



## CHEMICAL UPDATE WORKSHEET

<b>Chemical Name:</b>	n-Hexane
<b>CAS #:</b>	110-54-3
<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)	86.18	86.18	EPI	EXP
Physical State at ambient temp	liquid	Liquid	MDEQ	
Melting Point (°C)	---	-95.30	EPI	EXP
Boiling Point (°C)	68.7	68.70	EPI	EXP
Solubility (ug/L)	12000	9500	EPI	EXP
Vapor Pressure (mmHg at 25°C)	150	1.51E+02	EPI	EXP
HLC (atm-m <sup>3</sup> /mol at 25°C)	1.40E-2	1.80E+00	PP	EST
Log Kow (log P; octanol-water)	4.0	3.90	EPI	EXP
Koc (organic carbon; L/Kg)	1760	131.5	EPI	EST
Ionizing Koc (L/kg)		NR	NA	NA
Diffusivity in Air (Di; cm <sup>2</sup> /s)	0.08	7.31E-02	W9	EST
Diffusivity in Water (Dw; cm <sup>2</sup> /s)	8.0E-6	8.17E-06	W9	EST
Soil Water Partition Coefficient (Kd; inorganics)	NR	NR	NA	NA

	Part 201 Value	Updated Value	Reference Source	Comments
Flash Point (°C)	-7 F	-22	CRC	EXP
Lower Explosivity Level (LEL; unitless)	0.011	0.011	CRC	EXP
Critical Temperature (K)		508.00	EPA2004	EXP
Enthalpy of Vaporization (cal/mol)		6.90E+03	EPA2004	EXP
Density (g/mL, g/cm <sup>3</sup> )		0.6606	CRC	EXP
EMSOFT Flux Residential 2 m (mg/day/cm <sup>2</sup> )	2.38E-05	2.82E-05	EMSOFT	EST
EMSOFT Flux Residential 5 m (mg/day/cm <sup>2</sup> )	4.70E-05	6.94E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 2 m (mg/day/cm <sup>2</sup> )	3.30E-05	4.49E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 5 m (mg/day/cm <sup>2</sup> )	6.20E-05	1.10E-04	EMSOFT	EST

**(B) Toxicity Values/Benchmarks**

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
Reference Dose (RfD) (mg/kg/day)	4.1E-1	3E-1	PPRTV, 09/30/2009	
RfD details	<p>Per RD/EPBCCD: (NA from IRIS) Developed by SWQD...different from HEAST RfD because EPA considered a decrease in body weight gain to be significant. However, SWQD could not determine statistical significance &amp; considered low dose to be NOAEL. EPA considered low dose to be LOAEL. Critical effect = no observed effect. See justification. RD calculation date: 5/5/92.</p>	<p><b>Basis:</b> ATSDR is a Tier 2 source, no Tier 1 available</p> <p><b>Tier 1/IRIS Source:</b> <b>IRIS 12/23/2005:</b> An oral RfD is not available in IRIS. Per IRIS: <i>“An RfD for n-hexane cannot be derived in the absence of a suitable oral study of sufficient duration that evaluates an array of endpoints. The only study identified for oral exposure to n-hexane was of subchronic duration, utilized gavage exposure, and evaluated a small number (five/group) of animals (Krasavage et al., 1980). Several animals died in each dose group (two in the mid-dose and one in the high-dose groups, respectively) during the course of the study.”</i></p> <p><b>Tier 2 Sources:</b> <b>MRL:</b> No oral MRL available at this time.</p> <p><b>PPRTV. Final. 09/30/2009:</b> RfD = 3E-1 mg/kg/day <b>Critical Study:</b> Ono, Y., Y. Takeuchi and N. Hisanaga. (1981) A comparative study on the toxicity of n-hexane and its isomers on the peripheral nerve. Int. Arch. Occup. Environ. Health. 48:289–294. <b>Methods:</b> The effects of n-hexane on peripheral nerve transmission were evaluated by Ono et al. (1981). Male Wistar rats (5–7/group) were administered n-hexane (99% pure) by gavage in olive oil daily for 8 weeks. The exposure regimen consisted of administration of 0.4 mL solvent and 0.6 mL olive oil for the first 4 weeks, 0.6 mL solvent and 0.4 mL olive oil for a subsequent 2 weeks and 1.2 mL solvent and 0.8 mL olive oil for the final 2 weeks, while a control group received olive oil alone. Body weight was measured every 2 weeks during the experimental period, resulting in dose calculations of 811 mg/kg-day (after 2 weeks), 759 mg/kg-day (2–4 weeks), 1,047 mg/kg-day (4–6 weeks) and 2,022 mg/kg-day (6–8 weeks). Peripheral nerve activity was measured by administering a differential pulse to electrodes inserted at different points along</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		<p>the tail of unanaesthetized animals. Transmission of electrical charge was then detected at other points along the tail. The group mean motor nerve conduction velocity (MCV) was measured at the start of the experiment and every 2 weeks until termination. Histopathology examinations were not made.</p> <p><b>Critical effect:</b> neurotoxicity; decreased MCV</p> <p><b>End point or Point of Departure (POD):</b> The Ono et al. (1981) study was selected as the basis for the subchronic p-RfD for n-hexane. This study identified a LOAEL of 785 mg/kg-day for decreased MCV. This endpoint is supported by observed clinical signs and histological evidence of peripheral neuropathy at higher doses in the Krasavage et al. (1980) study. Krasavage et al. (1980) also observed changes in body weight at lower doses than the effects observed by Ono et al. (1981).</p> <p><b>Uncertainty Factors:</b> The composite UF of 3,000 is composed of the following:</p> <ul style="list-style-type: none"> <li>• An UF of 10 is applied for interspecies extrapolation to account for potential pharmacokinetic and pharmacodynamic differences between rats and humans.</li> <li>• An UF of 10 for interspecies differences is used to account for potentially susceptible individuals in the absence of information on the variability of response in humans.</li> <li>• An UF of 3 (10<sup>0.5</sup>) is applied for use of a LOAEL. Although nerve conduction velocity was reduced at the LOAEL of 785 mg/kg-day (Ono et al., 1981), there was no histopathologic evidence of damage to peripheral nerves at a similar dose, 814 mg/kg-day, or observable signs of nerve damage (e.g., limb dragging) at 1,140 mg/kg-day in the supporting study (Krasavage et al., 1980). Since nerve conduction normally decreases as a function of age, this delay in nerve conduction may represent an advancing of an age-related effect. Additionally, the weighted average dose method coupled with a fixed dose and increased body weight with time precluded identifying a NOAEL that was actually lower than the weighted average LOAEL value. For these reasons, a full UF of 10 is not warranted.</li> <li>• A database UF of 10 is applied. There are no two-generation reproductive studies or developmental studies. Although a large toxicological database exists for inhaled n-hexane, and supports peripheral nerve damage as the critical</li> </ul>		

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		<p>effect, the database for oral n-hexane exposure contains only two minimally adequate subchronic neurotoxicity studies. Confidence in the principal study and the supporting study is low.</p> <p><b>Tier 3 Source:</b> <b>MDEQ:</b> Per DEQ-CCD, WRD reports an RfD of 4.1E-1. CAS date = 04/01/1992; Calculation date = 05/05/1992. NOAEL of 570 mg/kg in male Charles River rats dosed by gavage, 5 days/week for 90 days (UF=1,000) (Krasavage, 1980). Per DEQ-CCD, RRD reports an RfD = 4.1E-1 adopted from SWQD and dated 05/05/1992.</p>		
<b>Oral Cancer Slope Factor (CSF) (mg/kg-day)<sup>-1</sup></b>	NA	NA	MDEQ, 2015	
<b>CSF details</b>		<p><b>Tier 1/IRIS Source:</b> <b>IRIS (12/23/2005):</b> there is inadequate information to assess the carcinogenic potential of n-hexane.</p> <p><b>Tier 2 Sources:</b> <b>PPRTV (09/30/2009):</b> Per PPRTV, no value at this time.</p> <p><b>MRL:</b> NA; MRLs are for non-cancer effects only.</p> <p><b>Tier 3 Source:</b> <b>MDEQ:</b> Per DEQ-CCD, no value at this time.</p>		Complete
<b>Reference Concentration (RfC) or Initial Threshold Screening Level (ITSL) (µg/m<sup>3</sup>)</b>	2.0E+2	7E+2	MDEQ, 2015	
<b>RfC/ITSL details</b>	(Air): Based on EPAs RfC, from Sanagi et al 1980 and Dunnick	<p><b>Basis:</b> IRIS is a Tier 1 source.</p> <p><b>Tier 1/IRIS Source (12/23/2005):</b> RfC = 7E+2 µg/m<sup>3</sup>.</p>		Complete

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
	et al 1989.	<p><b>Critical Study:</b> Huang, J; Kato, K; Shibata, E; et al. (1989) Effects of chronic n-hexane exposure on nervous system-specific and muscle-specific proteins. Arch Toxicol 63:381-385.</p> <p><b>Methods:</b> Male Wistar rats (8/group) were exposed to 0, 500, 1,200, or 3,000 ppm (0, 1,762, 4,230, 10,574 mg/m<sup>3</sup>) n-hexane (&gt;99% pure) for 12 hours/day, 7 days/week for 16 weeks. The authors measured motor nerve conduction velocity (MCV) in the tail nerve along with body weight before exposure and after 4, 8, 12, and 16 weeks of exposure to n-hexane. One animal from each group was sacrificed at 16 weeks exposure for histopathological evaluation of the nerve fibers in the tail. In addition, Huang et al. (1989) measured the levels of neuron-specific enolase and beta-S-100. These nervous system-specific proteins are a family of calcium binding proteins that are involved in processes such as cell-to-cell communication, cell growth, intracellular signal transduction, and development and maintenance of the central nervous system.</p> <p><b>Critical effect:</b> Peripheral neuropathy (decreased MCV at 12 weeks) in male rats.</p> <p><b>End point or Point of Departure (POD):</b> The Huang et al. (1989) data set provided an adequate dose response for BMD modeling with an estimated point of departure of a BMCL<sub>HEC</sub> of 215 mg/m<sup>3</sup> (Section 5.2.2 and Appendix B of the Toxicological Review of n-Hexane [U.S. EPA, 2005a]). The neurophysiological deficits and histopathological effects that were evident in mid- and high-dose rats indicate a NOAEL of 500 ppm.</p> <p><b>Uncertainty Factors:</b> A total UF of 300 was applied to the point of departure of 215 mg/m<sup>3</sup>: 10 for intraspecies variation; 3 for interspecies extrapolation; 3 to extrapolate to chronic exposure from data in a less than lifetime study; and 3 to account for database deficiencies.</p> <p><b>Tier 2 Sources:</b></p> <p><b>PPRTV:</b> Per PPRTV, 09/30/2009, a subchronic p-RfC of 2 mg/m<sup>3</sup> (2E+3 µg/m<sup>3</sup>) was derived using the same study and data as used by EPA IRIS to derive the chronic RfC. A total uncertainty factor of 100 was applied to derive the subchronic p-RfC (10 for intraspecies variability, 3 for intraspecies variability,</p>		

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		<p>and 3 for database deficiency). The critical effect was peripheral neuropathy. Updated literature searches did not reveal additional data beyond those that were evaluated in the previous IRIS assessment.</p> <p><b>MRL:</b> Per ATSDR (05/19/1999), the chronic inhalation MRL = 0.6 ppm (= 2 mg/m<sup>3</sup> [based on 1 ppm = 3.52 mg/m<sup>3</sup>] = 2E+3 µg/m<sup>3</sup>)</p> <p><b>Critical study:</b> Sanagi, S. et al. (1980) Peripheral nervous system functions of workers exposed to n-hexane at a low level. Int. Arch. Occup. Environ. Health 47(1): 69-79.</p> <p><b>Method(s):</b> This is an epidemiology study on two age-matched groups consisting of 14 control workers and 14 exposed workers employed in a factory producing tungsten carbide alloys. Exposure was estimated with 22 personal samples taken from the breathing zones over a period of 2 years). The 8-hour time-weighted average exposure to solvent vapors consisted of n-hexane at 58±41 ppm and acetone at 39±30 ppm. The exposure duration ranged from 1 to 12 years, with an average of 6.2 years. Both groups completed questionnaires and underwent clinical neurological examinations and neurophysiological and nerve stimulation studies.</p> <p><b>Critical Effect:</b> neurotoxicity; reduced motor nerve conduction velocity in occupationally exposed workers.</p> <p><b>End point or point of departure (POD):</b> The LOAEL was identified as 58 ppm.</p> <p><b>Uncertainty factors:</b> 100 (10 for LOAEL-to-NOAEL extrapolation, 10 for intraspecies variability). Final. 07/1999.</p> <p><b>Tier 3 Source:</b> <b>MDEQ-AQD:</b> Per DEQ-CCD, AQD ITSL = 700 ug/m<sup>3</sup> (24 hr. averaging time). Based on EPAs RfC, from Huang et al (1989) - a 16 week rat inhalation study that change motor nerve conduction velocity. BMDS methods were used to develop this RfC. AQD calculation date: 01/04/2006.</p>		
Inhalation Unit Risk Factor (IURF) ((µg/m <sup>3</sup> ) <sup>-1</sup> )	NA	NA	MDEQ, 2015	



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
<b>IURF details</b>		<p><b>Tier 1/IRIS Source:</b>  <b>IRIS 12/23/2005:</b>  <b>WOE Characterization:</b> There is inadequate information to assess the carcinogenic potential of n-hexane. Studies indicate that n-hexane is mostly nongenotoxic in short-term testing protocols. n-Hexane showed a minimal response in <i>Saccharomyces cerevisiae</i> D61.M (Mayer and Goin, 1994) and induced an increased incidence in the number of chromosomal mutations in albino rat bone marrow cells (Hazleton Laboratories, 1992). Also, the low pKa of exocyclic amino functional groups of DNA (&lt;5) would preclude reaction with 2,5-hexanedione to yield pyrrole adducts. Thus, these data suggest a lack of mutagenic potential of n-hexane.</p> <p><b>Tier 2 Sources:</b>  <b>PPRTV (09/30/2009):</b> No cancer assessment in the PPRTV document.</p> <p><b>MRL:</b> NA; MRLs are for non-cancer effects only.</p> <p><b>Tier 3 Source:</b>  <b>MDEQ-AQD:</b> Per DEQ-CCD, AQD does not report an IURF at this time.</p>		Complete
<b>Mutagenic Mode of Action (MMOA)? (Y/N)</b>	--	No	USEPA, 2014	
<b>MMOA Details</b>	--			
<b>Developmental or Reproductive Effector? (Y/N)</b>	No	No, the RfD [or RfC/ITSL] is not based on a reproductive-developmental effect.	MDEQ, 2014	
<b>Developmental or Reproductive Toxicity Details</b>				
<b>State Drinking Water Standard (SDWS) (µg/L)</b>	NA	NO	SDWA, 1976	
<b>SDWS details</b>		MI Safe Drinking Water Act (SDWA) 1976 PA 399		



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
<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? (Y/N)</b>	No	Not evaluated.	NA	
<b>Aesthetic value details</b>	NA	NA		
<b>Is there a 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> )		1.0	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>	NA
<b>Updated GSI value (µg/L)</b>	NA
<b>Rule 57 Drinking Water Value (µg/L)</b>	NA

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

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>	NA	MDEQ, 2015
<b>Target Detection Limit – Water (<math>\mu\text{g}/\text{L}</math>)</b>	NA	MDEQ, 2015
<b>Target Detection Limit – Air (ppbv)</b>	2.00E+02	MDEQ, 2015
<b>Target Detection Limit – Soil Gas (ppbv)</b>	6.60E+03	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 OEHHHA	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