CHEMICAL UPDATE WORKSHEET

Chemical Name:	**1,4-Dioxane**
CAS #:	**123-91-1**
Revised By:	RRD Toxicology Unit
Revision Date:	August 17, 2015

(A) Chemical-Physical Properties

	Part 201 Value	Updated Value	Reference Source	Comments
Molecular Weight (g/mol)	88.11	88.11	EPI	EXP
Physical State at ambient temp	Liquid	Liquid	MDEQ	
Melting Point (˚C)	285	11.80	EPI	EXP
Boiling Point (˚C)	101.5	101.50	EPI	EXP
Solubility (ug/L)	9.00E+8	1E+09	EPI	EXP
Vapor Pressure (mmHg at 25˚C)	38	3.81E+01	EPI	EXP
HLC (atm-m^3/mol at 25˚C)	4.90E-6	4.80E-06	EPI	EXP
Log Kow (log P; octanol-water)	-0.39	-0.27	EPI	EXP
Koc (organic carbon; L/Kg)	0.588	2.633	EPI	EST
Ionizing Koc (L/kg)		NR	NA	NA
Diffusivity in Air (Di; cm^2/s)	0.23	8.74E-02	W9	EST
Diffusivity in Water (Dw; cm^2/s)	1.0E-5	1.0541E-05	W9	EST

	Part 201 Value	Updated Value	Reference Source	Comments
Soil Water Partition Coefficient (Kd; inorganics)	NR	NR	NA	NA
Flash Point (˚C)	55 F	12	CRC	EXP
Lower Explosivity Level (LEL; unit less)	0.02	0.02	CRC	EXP
Critical Temperature (K)		587.3	CRC	EXP
Enthalpy of Vaporization (cal/mol)		8.16E+03	CRC	EXP
Density (g/mL, g/cm^3)		1.0337	CRC	EXP
EMSOFT Flux Residential 2 m (mg/day/cm^2)	1.57E-05	1.84E-05	EMSOFT	EST
EMSOFT Flux Residential 5 m (mg/day/cm^2)	1.84E-05	2.38E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 2 m (mg/day/cm^2)	2.01E-05	2.60E-05	EMSOFT	EST
EMSOFT Flux Nonresidential 5 m (mg/day/cm^2)	2.20E-05	3.03E-05	EMSOFT	EST

(B) Toxicity Values/Benchmarks

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
Reference Dose (RfD) (mg/kg/day)	--	3.0E-2	IRIS, 2010	
RfD details	Per CCD/RRD: IRIS (2000) file empty.	**Tier 1 Source:** **IRIS:** **Basis:** IRIS (2010) RfD = 3.0E-2 mg/kg-day. IRIS selected since it is a Tier 1 source and the assessment is very similar to the more recent ATSDR MRL. **Critical Study**: Kociba RJ; McCollister SB; Park C; Torkelson TR; Gehring PJ (1974). 1,4-dioxane I Results of a 2-year ingestion study in rats. Toxicol Appl Pharmacol, 30: 275-286. **Methods**: 8-week-old Sherman rats (60/grp) were given 0, 0.01, 0.1, or 1.0% 1,4-dioxane in drinking water for up to 716 days. The calculated mean daily doses are 9.6, 94, and 1,015 mg/kg-day for male rats and 19, 148, and 1,599 mg/kg-day for female rats during days 114–198 for the 0.01, 0.1, and 1.0% concentration levels, respectively. **Critical effect**: Liver and kidney toxicity **End point or Point of Departure (POD):** NOAEL = 9.6 mg/kg-day **Uncertainty Factors**: UF = 300 (10 each for intraspecies variability and interspecies extrapolation, and 3 for database deficiency) **Source and date:** IRIS, Last revision date - 8/11/2010. A Toxicological Review is available. **Tier 2 Sources**: **PPRTV:** No PPRTV record is available at this time. **MRL:** Per ATSDR (4/2012), oral chronic MRL = 0.1 mg/kg-day. **Critical Study:** Kociba RJ, McCollister SB, Park C, et al. 1974. 1,4-Dioxane. I. Results of a 2-year ingestion study in rats. Toxicol Appl Pharmacol 30:275-286. **Methods:** Groups of Sherman rats (60/sex/dose level) were treated with 1,4-dioxane in the drinking water at levels of 0 (controls), 0.01, 0.1, or 1% for 716 days. Based on body weight and water consumption data, the investigators estimated that the water provided doses of 1,4-dioxane of 0, 9.6, 94, and 1,015 mg/kg/day for males and 0, 19, 148, and 1,599 mg/kg/day for females. **Critical effect:** liver lesions consisted of various degrees of hepatocellular degeneration and necrosis **End point or Point of Departure (POD):** NOAEL = 9.6 mg/kg-day **Uncertainty Factors:** UF = 100 (10 each for intraspecies variability and		Complete

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		interspecies extrapolation) **Source and date:** ATSDR, 4/2012. A Toxicological Profile is available. Also Intermediate oral MRL = 0.5 mg/kg/day; Acute oral MRL = 5 mg/kg/day. **Tier 3 Source:** **MDEQ:** Per DEQ-CCD, RRD/WRD adopted 2000 IRIS RfD.		
Oral Cancer Slope Factor (CSF) (mg/kg-day)$^{-1}$)	1.0E-2	1.0E-1	IRIS, 2013	
CSF details	Liver adenomas/carcinomas in female B6C3F1 mice exposed via the drinking water for 90 weeks (NCI, 1978). Source: SWQD CCD/WRD date: 1/28/2000	**Tier 1 Source:** **IRIS:** **Basis:** IRIS presents a recent assessment. IRIS (2013) CFS = 1.0E-1 (mg/kg-day)$^{-1}$. **Critical Study**: Kano, H; Umeda, Y; Kasai, T; Sasaki, T; Matsumoto, M; Yamazaki, K; Nagano, K; Arito, H; Fukushima, S.(2009). Carcinogenicity studies of 1,4-dioxane administered in drinking-water to rats and mice for 2 years. Food Chem Toxicol 47: 2776-2784. The Japanese Bioassay Research Center conducted a 2-year drinking water study on the effects of 1,4-dioxane in both sexes of rats and mice. The results from that study were reported several times, once as conference proceeding (Yamazaki et al., 1994), once as a detailed laboratory report (JBRC, 1998b), and once as a published manuscript (Kano et al., 2009). **Methods**: 1) *Dose response data*: *Tumor Type* - hepatocellular adenoma and carcinoma; *Test Species* - female BDF1 mouse; *Route* - Oral, drinking water at 0, 66, 278 and 964 mg/kg-day. 2) *Extrapolation method*: Multi-tumor dose-response model with linear extrapolation **Carcinogen Weight-of-Evidence (WOE) Class**: "likely to be carcinogenic to humans" by all routes of exposure. **IRIS WOE Basis**: based on the following findings: (1) inadequate evidence of carcinogenicity in humans, and (2) sufficient evidence in animals (i.e., hepatic tumors in multiple species [three strains of rats, two strains of mouse, and in guinea pigs]; mesotheliomas of the peritoneum, mammary, and nasal tumors have also been observed in rats following 2 years of oral exposure to 1,4-dioxane). **Source and Date**: IRIS, Last revision date - 9/20/2013. A Toxicological Review is available.		Complete.

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		Tier 2 Sources: **PPRTV:** No PPRTV record is available at this time. **MRL:** NA; MRLs are for non-cancer effects only. **Tier 3 Source:** **MDEQ:** Per DEQ-CCD/WRD (1/28/2000), CSF – 1.0E-2 (mg/kg-day)-1. See Part 201 CSF details.		
Reference Concentration (RfC) or Initial Threshold Screening Level (ITSL) (µg/m³)	--	3.0E+1	IRIS, 2013	
RfC/ITSL details	NA	**Tier 1 Source:** **IRIS:** **Basis:** IRIS is a Tier 1 source and the assessment is very similar to the assessment conducted by ATSDR. IRIS (2013) RfC = 3.0E-2 mg/m^3. **Critical Study**: Kasai, T; Kano, H; Umeda, Y; Sasaki, T; Ikawa, N; Nishizawa, T; Nagano, K; Arito, H; Nagashima, H; Fukushima, S. (2009). Two-year inhalation study of carcinogenicity and chronic toxicity of 1,4-dioxane in male rats. Inhal Toxicol 21: 889-897. **Methods**: male 6 week old F344/DuCrj rats (50/group) were exposed via inhalation to 0 (clean air), 50, 250, and 1,250 ppm (0, 180, 900, and 4,500 mg/m3, respectively) of vaporized 1,4-dioxane (>99% pure) for 6 hours/day, 5 days/week, for 104 weeks (2 years) in whole body inhalation chambers. **Critical effect**: Atrophy and respiratory metaplasia of the olfactory epithelium **End point or Point of Departure (POD):** LOAEL = 50 ppm; LOAEL POD_{HEC} = 32.2 mg/m^3 **Uncertainty Factors**: UF = 1,000 (10 each for intraspecies variability and interspecies extrapolation, and 3 for database deficiency) **RfC:** 3.0E-2 mg/m^3 **Source and date:** IRIS, Last revision date - 9/20/2013. A Toxicological Review is available. **Tier 2 Source**: **PPRTV:** No PPRTV record is available at this time. **MRL:** Per ATSDR List (12/2014), inhalation chronic MRL = 0.03 ppm or 1.1E-1 mg/m^3 (MW = 88.11 g/mol).		Complete

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		Critical Study: Kasai T, Kano H, Umeda Y, et al. 2009. Two-year inhalation study of carcinogenicity and chronic toxicity of 1,4-dioxane in male. Inhal Toxicol 21:889-897. **Methods:** Groups of male F344/DuCrj rats (50/group) were exposed whole-body to target concentrations of 0, 50, 250, or 1,250 ppm 1,4-dioxane vapors 6 hours/day, 5 days/week for 104 weeks; controls were exposed to clean air. **Critical effect:** liver lesions consisted of various degrees of hepatocellular degeneration and necrosis **End point or Point of Departure (POD):** The lowest exposure concentration tested, 50 ppm 1,4-dioxane, is a LOAEL for nasal lesions (atrophy of the olfactory epithelium), a NOAEL was not defined in this study. **Uncertainty Factors:** UF = 300 (10 for use of a LOAEL; 3 for extrapolation from animals to humans with dosimetric adjustment; 10 for human variability. **Source and date:** ATSDR, 4/2012. A Toxicological Profile is available. **Tier 3 Source:** **MDEQ:** Per DEQ-CCD/AQD ITSL = 1.0E+2 ug/m^3. **Basis**: The inhalation ITSL was derived from the USEPA oral potency 1.0E-1 (mg/kg-day) using 70 kg person breaths 20 m3 a day. Key study is mice 2-year drinking water study by Kano et al 2009. Female mice developed hepatocellular adenomas and carcinomas with incidence of 5/50, 35/50, 41/50, and 46/50 a doses of 0, 66, 278 and 964 mg/kg. **Source and date:** MDEQ-CCD/AQD, 8/11/2010		
Inhalation Unit Risk Factor (IURF) (($\mu g/m^3$)$^{-1}$)	--	5.0E-6	IRIS, 2013	
IURF details	Record previous value (pre 2002)	**Tier 1 Source:** **IRIS:** **Basis:** IRIS is a Tier 1 source and the only available Tier 1 or 2 source. IRIS (2013) IURF = 5.0E-6 ($\mu g/m^3$)$^{-1}$. **Critical Study**: Kasai, T; Kano, H; Umeda, Y; Sasaki, T; Ikawa, N; Nishizawa, T; Nagano, K; Arito, H; Nagashima, H; Fukushima, S. (2009). Two-year inhalation study of carcinogenicity and chronic toxicity of 1,4-dioxane in male rats. Inhal Toxicol 21: 889-897. **Methods**: male 6 week old F344/DuCrj rats (50/group) were exposed via inhalation to 0 (clean air), 50, 250, and 1,250 ppm (0, 180, 900, and 4,500 mg/m3, respectively) of vaporized 1,4-dioxane (>99% pure) for 6 hours/day, 5 days/week, for 104 weeks (2 years) in whole body inhalation chambers.		Complete

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		1) *Dose response data*: *Tumor Type* - multiple (nasal, liver, kidney, peritoneal, mammary gland, and Zymbal gland); *Test Species* - male F344 rats; *Route* - inhalation 2) *Extrapolation method*: Multi-tumor dose-response model with linear extrapolation from the POD (BMCL10HEC) associated with 10% extra cancer risk **Carcinogen Weight-of-Evidence (WOE) Class**: "likely to be carcinogenic to humans." by all routes of exposure. **IRIS WOE Basis**: based on the following findings: (1) inadequate evidence of carcinogenicity in humans, and (2) sufficient evidence in animals (i.e., hepatic tumors in multiple species [three strains of rats, two strains of mouse, and in guinea pigs]; mesotheliomas of the peritoneum, mammary, and nasal tumors have also been observed in rats following 2 years of oral exposure to 1,4-dioxane). **Source and Date**: IRIS, Last revision date - 9/20/2013. A Toxicological Review is available. **Tier 2 Sources**: **PPRTV:** No PPRTV record is available at this time. **MRL:** NA; MRLs are for non-cancer effects only. **Tier 3 Source:** **MDEQ:** Per DEQ-CCD/AQD (8/11/2010), IURF = 2.9E-5 $(\mu g/m^3)^{-1}$ **Basis**: The inhalation potency was derived from the USEPA oral potency 1x10-1 (mg/kg) using 70 kg person breaths 20 m3 a day. Key study is mice 2-year drinking water study by Kano et al 2009. Female mice developed hepatocellular adenomas and carcinomas with incidence of 5/50, 35/50, 41/50, and 46/50 a doses of 0, 66, 278 and 964 mg/kg.		
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		

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
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 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	
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 (ABSgi)	---	1.0	MDEQ, 2015/USEPA RAGS-E	
ABSgi details		RAGS E (EPA, 2004) Default Value		
Skin absorption efficiency value (AEd)	---	0.1	MDEQ, 2015	
AEd details		RAGS E (EPA, 2004) Default Value		
Ingestion Absorption Efficiency (AEi)		1.0	MDEQ, 2015	
AEi 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)	2,800 (X)
Updated GSI value (µg/L)	2,800 (X)
Rule 57 Drinking Water Value (µg/L)	34

	Rule 57 Value (µg/L)	Verification Date
Human Non-cancer Values- Drinking water source (HNV-drink)	4,000	6/1998
Human Non-Cancer Values- Non-drinking water sources (HNV-Non-drink)	320,000	6/1998
Wildlife Value (WV)	NA	NA
Human Cancer Values for Drinking Water Source (HCV-drink)	34	6/1998
Human Cancer values for non-drinking water source (HCV-Non-drink)	2,800	6/1998
Final Chronic Value (FCV)	22,000	6/1998
Aquatic maximum value (AMV)	200,000	6/1998
Final Acute Value (FAV)	390,000	6/1998

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 (μg/kg)	500	MDEQ, 2015
Target Detection Limit – Water (μg/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