text{L}</math>)</b>	0.2	MDEQ, 2015
<b>Target Detection Limit – Air (ppbv)</b>	4.80E-03	MDEQ, 2015
<b>Target Detection Limit – Soil Gas (ppbv)</b>	1.60E-01	MDEQ, 2015

**CHEMICAL UPDATE WORKSHEET ABBREVIATIONS:**

CAS # - Chemical Abstract Service Number.

**Section (A) Chemical-Physical Properties****Reference Source(s):**

CRC	Chemical Rubber Company Handbook of Chemistry and Physics, 95th edition, 2014-2015
EMSOFT	USEPA Exposure Model for Soil-Organic Fate and Transport (EMSOFT) (EPA, 2002)
EPA2001	USEPA (2001) Fact Sheet, Correcting the Henry's Law Constant for Soil Temperature. Office of Solid Waste and Emergency Response, Washington, D.C.
EPA4	USEPA (2004) User's Guide for Evaluating Subsurface Vapor Intrusion into Buildings. February 22, 2004.
EPI	USEPA's Estimation Programs Interface SUITE 4.1, Copyright 2000-2012
HSDB	Hazardous Substances Data Bank
MDEQ	Michigan Department of Environmental Quality
NPG	National Institute for Occupational Safety and Health Pocket Guide to Chemical Hazards
PC	National Center for Biotechnology Information's PubChem database
PP	Syracuse Research Corporation's PhysProp database
SCDM	USEPA's Superfund Chemical Data Matrix
SSG	USEPA's Soil Screening Guidance: Technical Background Document, Second Edition, 1996
USEPA/EPA	United States environmental protection agency's Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment). July, 2004.

W9 USEPA's User Guide for Water9 Software, Version 2.0.0, 2001

**Basis/Comments:**

EST	estimated
EXP	experimental
EXT	extrapolated
NA	not available or not applicable
NR	not relevant

**Section (B) Toxicity Values/Benchmarks****Sources/References:**

ATSDR	Agency for Toxic Substances and Disease Registry
CALEPA	California Environmental Protection Agency
CAL DTSC	California Department of Toxic Substances Control
CAL OEHTA	CAEPA Office of Environmental Health Hazard Assessment
CCD	MDEQ Chemical Criteria Database
ECHA	European Chemicals Agency (REACH)
OECD HPV	Organization for Economic Cooperation and Development HPV Database
HEAST	USEPA's Health Effects Assessment Summary Tables
IRIS	USEPA's Integrated Risk Information System
MADEP	Massachusetts Department of Environmental Protection
MDEQ/DEQ	Michigan Department of Environmental Quality
DEQ-CCD/AQD	MDEQ Air Quality Division
DEQ-CCD/RRD	MDEQ Remediation and Redevelopment Division
DEQ-CCD/WRD	MDEQ Water Resources Division
MNDOH	Minnesota Department of Health

NJDEP	New Jersey Department of Environmental Protection
NYDEC	New York State Department of Environmental Conservation
OPP/OPPT	USEPA's Office of Pesticide Programs
PPRTV	USEPA's Provisional Peer Reviewed Toxicity Values
RIVM	The Netherlands National Institute of Public Health and the Environment
TCEQ	Texas Commission on Environmental Quality
USEPA	United States Environmental Protection Agency
USEPA OSWER	USEPA Office of Solid Waste and Emergency Response
USEPA MCL	USEPA Maximum Contaminant Level
WHO	World Health Organization
WHO IPCS	International Programme on Chemical Safety (IPCS/INCHEM)
WHO IARC	International Agency for Research on Cancers
NA	Not Available.
NR	Not Relevant.

**Toxicity terms:**

BMC	Benchmark concentration
BMCL	Lower bound confidence limit on the BMC
BMD	benchmark dose
BMDL	Lower bound confidence limit on the BMD
CSF	Cancer slope Factor
CNS	Central nervous system
IURF or IUR	Inhalation unit risk factor
LOAEL	Lowest observed adverse effect level
LOEL	Lowest observed effect level
MRL	Minimal risk level (ATSDR)
NOAEL	No observed adverse effect level
NOEL	No observed effect level

RfC	Reference concentration
RfD	Reference dose
p-RfD	Provisional RfD
aRfD	Acute RfD
UF	Uncertainty factor
WOE	Weight of evidence

**Section (C) Chemical-specific Absorption Factors**

MDEQ	Michigan Department of Environmental Quality
USEPA RAGS-E	United States Environmental Protection Agency's Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part E, Supplemental Guidance for Dermal Risk Assessment). July, 2004.

**Section (D) Rule 57 Water Quality Values and GSI Criteria**

GSI	Groundwater-surface water interface
NA	A value is not available or not applicable.
ID	Insufficient data to derive value
NLS	No literature search has been conducted