



CHEMICAL UPDATE WORKSHEET

Chemical Name:	4-Chloroaniline
CAS #:	106-47-8
Revised By:	RRD Toxicology Unit
Revision Date:	August 14, 2015

(A) Chemical-Physical Properties

	Part 201 Value	Updated Value	Reference Source	Comments
Molecular Weight (g/mol)	127.57	127.57	EPI	EXP
Physical State at ambient temp	Solid	Solid	MDEQ	
Melting Point (°C)	72.5	72.50	EPI	EXP
Boiling Point (°C)	449.6	232.00	EPI	EXP
Solubility (ug/L)	3.90E+6	3.90E+06	EPI	EXP
Vapor Pressure (mmHg at 25°C)	0.027	2.70E-02	EPI	EXP
HLC (atm-m³/mol at 25°C)	1.16E-6	3.31E-07	SSG	EXP
Log Kow (log P; octanol-water)	1.83	1.83	EPI	EXP
Koc (organic carbon; L/Kg)	63	112.7	EPI	EST
Ionizing Koc (L/kg)		NR	NA	NA
Diffusivity in Air (Di; cm²/s)	4.83E-2	7.04E-02	W9	EST
Diffusivity in Water (Dw; cm²/s)	1.01E-5	1.0253E-05	W9	EST
Soil Water Partition Coefficient (Kd; inorganics)	NR	NR	NA	NA

	Part 201 Value	Updated Value	Reference Source	Comments
Flash Point (°C)	220 F	104	NPG	EXP
Lower Explosivity Level (LEL; unit less)	NA	NA	NA	NA
Critical Temperature (K)		754.00	EPA2001	EXP
Enthalpy of Vaporization (cal/mol)		1.17E+04	EPA2001	EXP
Density (g/mL, g/cm3)		1.429	CRC	EXP
EMSOFT Flux Residential 2 m (mg/day/cm ²)	2.46E-06	2.21E-06	EMSOFT	EST
EMSOFT Flux Residential 5 m (mg/day/cm ²)	2.46E-06	2.21E-06	EMSOFT	EST
EMSOFT Flux Nonresidential 2 m (mg/day/cm ²)	2.94E-06	2.79E-06	EMSOFT	EST
EMSOFT Flux Nonresidential 5 m (mg/day/cm ²)	2.94E-06	2.79E-06	EMSOFT	EST

(B) Toxicity Values/Benchmarks

	Part 201 Value	Updated Value	Source*/Reference /Date	Comments/Notes /Issues
Reference Dose (RfD) (mg/kg/day)	--	5.0E-4	PPRTV, 2008	
RfD details	NA	<p>Tier 2 Source: PPRTV: Basis: PPRTV assessment is more recent than IRIS. MDEQ applied a UF = 1 for use of a subchronic RfD to derive the chronic p-RfD; this chronic RfD is lower than the IRIS and MDEQ chronic values. In addition, there was a precipitous drop (~50% reduction) in methemoglobin levels at the 12-month time point compared to the 6-month time point in male and female rats orally exposed at the LOAEL of 1.4 mg/kg-day thereby making an additional UF unnecessary. PPRTV subchronic p-RfD = 5.0E-4 mg/kg-day Critical Study(ies): NTP (1989)/Chhabra et al. (1991) - NTP (National Toxicology Program). 1989. Toxicology and carcinogenesis studies of parachloroaniline hydrochloride (CAS No. 20265-96-7) in F344/N rats and B6C3F1 mice (gavage studies). NTP-TR-351. NIH Pub. No. 89-2806. - Chhabra, R.S., J.E. Huff, J.K. Haseman et al. 1991. Carcinogenicity of p-chloroaniline in rats and mice. Food Chem. Toxicol. 29:119-124. Method(s): An oral gavage study in B6C3F1 mice exposed to 0, 3, 10, or 30 mg/kg-day, 5 days/week for 103 weeks. Duration-adjusted average daily doses are 0, 2.1, 7.1, or 21.4 mg/kg-day, respectively. Critical effect: increased incidence of hemosiderosis in the liver End point or Point of Departure (POD): LOAEL = 21.4 mg/kg-day; adjusted LOAEL = 1.4 mg/kg-day Data for methemoglobin levels were initially selected for benchmark dose (BMD) modeling. However, the duration adjusted BMDL1SD for methemoglobin levels in female rats does not provide a lower POD than the duration adjusted LOAEL. Therefore, the LOAEL was used as basis for deriving the RfD. Uncertainty Factors: UF = 3,000 (10 each for intraspecies variability and interspecies extrapolation, and database deficiencies and 3 for use of a LOAEL). Source: PPRTV, 9/30/08</p>	Complete	



	Part 201 Value	Updated Value	Source*/Reference /Date	Comments/Notes /Issues
		<p>Tier 1 and 2 Sources: IRIS: Per IRIS (2/01/1995), IRIS RfD = 4.0E-3 mg/kg-day. An EPA screening-level literature review on August 2003 identified one or more significant new studies. Critical Study (ies): NCI (National Cancer Institute). 1979. Bioassay of p-chloroaniline for possible carcinogenicity. NCI Carcinogenesis Tech. Rep. Ser. No. 189. NTIS PB 295896. Method(s): Groups of 20 and 50 F344 rats of each sex were exposed to p-chloroaniline in the diet at concentration of 0, 250 or 500 ppm for 78 weeks followed by an observation period of 24 weeks. Critical effect: Nonneoplastic lesions of splenic capsule. End point or Point of Departure (POD): LOAEL = 250 ppm in diet converted to 12.5 mg/kg-day Uncertainty Factors: UF = 3,000 (10 each for interspecies variability, interspecies extrapolation and use of a LOAEL, and 3 for lack of supporting reproductive and other toxicity data) Source and date: IRIS, Last revision date – 2/1/1995</p> <p>MRL: No MRL record available at this time.</p> <p>Tier 3 Source: MDEQ: Per DEQ/RRD, RfD = 1.43E-3 mg/kg-day: Critical Study: Chhabra, R.S. et al., (1991). Carcinogenicity of p-Chloroaniline in Rats and Mice. Food Chem. Toxicol. 29(2): 119-24. Method(s): 4-CA was administered to F344/N rats and B6C3F1 mice (50/specie/sex/dose group) by oral gavage five days per week for 103 weeks. Rats received doses of 0, 2, 6, or 18 mg/kg/d, while mice received doses of 0, 3, 10, or 30 mg/kg-day. Critical effect: fibrosis of the spleen and bone marrow hyperplasia End point or Point of Departure (POD): LOAEL = 2 mg/kg-day Uncertainty Factors: UF = 1,000 (10 each for interspecies variability, interspecies extrapolation and LOAEL to NOAEL extrapolation). Source and date: MDEQ/RRD, August 2008. See Toxicology Assessment. RRD</p>		

	Part 201 Value	Updated Value	Source*/Reference /Date	Comments/Notes /Issues
		literature review was conducted on 2008 and 2010.		
Oral Cancer Slope Factor (CSF) (mg/kg-day)⁻¹	--	2.0E-1	PPRTV, 2008	
CSF details	NA	<p>Tier 2 Source: PPRTV: Basis: PPRTV is the only available value and a Tier 2 source. PPRTV (9/30/2008) CSF = 0.2 (mg/kg-day)⁻¹. Per PPRTV, the OSF for p-chloroaniline should not be used with exposures exceeding the point of departure (BMDL₁₀ HED = 0.531 mg/kg-day) because above this level the fitted dose-response model better characterizes what is known about the carcinogenicity of p-chloroaniline. Critical Study(ies): NTP (National Toxicology Program). 1989. Toxicology and carcinogenesis studies of parachloroaniline hydrochloride (CAS No. 20265-96-7) in F344/N rats and B6C3F1 mice (gavage studies). NTP-TR-351. NIH Pub. No. 89-2806. Method(s):</p> <ol style="list-style-type: none"> 1) <i>Dose response data:</i> Tumor Type - adrenal tumors; Test Species – male rats; Route - oral 2) <i>Extrapolation method:</i> multistage-cancer model for dichotomous data. In order to linearly extrapolate cancer risks from the BMDL_{10HED} to the origin, a cancer OSF was calculated as the ratio of 0.1/BMDL_{10HED}. Taking the BMDL_{10HED} of 0.531 mg/kg-day for adrenal medulla tumors in male rats as the POD, a provisional OSF is calculated as follows: 0.1/BMDL_{10HED} = 0.1/0.532 mg/kg-day = 0.2 (mg/kg-day)⁻¹ <p>Carcinogen Weight-of-Evidence (WOE) and Basis: Likely to be carcinogenic to humans based on positive tumor development in multiple animal species. Per PPRTV, available data are insufficient to identify key events in the development of p-chloroaniline-induced tumors in rats (splenic and adrenal gland tumors) and mice (liver tumors).</p> <p>Tier 1 and 2 Sources:</p>		Complete



	Part 201 Value	Updated Value	Source*/Reference /Date	Comments/Notes /Issues
		IRIS: Per IRIS (8/22/1988), no value at this time. MRL: NA; MRLs are for non-cancer effects only.		
Reference Concentration (RfC) or Initial Threshold Screening Level (ITSL) (µg/m³)	--	NA	MDEQ, 2015	
RfC/ITSL details	NA	<p>Tier 1 and 2 Sources: IRIS: Per IRIS (8/22/1988), no value at this time. PPRTV: Per PPRTV (9/30/2008), no value at this time. A limited number of sub chronic animal inhalation studies are available; these studies are limited in design and/or reporting detail and are, thus, inadequate for derivation of a sub chronic p-RfC. Human case reports of hematological effects (anemia, cyanosis, increased methemoglobin and sulfhemoglobin, and reduced hemoglobin) associated with occupational exposures (Pacseri et al., 1958, as reported in IPCS, 2003; Monsanto Co., 1986, as reported in IPCS, 2003) and accidental exposures of neonates (IPCS, 2003) did not provide sufficient details of study methodology, exposure, and response adequate for the derivation of a sub chronic or chronic inhalation RfC for <i>p</i>-chloroaniline. MRL: No MRL record available at this time.</p> <p>Tier 3 Source: MDEQ: Per DEQ-CCD, no value at this time.</p>		Complete
Inhalation Unit Risk Factor (IURF) ((µg/m³) ⁻¹)	--	NA	MDEQ, 2015	
IURF details	NA	<p>Carcinogen Weight-of-Evidence (WOE) Class: likely to be carcinogenic to humans WOE Basis: based on positive tumor development in multiple animal species. Per PPRTV, available data are insufficient to identify key events in the development of <i>p</i>-chloroaniline-induced tumors in rats (splenic and adrenal gland tumors) and mice (liver tumors).</p>		Complete



	Part 201 Value	Updated Value	Source*/Reference /Date	Comments/Notes /Issues
		<p>Source: IRIS, 8/22/1988</p> <p>Tier 1 and 2 Sources: IRIS: No value at this time. PPRTV: Per PPRTV (9/30/2008), 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>		
Mutagenic Mode of Action (MMOA)? (Y/N)	--	NO	USEPA, 2015	
MMOA Details	--	This substance is not listed as a carcinogen with mutagenic MOA in the USEPA OSWER 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	NA		
State Drinking Water Standard (SDWS) (ug/L)	--	NA	SDWA, 1976	
SDWS details	NA	MI Safe Drinking Water Act (SDWA) 1976 PA 399		
Secondary Maximum Contaminant Level (SMCL) (ug/L)	--	NA	SDWA,1976 and USEPA SMCL List	
SMCL details	NA	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	



	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)	---	NA	MDEQ, 2015	
AE_d details				
Ingestion Absorption Efficiency (AE_i)		1.0	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)	10 (M); 2

	Rule 57 Value (µg/L)	Verification Date
Human Non-cancer Values- Drinking water source (HNV-drink)	39	5/2008
Human Non-Cancer Values- Non-drinking water sources (HNV-Non-drink)	1,400	5/2008
Wildlife Value (WV)	NA	NA
Human Cancer Values for Drinking Water Source (HCV-drink)	2	5/2008
Human Cancer values for non-drinking water source (HCV-Non-drink)	72	5/2008
Final Chronic Value (FCV)	ID	4/2008
Aquatic maximum value (AMV)	ID	4/2008
Final Acute Value (FAV)	ID	4/2008

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 ($\mu\text{g}/\text{kg}$)	330	MDEQ, 2015
Target Detection Limit – Water ($\mu\text{g}/\text{L}$)	10	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