



CHEMICAL UPDATE WORKSHEET

Chemical Name:	4-Methyl-2-pentanone (Methyl isobutyl ketone (MIBK) (DD)
CAS #:	108-10-1
Revised By:	RRD Toxicology Unit
Revision Date:	September 21, 2015

(A) Chemical-Physical Properties

	Part 201 Value	Updated Value	Reference Source	Comments
Molecular Weight (g/mol)	100.2	100.16	EPI	EXP
Physical State at ambient temp	Liquid	Liquid	MDEQ	
Melting Point (°C)	188	-84.00	EPI	EXP
Boiling Point (°C)	116.5	116.50	EPI	EXP
Solubility (ug/L)	2.00E+7	19000000	EPI	EXP
Vapor Pressure (mmHg at 25°C)	19	1.99E+01	EPI	EXP
HLC (atm-m³/mol at 25°C)	1.20E-4	1.38E-04	PP	EST
Log Kow (log P; octanol-water)	1.18	1.31	EPI	EXP
Koc (organic carbon; L/Kg)	14.5	12.6	EPI	EST
Ionizing Koc (L/kg)		NR	NA	NA
Diffusivity in Air (Di; cm²/s)	0.075	6.98E-02	W9	EST
Diffusivity in Water (Dw; cm²/s)	7.8E-6	8.35E-06	W9	EST
Soil Water Partition Coefficient (Kd; inorganics)	NR	NR	NA	NA

	Part 201 Value	Updated Value	Reference Source	Comments
Flash Point (°C)	64 F	18	CRC	EXP
Lower Explosivity Level (LEL; unit less)	NA	0.012	CRC	EXP
Critical Temperature (K)		571.00	EPA2004	EXP
Enthalpy of Vaporization (cal/mol)		8.24E+03	EPA2004	EXP
Density (g/mL, g/cm ³)		0.7965	CRC	EXP
EMSOFT Flux Residential 2 m (mg/day/cm ²)	2.26E-05	2.56E-05	EMSOFT	EST
EMSOFT Flux Residential 5 m (mg/day/cm ²)	4.09E-05	5.41E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 2 m (mg/day/cm ²)	3.10E-05	3.99E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 5 m (mg/day/cm ²)	5.25E-05	8.01E-05	EMSOFT	EST

(B) Toxicity Values/Benchmarks

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
Reference Dose (RfD) (mg/kg/day)	2.5E-1	5.0E-2	MDEQ, 2010	
RfD details	<p>Withdrawn from IRIS 3/1/91, (under review); 13-week rat gavage study; NOAEL = 250 mg/(kg-d); UF = 1000; Critical effects = liver & kidney effects (Microbiology Assos., 1986); (US EPA, 1987). HEAST # subject to change.</p>	<p>Tier 3 Source: MDEQ: Basis: MDEQ (2010) value based on a no effect NOEL of 50 mg/kg-day from a subchronic rat study (Microbiological Associates, 1986) and UF of 1,000. Massachusetts derived the same value as MDEQ using the same approach. HEAST (1997) used the same study but identified a higher NOAEL (250 mg/kg-day) at which effects that “are not clearly adverse were observed”. Minnesota and Texas adopted the HEAST RfD of 8.0E-2 mg/kg-day. The derivation of the RIVM and ECHA are not clearly presented in the source documents. See details below.</p> <p>Tier 1 and 2 Sources: IRIS: Per IRIS (04/25/2003), no oral RfD was developed for MIBK because no critical effect was identified after subchronic exposure. Since no chronic oral studies were available, it is uncertain whether chronic exposure at the same exposure levels would have induced biologically significant adverse effects. The database was limited to two subchronic oral exposure studies: one 13 week gavage exposure study (Microbiol. Assoc. Inc., 1986) and one 90 day <i>ad libitum</i> drinking water study (Carnegie-Mellon Institute, 1977a, b). Effects that may be associated with changes in the liver or kidney occurred at approximately 1,000 mg/kg-day in both studies and at 250 mg/kg-day in the gavage study, but the effects were not considered to be clearly adverse for reasons discussed in the Toxicological Review (U.S. EPA, 2003). PPRTV: No PPRTV record for 4-methyl-2-pentanone is available at this time. MRL: No ATSDR Toxicological Profile for 4-methyl-2-pentanone is available at this time.</p> <p>Tier 3 Sources: MDEQ/WRD (03/24/2010): RfD = 5.0E-2 mg/kg-day. Critical Study: Microbiological Associates (1986). Subchronic Toxicity of methyl</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		<p>isobutyl ketone in Sprague-Dawley rats. Preliminary report for Research Triangle Institute, RTP, NC. Study No. 5221.04.</p> <p>Methods: Sprague-Dawley rats (30 animals/sex/group) were administered 0, 50, 250, or 1,000 mg/kg/d MIBK via gavage in corn oil for 13 weeks.</p> <p>Critical Effects: An increase in serum glutamic-pyruvic transaminase (SGPT) occurred in female rats in the 250 and 1,000 mg/kg/d dose groups. Increased relative kidney weights occurred in both sexes at the highest dose and to a lesser extent in the 250 mg/kg/d dose groups. Enlarged livers in both sexes at the high dose.</p> <p>Point Of Departure (POD): NOEL of 50 mg/kg/day (oral) in male and female SD rats dosed by gavage for 13 weeks.</p> <p>Uncertainty Factors: UF = 1,000 (10 each for intraspecies variability and, interspecies and subchronic to chronic extrapolation).</p> <p>Basis: Per DEQ-WRD (03/24/2010), RfD = 0.05 mg/kg/day is used by WRD to develop a human noncancerous <i>screening</i> value only. EPA (2003) could not determine whether the effects found in the Microbiological Associates (1986) study were adverse. EPA concluded that “the degree of their biological adversity is uncertain, particularly since treatment-related corroborative gross pathologies or histopathological lesions were not discussed”. For this review, there is sufficient concern about the effects found in the study to use the NOEL of 50 mg/kg-day as the basis for a <i>screening</i> level.</p> <p>Source: DEQ-WRD, 3/24/2010.</p> <p>HEAST: RfD = 8.0E-2 mg/kg/day: Key Study/Reference: Microbiological Associates. 1986. Subchronic Toxicity Of Methyl Isobutyl Ketone In Sprague-Dawley Rats. Performed For Research Triangle Institute. Po Box 12194. Research Triangle Park. Nc. 27709. Final Report. Study No 522104. Methods: 13 week rat study; oral (gavage) Critical effects: whole body lethargy, liver: increased relative weight and increased absolute weight in females, and kidney: increased relative weight, increased absolute weight, and increased urinary protein levels in females.</p>		

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		<p>Endpoint: NOAEL = 250 mg/kg-day Uncertainty Factors: UF = 3,000 Chronic [RfD] Comment: withdrawn from IRIS (03/01/91). Under review. Source: HEAST Summary 1997, p. 1-67</p> <p>Massachusetts DEP: RfD = 5.0E-2 mg/kg-day used to generate the ORSG (Drinking Water Guidelines) of 0.35 mg/L. Per MADEP, this RfD has been withdrawn from IRIS. RfD was derived as follows: RfD: 5.0E-2 mg/kg/day (U.S. EPA, 1988; U.S. EPA, 1991) Uncertainty Factors: UF = 1,000 (10 each for intraspecies, interspecies and sub chronic to chronic extrapolations); Modification Factor = 1. Critical study and Endpoint: A NOAEL of 50 mg/kg/day was identified from a subchronic gavage study in rats (U.S. EPA, 1986). Critical effects: liver and kidneys effects Cancer Assessment: Under U.S. EPA's draft revised cancer guidelines (U.S. EPA, 1999), the data for methyl isobutyl ether are inadequate for an assessment of human carcinogenic potential. Both in vivo and in vitro genotoxicity studies of MIBK are overwhelmingly negative. Source: Massachusetts Drinking Water Standards (MMCLs), 2015.</p> <p>Minnesota PCA: RfD= 8.0E-02 mg/kg-day based on HEAST 1997.</p> <p>Texas CEQ: RfD= 8.0E-02 mg/kg-day based on HEAST 1997.</p> <p>RIVM: Tolerable Daily Intake (TDI) = 8.0E-1 mg/kg-day: Critical study: Rat, oral 13 weeks exposure Endpoint: NOAEL = 250 mg/kg-day (RIVM, 2001); USEPA (2003) IRIS file: NOAEL>1000 mg/kg-day Sources: 1) RIVM (2001) AD-HOC ADVIES, Betreft: Diisobutylketon (CAS-number 108-83-8). Afleiding voorlopige huamantoxicologische MTR t.b.v. afleiding voorlopige EBVChumaan. RIVM/CSR advises d.d. 9-1-2001.</p>		

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		<p>2)US-EPA (2003) IRIS-file voor Methyl Isobutyl Ketone (MIBK) (CASRN Reference: Afleiding van 41 ad hoc MTR's 2007 (in Dutch) p. 73-78</p> <p>ECHA (REACH): Derived No Effect Level (DNEL) = 4.2 mg/kg bw-day: <u>Key study:</u> "study report", 1986 (From EPA (U.S. Environmental Protection Agency). 2003. TOXICOLOGICAL REVIEW OF METHYL ISOBUTYL KETONE (CAS No. 108-10-1). In Support of Summary Information on the Integrated Risk Information System (IRIS). Per IRIS, this study is: "Microbiological Associates (1986). Sub chronic Toxicity of methyl isobutyl ketone in Sprague-Dawley rats. Preliminary report for Research Triangle Institute, RTP, NC. Study No. 5221.04." <u>Methods:</u> subchronic; Sprague-Dawley rats (30/sex/dose) were exposed 0 (vehicle control), 50, 250, or 1000 mg/kg-day MIBK by gavage in corn oil for 13 consecutive weeks and evaluated for exposure-related changes in body weight, food consumption, mortality, clinical signs, ophthalmological parameters, and terminal organ weights (heart, liver, spleen, brain, kidney, gonads, adrenals, thyroid, and parathyroid). <u>Endpoints and Effects:</u> NOAEL - 250 mg/kg bw/d; increases in relative kidney weights for male and female rats but without histological lesions NOEL – 50 mg/kg bw/day; no treatment-related effects of any kind. Adjustment factors: none specified Note: the DNEL value derivation is not clearly presented in this document. Source: ECHA REACH Database for MIBK</p> <p>Other Tier 3: No value is available at this time from these Tier 3 sources/databases: NTP ROC, health and environmental agencies of California, New Jersey and New York, Canada, WHO (IARC), WHO (IPCS/INCHEM) and OECD HPV.</p>		
Oral Cancer Slope Factor (CSF) (mg/kg-day)⁻¹	NA	NA	MDEQ, 2015	
CSF details	NA	The available data are inadequate for an assessment of human carcinogenic potential. No data were located regarding the existence of an association		

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		<p>between cancer and MIBK exposure in humans, but studies of the in vivo and in vitro genotoxicity of MIBK overwhelmingly provided negative responses. Source: IRIS, 04/25/2003.</p> <p>Tier 1 and 2 Sources: IRIS: No value at this time. PPRTV: No PPRTV record for 4-methyl-2-pentanone is available at this time. MRL: NA; MRLs are for non-cancer effects only.</p> <p>Tier 3 Source: MDEQ: Per DEQ-CCD, no value for 4-methyl-2-pentanone is available at this time.</p>		Complete
Reference Concentration (RfC) or Initial Threshold Screening Level (ITSL) (µg/m³)	2.05E+3	3.0E+3	IRIS, 2003	
RfC/ITSL details	AIR: Based on 1% of the TWA-TLV.	<p>Tier 1 Source: Basis: IRIS is a Tier 1 source. IRIS RfC = 3 mg/m³ (= 3E+3 µg/m³) Critical Study: Tyl, R.W. et al. (1987) Developmental toxicity evaluation of inhaled methyl isobutyl ketone in Fischer 344 rats and CD-1 mice. Fund. Appl. Toxicol. 8:310-327. Methods: Developmental and maternal toxicity were evaluated in groups of 35 pregnant Fischer 344 rats and 30 pregnant CD-1 mice exposed by inhalation exposure to 0, 300, 1,000, or 3,000 ppm (0, 307, 1026, 3073 mg/m³) MIBK for 6 hours/day on gestation days 6-15. Animals were sacrificed on gestation day 21 (rats) or 18 (mice). Dams were evaluated for exposure-related changes in clinical signs, body weight, food consumption, organ weights (kidney, liver and gravid uterus), and reproductive parameters; fetuses were evaluated for exposure-related changes in body weight and viability and for external, skeletal, and thoracic and peritoneal visceral alterations. Critical effect: Reduced fetal body weight, skeletal variations, and increased fetal</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		<p>death in mice, and skeletal variations in rats. End point or Point of Departure (POD): NOAEL_{HEC} = 1,026 mg/m³ and LOAEL_{HEC} = 3,073 mg/m³. Uncertainty Factors: UF = 300. UF = 3 for interspecies extrapolation (10 not used because animal to human dosimetric adjustments were made); UF = 10 for intraspecies variability; UF = 10 for database deficiency based on the lack of developmental neurotoxicity data and definitive neurotoxicity data in general, and based on the lack of any chronic toxicity data. Source: IRIS, 04/25/2003</p> <p>Tier 2 Sources: PPRTV: No PPRTV record for 4-methyl-2-pentanone is available at this time. MRL: No MRL record for 4-methyl-2-pentanone is available at this time.</p> <p>Tier 3 Source: MDEQ/AQD: Per DEQ-CCD (4/25/2003), ITSL based on EPA's RfC of 3 mg/m³. RfC is based on rat and mouse developmental effects (reduced fetal weight, increased skeletal variations, increased fetal mortality) reported by Tyl et al. (1987). The NOAEL(HEC) = 1,026 mg/m³ from the low dose exposed to 300 ppm 6/24 hours per day on gestation days 6-15. UF = 300. EPA considers this to be a category 3 gas with the blood: gas partition unknown defaulting to a ratio of 1.</p>		
Inhalation Unit Risk Factor (IURF) ((µg/m³)⁻¹)	NA	NA	MDEQ, 2015	
IURF details	NA	<p>Tier 1 and 2 Sources: IRIS: Per IRIS (04/25/2003), no quantitative estimate of carcinogenic risk from inhalation exposure was derived because no cancer epidemiology studies in humans and no carcinogenicity assays in animals were located. PPRTV: No PPRTV record for 4-methyl-2-pentanone is available at this time. MRL: NA; MRLs are for non-cancer effects only.</p> <p>Tier 3 Source: MDEQ: Per DEQ-CCD, no inhalation toxicity value for 4-methyl-2-pentanone is</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		available at this time.		
Mutagenic Mode of Action (MMOA)? (Y/N)	--	No	USEPA, 2015	
MMOA Details	--	Not listed as a carcinogen with mutagenic MOA in the USEPA OSWER List.		
Developmental or Reproductive Effector? (Y/N)	--	Yes - inhalation, the RfC is based on a reproductive-developmental effect. Inhalation Exposure Pathways- Single Exposure No – oral exposure. The RfD is not based on a reproductive-developmental effect.	MDEQ, 2015	
Developmental or Reproductive Toxicity Details	--	Critical Study: Tyl, R.W. et al. (1987) Developmental toxicity evaluation of inhaled methyl isobutyl ketone in Fischer 344 rats and CD-1 mice. Fund. Appl. Toxicol. 8:310-327. Methods: Developmental and maternal toxicity were evaluated in groups of 35 pregnant Fischer 344 rats and 30 pregnant CD-1 mice exposed by inhalation exposure. Critical effect: Reduced fetal body weight, skeletal variations, and increased fetal death in mice, and skeletal variations in rats.		
State Drinking Water Standard (SDWS) (ug/L)	NA	NO	SDWA, 1976	
SDWS details		MI Safe Drinking Water Act (SDWA) 1976 PA 399		
Secondary Maximum Contaminant Level (SMCL) (ug/L)	NA	NO	SDWA, 1976 and USEPA SMCL List	
SMCL details	--	NA		
Is there an aesthetic value for drinking water? (Y/N)	No	Not evaluated.	NA	



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
Aesthetic value (ug/L)	NA	NA	NA	
Aesthetic Value details	NA	NA		
Phytotoxicity Value? (Y/N)	No	Not evaluated.	NA	
Phytotoxicity details	NA	NA	NA	
Others				

(C) Chemical-specific Absorption 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 (AEd)	---	0.1	MDEQ, 2015	
AEd details				
Ingestion Absorption Efficiency (AE _i)		1.0	MDEQ, 2015	
AE _i 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)	ID

	Rule 57 Value (µg/L)	Verification Date
Human Non-cancer Values- Drinking water source (HNV-drink)	ID	3/2010
Human Non-Cancer Values- Non-drinking water sources (HNV-Non-drink)	ID	3/2010
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	6/2009
Aquatic maximum value (AMV)	ID	6/2009
Final Acute Value (FAV)	ID	6/2009

Sources:

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



(E) Target Detection Limits (TDL)

	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)	7.30E+02	MDEQ, 2015
Target Detection Limit – Soil Gas (ppbv)	2.40E+04	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