



CHEMICAL UPDATE WORKSHEET

Chemical Name:	1,2,3-Trimethylbenzene
CAS #:	526-73-8
Revised By:	RRD Toxicology Unit
Revision Date:	September 1, 2015

(A) Chemical-Physical Properties

	Part 201 Value	Updated Value	Reference Source	Comments
Molecular Weight (g/mol)	120.2	120.20	EPI	EXP
Physical State at ambient temp	Liquid	Liquid	MDEQ	
Melting Point (°C)	-25.4	-25.40	EPI	EXP
Boiling Point (°C)	349	176.10	EPI	EXP
Solubility (ug/L)	7.52E+4	75200	EPI	EXP
Vapor Pressure (mmHg at 25°C)	1.69	1.69E+00	EPI	EXP
HLC (atm-m ³ /mol at 25°C)	4.36E-3	4.36E-03	EPI	EXP
Log Kow (log P; octanol-water)	3.66	3.66	EPI	EXP
Koc (organic carbon; L/Kg)	4000	626.9	EPI	EST
Ionizing Koc (L/kg)		NR	NA	NA
Diffusivity in Air (Di; cm ² /s)	0.08	6.13E-02	W9	EST
Diffusivity in Water (Dw; cm ² /s)	8.0E-6	8.02E-06	W9	EST
Soil Water Partition Coefficient (Kd; inorganics)	NR	NR	NA	NA

	Part 201 Value	Updated Value	Reference Source	Comments
Flash Point (°C)	111.2	44	CRC	EXP
Lower Explosivity Level (LEL; unit less)	0.008	0.008	CRC	EXP
Critical Temperature (K)		664.50	HSDB	EXP
Enthalpy of Vaporization (cal/mol)		1.17E+04	HSDB	EXP
Density (g/mL, g/cm ³)		0.8944	CRC	EXP
EMSOFT Flux Residential 2 m (mg/day/cm ²)	1.82E-05	2.59E-05	EMSOFT	EST
EMSOFT Flux Residential 5 m (mg/day/cm ²)	2.42E-05	5.58E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 2 m (mg/day/cm ²)	2.39E-05	4.04E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 5 m (mg/day/cm ²)	2.92E-05	8.32E-05	EMSOFT	EST

(B) Toxicity Values/Benchmarks

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
Reference Dose (RfD) (mg/kg/day)	--	2.0E-2	IRIS, 2013	
RfD details	NA	<p>Tier 1 Source: IRIS: Basis: IRIS is the only available value. IRIS RfD is based on a surrogate chemical 1,2,4-trimethylbenzene. Per EPA Toxicological Review of Trimethylbenzene (August 2013 Revised External Review Draft), the available oral database is inadequate to derive an RfD for 1,2,3-TMB. However, there are sufficient similarities between isomers regarding observed toxicological effects that support adopting the RfD for 1,2,4-TMB, 2.0E-2 mg/kg-day, as the RfD for 1,2,3-TMB. Specifically, the qualitative pattern of neurotoxic effects following short-term and subchronic inhalation exposures is similar between TMB isomers. Particularly important to this determination is that, although 1,2,3-TMB is observed to decrease pain sensitivity at lower concentrations than 1,2,4-TMB, the magnitude of decreased pain sensitivity is similar for 1,2,4-TMB and 1,2,3-TMB, especially at the low-and mid-concentrations. Similarities in blood: air and tissue: air partition coefficients and degree of absorption into the bloodstream between 1,2,4-TMB and 1,2,3-TMB support the conclusion that internal blood dose metrics for 1,2,3-TMB would be similar to those calculated for 1,2,4-TMB using that isomer’s available PBPK model. Also, the qualitative metabolic profiles for the two isomers are similar such that first-pass metabolism through the liver is not expected to differ greatly between 1,2,4-TMB and 1,2,3-TMB.</p> <p>Per IRIS (4/24/2015), the August 2013 Revised External Review Draft RfD = 2.0E-2 mg/kg/day is based on 1,2,4-trimethylbenzene surrogate. “Given the similarities in chemical properties, toxicokinetics, and toxicity, the RfD derived for 1,2,4-TMB, 2 × 10⁻² mg/kg-day was adopted as the RfD for 1,2,3-TMB.”</p> <p>Critical Study: Korsak, Z; Rydzyński, K (1996) Neurotoxic effects of acute and subchronic inhalation exposure to Trimethylbenzene isomers (pseudocumene, mesitylene, hemimellitene) in rats. International Journal of Occupational Medicine and Environmental Health. 9:341-349.</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		<p>Methods: subchronic inhalation exposure to Wistar rats at 1,2,3-TMB at concentrations of 25, 100 and 250 ppm (1 ppm = ~4.92 mg/m³) for 6h/day, 5 days/week, until 3-months</p> <p>Critical effect: decrease pain sensitivity</p> <p>Endpoint or Point of Departure (POD): POD_{HED} = 6.3 mg/kg/day; human PBPK model was run to determine what oral exposure would yield an equivalent weekly average blood concentration, and then the resulting value of <u>6.3 mg/kg-day</u> was used as the human equivalent dose POD (PODHED) for the RfD derivation</p> <p>Uncertainty factors: UF = 300</p> <p>Source and date: Toxicological Review of Trimethylbenzenes - In support of summary information on the integrated risk information system (IRIS), August 2013 Revised External Review</p> <p>Tier 1 and 2 Sources: IRIS: No IRIS final file is available at this time. PPRTV: Per PPRTV (6/28/2010), no value at this time. MRL: No MRL record is available at this time.</p> <p>Tier 3 Source: MDEQ: Per DEQ-CCD, no value at this time. An MDEQ-RRD Toxicological Assessment in December, 2008 showed no studies were located for RfD development.</p>		
Oral Cancer Slope Factor (CSF) (mg/kg-day)⁻¹	--	NA	MDEQ, 2015	
CSF details	NA	<p>Carcinogen Weight-of-Evidence (WOE) Class: Inadequate Information to Assess [the] Carcinogenic Potential”</p> <p>IRIS WOE Basis: Studies evaluating the carcinogenic potential of oral or inhalation exposure to 1,2,3-TMB in humans or animals were not identified in the available literature</p> <p>Source and Date: PPRTV, 6/28/2010</p> <p>Tier 1 and 2 Sources:</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		<p>IRIS: No IRIS value is available at this time. PPRTV: Per PPRTV (6/28/2010), no value at this time. MRL: NA; MRLs are for non-cancer effects only.</p> <p>Tier 3 Source: MDEQ: Per DEQ-CCD, no value at this time.</p>		
Reference Concentration (RfC) or Initial Threshold Screening Level (ITSL) ($\mu\text{g}/\text{m}^3$)	1,230	5.0E+0	PPRTV, 2010	
RfC/ITSL details	(QD had previously (1996) generated an ITSL value for 1,2,3-TMB of 1230 $\mu\text{g}/\text{m}^3$ (8-hour averaging) for the combined impact of all TMB isomers. The AQD staff determined that “there was some concern that the key study on which the occupational standard is based is outdated and lacks good exposure characterization”	<p>Tier 2 Source: PPRTV: Basis: PPRTV’s RfC is preferred over IRIS value as IRIS is still a draft value. PPRTV chronic p-RfC = 5.0E-3 mg/m^3 Critical Study: Korsak, Z. and K. Rydzynski. 1996. Neurotoxic effects of acute and subchronic inhalation exposure to Trimethylbenzene isomers (pseudocumene, mesitylene, hemimellitene) in rats. Int. J. Occup. Med. Environ. Health. 9:341–349. Methods: Wistar rats were exposed to 0, 123, 492, or 1230 mg/m^3 1,2,3-TMB for 6 hours/day, 5 days/week, for 3 months. Neurobehavioral effects were assessed using performance testing. Critical effect: decreased pain sensitivity in rats End point or Point of Departure (POD): $\text{BMCL}_{\text{HEC}} = 16 \text{ mg}/\text{m}^3$ ($\text{BMCL}_{1\text{SD}} = 97 \text{ mg}/\text{m}^3$) Uncertainty Factors: UF = 3,000 (10 each for intraspecies variability, use of a subchronic study, and database insufficiencies; and 3 for interspecies extrapolation) Source and date: PPRTV, 6/28/2010</p> <p>Tier 1 and 2 Sources: IRIS: No IRIS file is available at this time. An IRIS draft chronic RfC = 5.0E-2 mg/m^3 is available. Toxicological Review of Trimethylbenzenes - In support of summary</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
	(AQD, 2006). The new ITSL value for 1,2,3-TMB, 220 µg/m ³ (24-hour average), was developed from the subchronic animal inhalation study of Korsak et.al., (2000). CCD-AQD, 2006 (Note: The 2012 Part 201 inhalation-based cleanup criteria are developed using this ITSL value.)	<p>information on the integrated risk information system (IRIS), August 2013 Revised External Review Draft.</p> <p>Critical Study: Korsak, Z; Rydzyński, K (1996) Neurotoxic effects of acute and subchronic inhalation exposure to Trimethylbenzene isomers (pseudocumene, mesitylene, hemimellitene) in rats. International Journal of Occupational Medicine and Environmental Health. 9:341-349.</p> <p>Methods: subchronic inhalation exposure to Wistar rats at 1,2,3-TMB at concentrations of 25, 100 and 250 ppm (1 ppm = ~4.92 mg/m³) for 6h/day, 5 days/week, until 3-months</p> <p>Critical effect: decrease pain sensitivity</p> <p>Endpoint or Point of Departure (POD): POD_{HEC} = 16.3 mg/m³</p> <p>Uncertainty factors: UF = 300</p> <p>MRL: No MRL record is available at this time.</p> <p>Tier 3 Source:</p> <p>MDEQ: Per DEQ-CCD (1/26/2012), AQD established two ITSLs: 50 µg/m³ with annual averaging time and a second ITSL of 1200 µg/m³ with 8-hour averaging time. These are applied to all 3 TMB isomers in combination. The acute value is protective of irritancy and other potential effects, based on human experimental studies and occupational experience. The annual value is partially consistent with the PPRTVs (chronic) of 5 µg/m³ (1,2,3-TMB) and 7 µg/m³ (1,2,4-TMB) which were based on rat studies and CNS effects. For the PPRTVs, EPA employed database UF of 10 which was not employed in the derivation of the chronic ITSL. The PPRTVs apply only to each specific isomer, and no PPRTV is available for 1,3,5-TMB; the AQD justified grouping the 3 isomers together. AQD does not routinely apply database UF =10 in their own risk assessments. AQD footnote #14: The combined ambient impacts for the isomers of Trimethylbenzene, or any mixture thereof, cannot exceed the screening level(s).</p>		
Inhalation Unit Risk Factor (IURF) ((µg/m ³) ⁻¹)	--	NA	MDEQ, 2015	

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
IURF details	NA	<p>Carcinogen Weight-of-Evidence (WOE) Class: Inadequate Information to Assess [the] Carcinogenic Potential”</p> <p>IRIS WOE Basis: Studies evaluating the carcinogenic potential of oral or inhalation exposure to 1,2,3-TMB in humans or animals were not identified in the available literature</p> <p>Source and Date: PPRTV, 6/28/2010</p> <p>Tier 1 and 2 Sources:</p> <p>IRIS: No IRIS value is available at this time.</p> <p>PPRTV: Per PPRTV (6/28/2010), no value at this time.</p> <p>MRL: NA; MRLs are for non-cancer effects only.</p> <p>Tier 3 Source:</p> <p>MDEQ: Per DEQ-CCD, no value at this time.</p>		Complete
Mutagenic Mode of Action (MMOA)? (Y/N)	--	NO	USEPA, 2015	
MMOA 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/ITSL is not based on a reproductive-developmental effect.	MDEQ, 2015	
Developmental or Reproductive Toxicity Details	NA	NA		
State Drinking Water Standard (SDWS) (ug/L)	--	NO	SDWA, 1976	
SDWS details	NA	MI Safe Drinking Water Act (SDWA) 1976 PA 399		
Secondary Maximum Contaminant Level (SMCL) (ug/L)	--	NO	SDWA, 1976 USEPA SMCL List, 2015	

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
SMCL details	NA	MI Safe Drinking Water Act (SDWA) 1976 PA 399 and USEPA SMCL List, 2015		
Is there an aesthetic value for drinking water? (Y/N)	NO	YES	MDEQ, 2015	
Aesthetic value (ug/L)	--	125	Pirnie Report, 1996	
Aesthetic Value details		Threshold Odor Concentration using EPA Method 2150B. Prepared for MDEQ under contract to Malcolm Pirnie by St. Croix Sensory. See diethyl ether file for report. Source: Malcolm Pirnie, Inc. (1998). Technical Memorandum No. 8303. Determination of Threshold Odor Concentrations for Four Chemicals in Water. MDNR Contract No. 9499. Prepared by St. Croix Sencory, Inc., Stillwater, MN. (unpublished)		
Phytotoxicity Value? (Y/N)	NO	Not evaluated	NA	
Phytotoxicity details	NA	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 (AE _d)	---	NA	MDEQ, 2015	
AE _d details				
Ingestion Absorption Efficiency (AE _i)		NA	MDEQ, 2015	
AE _i Details				
Relative Source Contribution for Water (RSC _w)		NA	MDEQ, 2015	
Relative Source Contribution for Soil (RSC _s)		NA	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)	290

	Rule 57 Value (µg/L)	Verification Date
Human Non-cancer Values- Drinking water source (HNV-drink)	290	9/2006
Human Non-Cancer Values- Non-drinking water sources (HNV-Non-drink)	650	9/2006
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	9/2006
Aquatic maximum value (AMV)	ID	9/2006
Final Acute Value (FAV)	ID	9/2006

Sources:

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



(E) Analytical Information

	Value	Source
Target Detection Limit – Soil ($\mu\text{g}/\text{kg}$)	250	MDEQ, 2015
Target Detection Limit – Water ($\mu\text{g}/\text{L}$)	5	MDEQ, 2015
Target Detection Limit – Air (ppbv)	4.40E+01	MDEQ, 2015
Target Detection Limit – Soil Gas (ppbv)	1.50E+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 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