



CHEMICAL UPDATE WORKSHEET

Chemical Name:	4,4'-Methylene-bis-2- chloroaniline
CAS #:	101-14-4
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)	267.17	267.16	EPI	EXP
Physical State at ambient temp	Solid	Solid	MDEQ	
Melting Point (°C)	---	110.00	EPI	EXP
Boiling Point (°C)	378.9	378.90	EPI	EXP
Solubility (ug/L)	14000	13900	EPI	EXP
Vapor Pressure (mmHg at 25°C)	0.000000013	2.86E-07	PP	EST
HLC (atm-m ³ /mol at 25°C)	4.10E-11	4.06E-11	PP	EST
Log Kow (log P; octanol-water)	3.92	3.91	EPI	EXP
Koc (organic carbon; L/Kg)	7140	5698	EPI	EST
Ionizing Koc (L/kg)		NR	NA	NA
Diffusivity in Air (Di; cm ² /s)	0.08	2.55E-02	W9	EST
Diffusivity in Water (Dw; cm ² /s)	8.0E-6	6.61E-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	113	PC	EXP
Lower Explosivity Level (LEL; unit less)	NA	NA	NA	NA
Critical Temperature (K)		NA	NA	NA
Enthalpy of Vaporization (cal/mol)		NA	NA	NA
Density (g/mL, g/cm ³)		1.44	PC	EXP
EMSOFT Flux Residential 2 m (mg/day/cm ²)	NA	3.18E-10	EMSOFT	EST
EMSOFT Flux Residential 5 m (mg/day/cm ²)	NA	3.18E-10	EMSOFT	EST
EMSOFT Flux Nonresidential 2 m (mg/day/cm ²)	NA	3.18E-10	EMSOFT	EST
EMSOFT Flux Nonresidential 5 m (mg/day/cm ²)	NA	3.18E-10	EMSOFT	EST

(B) Toxicity Values/Benchmarks

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
Reference Dose (RfD) (mg/kg/day)	7.3E-4	2.0E-3	PPRTV, 2006	
RfD details	<p>Per RD/CCD: the RfD is based on a chronic carcinogenicity study in dogs (Stula et al., 1977). Six female beagles were dosed at a single level via oral gelatin capsule for up to 9 years. LOAEL = 7.3 mg/kg/d (this was the only dose tested). UF = 10,000 (individual UF justifications not described in original RD RfD development). CRITICAL EFFECT = liver and bladder effects.</p>	<p>Tier 2 Source: PPRTV Basis: PPRTV chronic p-RfD represents the most current evaluation of Stula et al. (1977) study data. No Tier 1 source. PPRTV chronic p-RfD = 2.0E-3 mg/kg/d. Critical Study: Stula, E.F., et al. (1977). Urinary bladder tumors in dogs from 4,4'-methylene-bis(2-chloroaniline) (MOCA). J. Environ. Path. Toxicol. 1: 31-50. Methods: MBOCA (90% pure) in gelatin capsules was administered at 100 mg/day to 6 female purebred beagle dogs, 3 days per week for 6 weeks and then 5 days per week thereafter for up to 9 years. The average dose per treatment was 10.3 mg/kg and the average daily dose was 7.3 mg/kg/day, calculated from data provided by the investigators. Six control dogs received no treatment. Critical effects: Increase in mean serum ALT in treated dogs versus controls, and a statistically significant increase in nodular hyperplasia of the liver in the treated dogs (3/5 versus 0/6 in controls). No liver tumors were found in the dogs. The average daily dose of MOCA in treated dogs was 7.3 mg/kg-day. End point or Point of Departure (POD): LOAEL = 7.3 mg/kg-day Uncertainty Factors: UF = 3,000 (10 for use of a LOAEL, 10 to extrapolate from dogs to humans, 10 to protect sensitive individuals, and 3 for database deficiencies, including lack of reproductive or developmental toxicity studies). Source: PPRTV, 08/03/2006</p> <p>Tier 1 and 2 Sources: IRIS: No IRIS file for MBOCA is available at this time.</p> <p>ATSDR MRL (05/1994): Chronic oral MRL = 3E-3 mg/kg/day Critical study: Stula, E.F., et al. (1977) Urinary bladder tumors in dogs from 4,4'-methylene-bis(2-chloroaniline) (MOCA). J. Environ. Path. Toxicol. 1: 31-50. Methods: see PPRTV entry above for study details.</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		<p>Critical effect: Hepatic effects including nodular hepatic hyperplasia and disruption of liver architecture and a significant increase in serum SGPT.</p> <p>Point of Departure (POD): LOAEL = 10 mg/kg/d</p> <p>Uncertainty factors: 3,000 (10 each for interspecies extrapolation, intraspecies variability, and use of a LOAEL; 3 for database limitations).</p> <p>Tier 3 Source: MDEQ/RRD (03/01/1992): Per DEQ-CCD, RfD = 7.3E-4 based on a 9-year dog study. LOAEL = 7.3 mg/kg/day; critical effects = liver effects and bladder inflammation (Stula et al., 1977). Basis of total uncertainty factor (assumed to be 10,000) is not described.</p>		
Oral Cancer Slope Factor (CSF) (mg/kg-day)⁻¹	7.7E-1	7E-3	PPRTV, 2006	
CSF details	<p>Per RD: HEAST SF = 1.3E-1 mg/kg/day; 2-year oral rat study (Kommineni et al., 1979); MDEQ-CCD SF based on oral dog study (Stula, et al., 1977). SF revised based on species scaling factor (BWh/BWa) rose to the .25 power.</p>	<p>Tier 2 Source: PPRTV: Basis: PPRTV is a Tier 2 source, no Tier 1 available. PPRTV CSF = 7E-3 per mg/kg-day. Critical Study: Kommineni, C., et al. (1978) Determination of the tumorigenic potential of methylene-bis-ortho-chloroaniline. J. Environ. Path. Toxicol. 2: 149-171. Methods: Rats were exposed to dietary levels of 0, 250, 500, or 1,000 ppm of MBOCA for 18 months and observed for an additional 6 months. Doses of 0, 12.5, 25, and 50 mg/kg/day were estimated by assuming that a rat consumes 5% of its body weight per day. These doses were expanded to continuous exposure by multiplying by 18/24 months. Point of Departure (POD): The highest estimate of human cancer risk was based on the combined incidence of lung tumors (adenoma, adenocarcinoma, epidermoid carcinoma) in male rats (human 0.1/BMDL₁₀ = 0.10 per mg/kg-day, 1E-1 per mg/kg-day (rounded from 9.95E-2). The oral slope factor, calculated from adult exposure, is derived from the BMDL₁₀, the 95% lower bound on the exposure associated with an 10% extra cancer risk, by dividing the risk by the BMDL₁₀ and represents an upper bound risk estimate for continuous lifetime</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		<p>exposure without consideration of increased early-life susceptibility due to MOCA’s mutagenic mode of action: the slope of the linear extrapolation from the central estimate, human BMD₁₀ is 0.1/(14.37 mg/kg-day) = 7E-3 per mg/kg-day. The BMD₁₀ for humans was calculated from the BMD₁₀ for animals according to the same procedure for conversion of the BMDL₁₀ for animals to humans.</p> <p>Carcinogen Weight-of-Evidence (WOE) Class: According to the 2005 Cancer Guidelines, the descriptor “Likely to be carcinogenic to humans” is appropriate for MOCA. This descriptor is applied when “...the weight of the evidence is adequate to demonstrate carcinogenic potential to humans but does not reach the weight of evidence for the descriptor “Carcinogenic to Humans”. MOCA satisfies at least two of the illustrative examples described under this category including, “...an agent demonstrating a plausible (but not definitely causal) association between human exposure and cancer...” and “... an agent that has tested positive in animal experiments in more than one species, sex, strain, or exposure route, with or without evidence of carcinogenicity in humans”. Suggestive epidemiologic evidence is available and MOCA has tested positive in rats, mice, and dogs in adequate studies. IARC classified MOCA as “probably carcinogenic to humans.”</p> <p>Source: PPRTV, 8/03/2006</p> <p>Tier 1 and 2 Sources: IRIS: No IRIS file for MBOCA is available at this time. MRL: NA; MRLs are for non-cancer effects only.</p> <p>Tier 3 Source: MDEQ: RRD (01/18/2000): Per DEQ-CCD, RRD oral slope factor = 7.7E-1 per mg/kg/d based on oral dog study (Stula, et al., 1977). SF revised based on species scaling factor (BW_i/BW_a) rose to the 0.25 power.</p>		
Reference Concentration (RfC) or Initial Threshold Screening Level	NA	NA	MDEQ, 2015	



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
(ITSL) ($\mu\text{g}/\text{m}^3$)				
RfC/ITSL details	--	<p>Tier 1 and 2 Sources: IRIS: No IRIS file available for MBOCA at this time. PPRTV (08/03/2006): Per PPRTV, limited human studies found no noncancerous effects attributable to MBOCA but were primarily interested in cancer effects. No animal data regarding the toxicity of MBOCA following subchronic or chronic inhalation exposure are available. Therefore, derivation of subchronic or chronic p-RfC values for MBOCA is precluded. MRL (05/1994): No inhalation MRLs have been derived for any duration of exposure because of lack of data.</p> <p>Tier 3 Sources: MDEQ: Per DEQ-CCD, no inhalation toxicity value for MBOCA is available at this time.</p>		Complete
Inhalation Unit Risk Factor (IURF) ($(\mu\text{g}/\text{m}^3)^{-1}$)	3.7E-5	NA	MDEQ, 2015	
IURF details	Per AQD: Potency based on EPA IRIS evaluation of Kammineni et al 1979 and Stula et al 1975. Kammineni et al 1979 male rats exposed via diet to 0, 250, 500 or 1000 ppm developed lung tumors with an incidence of 1/100, 23/100,	<p>Tier 1 and 2 Sources: IRIS: No IRIS file for MBOCA is available at this time. PPRTV (08/03/2006): Per PPRTV, there are no suitable human or animal carcinogenicity data from which to derive a provisional inhalation unit risk for MBOCA. MRL: NA; MRLs are for non-cancer effects only.</p> <p>Tier 3 Source: MDEQ: Per DEQ-CCD, no inhalation toxicity value for MBOCA is available at this time.</p>		Complete

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
	28/75 and 35/50 respectively. IRSL rounded to 0.03 from 0.027 ug/m3. AQD calculation date: 12/4/84. No PPRTV IUR (11/21/11).			
Mutagenic Mode of Action (MMOA)? (Y/N)	--	Yes	USEPA, 2014	
MMOA Details	--	Listed as a carcinogen with mutagenic MOA in the USEPA Table 1b List.		
Developmental or Reproductive Effector? (Y/N)	No	No, the RfD is not based on a reproductive-developmental effect.	MDEQ, 2015	
Developmental or Reproductive Toxicity Details	NA	--		
State Drinking Water Standard (SDWS) (ug/L)	NA	NO	SDWA, 1976	
SDWS details	NA	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	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 (AE _d)	---	0.1	MDEQ, 2015	
AE _d 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)	NA
Updated GSI value (µg/L)	NA
Rule 57 Drinking Water Value (µg/L)	NA

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

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 ($\mu\text{g}/\text{kg}$)	500	MDEQ, 2015
Target Detection Limit – Water ($\mu\text{g}/\text{L}$)	1	MDEQ, 2015
Target Detection Limit – Air (ppbv)	NA	MDEQ, 2015
Target Detection Limit – Soil Gas (ppbv)	NA	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