



CHEMICAL UPDATE WORKSHEET

Chemical Name:	2-Hexanone
CAS #:	591-78-6
Revised By:	RRD Toxicology Unit
Revision Date:	August 18, 2015

(A) Chemical-Physical Properties

	Part 201 Value	Updated Value	Reference Source	Comments
Molecular Weight (g/mol)	100.16	100.16	EPI	EXP
Physical State at ambient temp	Liquid	Liquid	MDEQ	
Melting Point (°C)	---	-55.50	EPI	EXP
Boiling Point (°C)	127.6	127.60	EPI	EXP
Solubility (ug/L)	1.60E+7	17200000	EPI	EXP
Vapor Pressure (mmHg at 25°C)	11.62	1.16E+01	EPI	EXP
HLC (atm-m ³ /mol at 25°C)	9.57E-5	9.32E-05	PP	EST
Log Kow (log P; octanol-water)	1.4	1.38	EPI	EXP
Koc (organic carbon; L/Kg)	23.8	14.98	EPI	EST
Ionizing Koc (L/kg)		NR	NA	NA
Diffusivity in Air (Di; cm ² /s)	0.08	7.04E-02	W9	EST
Diffusivity in Water (Dw; cm ² /s)	8.0E-6	8.44E-06	W9	EST
Soil Water Partition Coefficient (Kd; inorganics)	NR	NR	NA	NA

	Part 201 Value	Updated Value	Reference Source	Comments
Flash Point (°C)	77 F	25	CRC	EXP
Lower Explosivity Level (LEL; unit less)	NA	0.01	CRC	EXP
Critical Temperature (K)		586.7	CRC	EXP
Enthalpy of Vaporization (cal/mol)		8.69E+03	CRC	EXP
Density (g/mL, g/cm ³)		0.8113	CRC	EXP
EMSOFT Flux Residential 2 m (mg/day/cm ²)	2.14E-05	2.49E-05	EMSOFT	EST
EMSOFT Flux Residential 5 m (mg/day/cm ²)	3.53E-05	5.01E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 2 m (mg/day/cm ²)	2.90E-05	3.85E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 5 m (mg/day/cm ²)	4.42E-05	7.25E-05	EMSOFT	EST

(B) Toxicity Values/Benchmarks

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
Reference Dose (RfD) (mg/kg/day)	1.4E-1	5.0E-3	MDEQ, 2009	
RfD details	143, 266, & 560 mg/kg in drinking water to male rats for 10-13 months. LD caused a decrease in body weight (critical effect), but no neuropathy seen in higher doses. LOAEL = 143 mg/kg; UF = 1000; (O'Donoghue et al., 1978). RD calculation date: 5/1/92.	<p>Tier 1 Source:</p> <p>IRIS:</p> <p>Basis: IRIS is a Tier 1 source and most recently updated value.</p> <p>IRIS (09/25/2009): oral RfD = 5E-3 mg/kg-day.</p> <p>Critical Study: O'Donoghue, JL; Krasavage, WJ; Terhaar, CJ. (1978) A comparative chronic toxicity study of methyl n-propyl ketone, methyl n-butyl ketone, and hexane by ingestion. Eastman Kodak Company, Rochester, NY; Report No. 104657Y. Submitted under TSCA Section 8ECP; EPA Document No. 88-920008233; NTIS No. OTS0555051.</p> <p>Method(s): O'Donoghue et al. (1978) conducted a 13-month study in male COBS/CD (SD) rats. The animals' drinking water contained 0, 0.25, 0.5, or 1.0% (0, 143, 266, or 560 mg/kg/d, respectively) 2-hexanone (96% pure, containing 3.2% methyl isobutyl ketone and 0.7% unknown contaminants).</p> <p>Critical effect: The critical endpoint selected from this study was the incidence of swollen axons in peripheral nerves of male rats. This endpoint was chosen because peripheral neuropathy is the most consistent and relevant effect identified in occupationally exposed humans and experimental animals that occurs following low-level exposures to 2-hexanone. Axonal swelling was observed in the peripheral nerve with high incidence at the lowest dose tested and is the most sensitive endpoint observed in this study. Although some studies have suggested that axonal swelling may occur without progression to nerve dysfunction, myofibrillar atrophy, an effect observed subsequent to axonal swelling, displayed a dose-dependent response in the present study.</p> <p>End point or Point of Departure (POD): BMDL₁₀: 5 mg/kg-day. EPA's BMD software (version 1.4.1c) was used to estimate a POD for deriving an RfD from data on axonal swelling of the peripheral nerve. The POD was defined as the 95% lower confidence limit on the BMDL associated with a BMR of 10% extra risk of axonal swelling.</p> <p>Uncertainty Factors: UF = 1,000 (10 for intraspecies variability; 10 for</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		<p>interspecies extrapolation; and 10 for database deficiencies). Source and date: IRIS, 09/25/2009.</p> <p>Tier 2 Sources: PPRTV: No PPRTV record available at this time. MRL (09/1992): Per ATSDR: Available information on acute-duration oral exposure in animals does not identify the most sensitive effect, and while available information on intermediate-duration oral exposure to 2-hexanone in animals suggests that neurotoxicity may be the most sensitive effect; data do not reliably identify the threshold for neurotoxicity. No information was located on effects of chronic-duration exposure to 2-hexanone in humans or animals. Therefore, no oral MRLs were derived.</p> <p>Tier 3 Sources: MDEQ: Per DEQ-CCD, WRD reports RfD of 1.43E-1 (CAS date is 11/01/1991 and calculation date of 05/22/1992. RRD reports RfD of 1.4E-1 based on same study as WRD (i.e., O'Donoghue, et al., 1979).</p>		
Oral Cancer Slope Factor (CSF) (mg/kg-day)⁻¹	NA	NA	MDEQ, 2015	
CSF details		<p>Per IRIS (2009), there are no animal carcinogenicity studies available that examine exposure to 2-hexanone, and there are no studies available that assert a mutagenic potential of 2-hexanone. The available occupational studies do not present evidence for carcinogenic action of 2-hexanone, although these are limited by frequent co-exposure to other chemicals (e.g., MEK).</p> <p>Tier 1 and 2 Sources: IRIS: No available value. PPRTV: No PPRTV record available at this time. MRL: NA; MRLs only address non-cancer effects.</p> <p>Tier 3 Sources: MDEQ: Per DEQ-CCD, no cancer slope factor value available at this time.</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
Reference Concentration (RfC) or Initial Threshold Screening Level (ITSL) ($\mu\text{g}/\text{m}^3$)	4.0E+1	3.0E+1	IRIS, 2009	
RfC/ITSL details		<p>Tier 1 Source: IRIS: Basis: IRIS is a Tier 1 source. IRIS inhalation RfC = $3\text{E}+1 \mu\text{g}/\text{m}^3$. Critical Study: Johnson, BL; Setzer, JV; Lewis, TR; et al. (1977) Effects of methyl n-butyl ketone behavior and the nervous system. Am Ind Hyg Assoc J 38(11):567–579. Method(s): The study by Johnson et al. (1977) was performed in monkeys and rats, with 8 and 10 animals per dose group, respectively. Two concentrations of commercial grade 2-hexanone were employed (100 and 1,000 ppm in air), with exposures occurring 6 hours/day, 5 days/week for a duration of 10 months. Concurrent control groups were used in both species. As part of this study, Johnson et al. (1977) conducted four neurological tests in each species (usually once per month) to identify effects in treated versus control animals. These four tests were (1) motor conduction velocity (MCV) of the right sciatic-tibial nerve, (2) MCV of the right ulnar nerve, (3) absolute refractory period of these two nerves, and (4) muscle action potentials in response to both sciatic and ulnar nerve stimulation. After approximately 6 months of exposure, monkeys and rats in the 1,000 ppm exposure group were removed from the study because neuropathy (characterized as hind-limb drag) had developed in these animals. Unit conversion: 1 ppm = $4.1 \text{ mg}/\text{m}^3$. Critical effect: Because monkeys have a similar respiratory tract and breathing patterns to humans and it is known that 2,5 hexanedione (the primary metabolite of 2-hexanone) typically affect long axons such as the sciatic-tibial nerve prior to other nerves, the decreased sciatic-tibial nerve MCV in monkeys was identified as the critical effect to derive the RfC. For comparison purposes, sciatic-tibial MCV in rats and ulnar MCV in both monkeys and rats were also considered potential</p>	Complete	



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		<p>critical effects for RfC derivation.</p> <p>End point or Point of Departure (POD): $BMCL_{05 [HEC]} = 90 \text{ mg/m}^3$. The available continuous models in U.S. EPA's BMDS, version 2.0, were used to estimate a POD (121 ppm) for deriving an RfC for 2-Hexanone from data on nerve MCV. Because the magnitude of variation in nerve MCVs between the 6- and 10-month data was similar and because more treatment groups were available for the 6-month exposure duration (i.e., two exposure groups plus control at 6 months versus one exposure group plus control at 10 months), the data at 6 months were used for BMD modeling. EPA determined that small changes in mean sciatic-tibial nerve MCV are biologically significant. A BMR of 5% extra risk was selected based on the following considerations: (1) this effect level is considered to be a minimal biologically significant change; (2) the potential for nerve fiber damage (i.e., axonal degeneration) with little to no change in MCV; and (3) the $BMDL_{05}$ falls within the low end of the range of the observable data. The POD was adjusted to account for the duration of exposure to 2-hexanone.</p> <p>Uncertainty Factors: UF = 3,000. (10 for intraspecies variability, 3 for interspecies extrapolation, 10 for subchronic-to-chronic extrapolation, and 10 for database deficiency).</p> <p>Source and date: IRIS, 09/25/2009.</p> <p>Tier 2 Sources: PPRTV: No PPRTV record available at this time. MRL: Per ATSDR, No data were located on effects of acute-duration or chronic duration inhalation exposure to 2-hexanone in humans or animals. Available information concerning effects of intermediate-duration inhalation exposure in humans and animals identifies neurological effects as the most sensitive indicator of toxicity, but this information does not reliably identify the threshold for this effect. Therefore, no inhalations MRLs were derived.</p> <p>Tier 3 Source: MDEQ-AQD: Per DEQ-CCD, AQD reports an ITSL of $30 \text{ }\mu\text{g/m}^3$ based on the EPA IRIS RfC in which subchronic exposure of rats and monkeys to 2-hexanone caused</p>		

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		nerve conduction damage (Johnson, et al, 1977).		
Inhalation Unit Risk Factor (IURF) (($\mu\text{g}/\text{m}^3$)⁻¹)	NA	NA	MDEQ, 2015	
IURF details		<p>Per IRIS, under the Guidelines for Carcinogen Risk Assessment (U.S. EPA, 2005a), the database for 2-hexanone is "inadequate to assess human carcinogenic potential." Specifically, there are no animal carcinogenicity studies available that examine exposure to 2-hexanone, and there are no studies available that assert a mutagenic potential of 2-hexanone. The available occupational studies do not present evidence for carcinogenic action of 2-hexanone, although these are limited by frequent co-exposure to other chemicals (e.g., MEK).</p> <p>Source: IRIS, 09/25/2009</p> <p>Tier 1 and 2 Sources: IRIS: No available value. PPRTV: No PPRTV record available at this time. MRL: NA; MRLs only address non-cancer effects.</p> <p>Tier 3 Source: MDEQ: Per DEQ-CCD, AQD does not report an IURF value at this time.</p>		Complete
Mutagenic Mode of Action (MMA)? (Y/N)	--	NO	USEPA, 2015	
MMA Details	--	NA Not listed as a carcinogen with mutagenic MOA in the USEPA OSWER List.		
Developmental or Reproductive Effector? (Y/N)	No	No, the RfD or RfC is not based on a reproductive-developmental effect.	MDEQ, 2015	
Developmental or Reproductive Toxicity Details		NA		
State Drinking Water Standard	NA	NO	SDWA, 1976	



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
(SDWS) (µg/L)				
SDWS details		MI Safe Drinking Water Act (SDWA) 1976 PA 399		
Secondary Maximum Contaminant Level (SMCL) (µg/L)	NA	NO	SDWA, 1976 and USEPA SMCL List	
SMCL details		MI Safe Drinking Water Act (SDWA) 1976 PA 399 and USEPA SMCL List		
Is there an aesthetic value for drinking water? (Y/N)	No	Not evaluated.	NA	
Aesthetic value details	NA	NA		
Phytotoxicity Value? (Y/N)	No	Not evaluated.	NA	
Phytotoxicity details	NA	NA		
Others:				

(C) Chemical-specific Exposure Factors

	Part 201 Value	Update	Source/Reference/ Dates	Comments/Notes /Issues
Gastrointestinal absorption efficiency value (ABS_{gi})	---	1.0	MDEQ, 2015/USEPA RAGS-E	
ABS_{gi} details		RAGS E (EPA, 2004) Default Value		
Skin absorption efficiency value (A_{Ed})	---	0.1	MDEQ, 2015	
A_{Ed} details				
Ingestion Absorption Efficiency (A_{Ei})		1.0	MDEQ, 2015	
A_{Ei} Details				
Relative Source Contribution for Water (RSC_w)		0.2	MDEQ, 2015	
Relative Source Contribution for Soil (RSC_s)		1.0	MDEQ, 2015	
Relative Source Contribution for Air (RSC_A)		1.0	MDEQ, 2015	
Others				

(D) Rule 57 Water Quality Values and GSI Criteria

Current GSI value (µg/L)	ID
Updated GSI value (µg/L)	ID
Rule 57 Drinking Water Value (µg/L)	9,700

	Rule 57 Value (µg/L)	Verification Date
Human Non-cancer Values- Drinking water source (HNV-drink)	9,700	9/2004
Human Non-Cancer Values- Non-drinking water sources (HNV-Non-drink)	630,000	9/2004
Wildlife Value (WV)	NA	NA
Human Cancer Values for Drinking Water Source (HCV-drink)	NA	NA
Human Cancer values for non-drinking water source (HCV-Non-drink)	NA	NA
Final Chronic Value (FCV)	ID	9/2004
Aquatic maximum value (AMV)	ID	9/2004
Final Acute Value (FAV)	ID	9/2004

Sources:

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

(E) Analytical Information

	Value	Source
Target Detection Limit – Soil ($\mu\text{g}/\text{kg}$)	2,500	MDEQ, 2015
Target Detection Limit – Water ($\mu\text{g}/\text{L}$)	50	MDEQ, 2015
Target Detection Limit – Air (ppbv)	7.40E+00	MDEQ, 2015
Target Detection Limit – Soil Gas (ppbv)	2.50E+02	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 OEHHA	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