



CHEMICAL UPDATE WORKSHEET

Chemical Name:	Lithium (DD)
CAS #:	7439-93-2
Revised By:	RRD Toxicology Unit
Revision Date:	November 4, 2015

(A) Chemical-Physical Properties

	Part 201 Value	Updated Value	Reference Source	Comments
Molecular Weight (g/mol)	6.941	6.94	EPI	EXP
Physical State at ambient temp	Inorganic	Inorganic	MDEQ	
Melting Point (°C)	---	180.50	CRC	EXP
Boiling Point (°C)	1342	1342.00	CRC	EXP
Solubility (ug/L)	NA	NA	NA	NA
Vapor Pressure (mmHg at 25°C)	NA	NR	NA	NA
HLC (atm-m³/mol at 25°C)	NR	NR	NA	NA
Log Kow (log P; octanol-water)	NR	NR	NA	NA
Koc (organic carbon; L/Kg)	NR	NR	NA	NA
Ionizing Koc (L/kg)		NR	NA	NA
Diffusivity in Air (Di; cm²/s)	NR	NR	NA	NA
Diffusivity in Water (Dw; cm²/s)	NR	NR	NA	NA
Soil Water Partition Coefficient (Kd; inorganics)	NA	NA	NA	NA

	Part 201 Value	Updated Value	Reference Source	Comments
Flash Point (°F)	NA	NA	NA	NA
Lower Explosivity Level (LEL; unitless)	NA	NA	NA	NA
Critical Temperature (K)		NR	NA	NA
Enthalpy of Vaporization (cal/mol)		NR	NA	NA
Density (g/mL, g/cm ³)		NR	NA	NA
EMSOFT Flux Residential 2 m (mg/day/cm ²)	NA	NR	EMSOFT	NA
EMSOFT Flux Residential 5 m (mg/day/cm ²)	NA	NR	EMSOFT	NA
EMSOFT Flux Nonresidential 2 m (mg/day/cm ²)	NA	NR	EMSOFT	NA
EMSOFT Flux Nonresidential 5 m (mg/day/cm ²)	NA	NR	EMSOFT	NA

(B) Toxicity Values/Benchmarks

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
Reference Dose (RfD) (mg/kg/day)	2.8E-2	2.0E-3	PPRTV, 2008	
RfD details	Prospective study of human exposure during first trimester of pregnancy. LOAEL = 2.8 Li/kg BW/day, UF = 100 (10 for intraspecies variability, 10 for use of a LOAEL rather than a NOAEL). Critical effect = developmental in human offspring manifested as increased body weight at birth (Jacobson et al, 1992). CCD/RRD date: 4/1/97.	<p>Tier 2 Source: PPRTV: Basis: PPRTV is a Tier 2 source, no Tier 1 available. RfD Basis: The lower bound of the therapeutic serum lithium concentration range of 6 mmol/L is selected as the basis for the provisional RfD. Methods: Based on pharmacokinetic considerations, to achieve a serum lithium concentration of 0.6 mmol Li/L, the daily ingestion of lithium by a 70-kg individual is calculated as approximately 1.8 mg Li/kg-day. At steady state, $D = (Cp \times Cl)/f$ where D is the dose (mg/kg-day), Cp is the plasma concentration (mg/L), Cl is the plasma clearance (L/kg-day) and f is the fraction of the dose absorbed. Assuming values of 0.5 L/kg-day for Cl and 1 for f (Baldessarini and Tarazi, 2001), a steady-state plasma concentration of 0.6 mmol/L (4.2 mg Li/L) corresponds to a daily dose of 2.1 mg Li/kg-day. Critical effect: adverse effects in several organs and systems and developmental effects, primarily involving the heart. End point or Point of Departure (POD): LOAEL = 2.1 mg/kg-day Uncertainty Factors: UF = 1,000 (10 each for intraspecies variability, LOAEL to NOAEL extrapolation, and database insufficiencies) Source and date: PPRTV, 6/12/2008</p> <p>Tier 1 and 2 Sources: IRIS: No IRIS file available at this time. MRL: No MRL record available at this time.</p> <p>Tier 3 Source: MDEQ: Per DEQ-CCD/RRD, RfD = 2.8E-2. See Part 201 Value RfD details. RRD Calculation date = 04/01/1997.</p>		Complete
Oral Cancer Slope Factor (CSF) (mg/kg-day) ⁻¹	--	NA	MDEQ, 2015	

	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
CSF details	NA	<p>Carcinogen Weight-of-Evidence (WOE) Class: "data are inadequate for an assessment of human carcinogenic potential". Due to the lack of data, derivation of an oral cancer slope factor and an inhalation cancer unit risk are precluded. Source and Date: PPRTV, 6/12/2008</p> <p>Tier 1 and 2 Sources: IRIS: IRIS file not available at this time. PPRTV: Per PPRTV (6/12/2008), 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>		Complete.
Reference Concentration (RfC) or Initial Threshold Screening Level (ITSL) (µg/m³)	--	3.5E+1	MDEQ, 2011	
RfC/ITSL details	NA	<p>Tier 3 Source: MDEQ: Basis: MDEQ-AQD value is based on route to route extrapolation of the oral toxicity value derived from a 1992 epidemiological study. The ECHA value is based on information from review articles. See details below.</p> <p>Tier 1 and 2 Sources: IRIS: No IRIS file available at this time. PPRTV 06/12/2008: No studies investigating the effects of acute, sub chronic or chronic inhalation exposure to lithium in humans were identified. The available studies in animals did not evaluate comprehensive histopathological, biochemical and clinical endpoints of inhalation exposure. MRL: No MRL record available at this time.</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		<p>Tier 3 Sources: MDEQ-AQD: ITSL = 35 µg/m³ (24-hour averaging time) Critical Study: Jacobson, S.J., K. Jones, K. Johnson et al. 1992. Prospective multicenter study of pregnancy outcome after lithium exposure during the first trimester. Lancet. 339:530-533. Methods: 148 women using lithium during the first trimester of pregnancy were prospectively recruited and followed. Each study patient was matched with a woman (control) of similar age (within 2 years). The mean lithium dose was 927 mg/day of lithium carbonate (2.5 mg Li/kg-day); the authors did not report serum lithium concentrations. Average maternal body weight = 62 kg; RfD = 0.01 mg/kg-day; oral to inhalation conversion assumed 70kg BW and 20m³ air breathing rate. Critical effect: Significant increase in neonate birth weight (macrosomia). End point or Point of Departure (POD): LOAEL = 2.8 mg/kg (174 mg Li/62 kg body weight) Uncertainty Factors: UF = 300 (10 for interspecies variability, 10 for use of a LOAEL and 3 for treatment duration of only the first trimester of pregnancy) Source and date: MDEQ-CCD/RRD: 6/06/2011</p> <p>ECHA (REACH): Derived No Effect Level (DNEL) = 1.8 mg/m³ (1.8E+3 µg/m³): Basis: route to route extrapolation of oral dose of 1.2 mg lithium/kg bw. Adjustment factors (AF): Per ECHA, recommended AF (for chronic exposure; ECHA REACH Guidance document R8, 2012) is one (1). References/Studies:</p> <ol style="list-style-type: none"> 1) Schatzberg, A.F.; Cole, O.J., DeBattista, C. (2007). Manual of clinical psychopharmacology. American Psychiatric Publishing. ISBN 158562317 2) Casarett, L.; Klassen, C.D; Curtis, D. (2007) Toxicology: the basic science of poisons. ISBN-10: 0-07-147051-4 3) Davis, B; Morris, T. (1993) Physiological Parameters on Laboratory animals and humans. Pharm. res. 10: 1093 <p>Methods: The effect level (NOAEL) determined for lithium for repeated dose toxicity by the</p>		



	Part 201 Value	Updated Value	Source/Reference/Date	Comments/Notes/Issues
		<p>oral route is based on human data and can be calculated in two ways that complete one another. One way is based on the therapeutic serum concentrations of 0.5 to 1.0 mmol lithium/L and the extracellular fluid (ECF) volume. A desired concentration of 1 mmol/L of lithium is expected to be sustained and reflected in the extracellular fluid (ECF) only and not in the intracellular fluid. Thus, the volume considered is the ECF only and is typically 15 L. Based on this data the derived NOAEL (considering a lithium concentration of 1mmol/L and an ECF volume of 15 L) is 1.5 mg/kg bw/day. This NOAEL value can be considered as a conservative value as it is based on an bioavailable dose in humans after absorption and on a smaller volume than its actual distribution volume. Another way to calculate NOAEL oral for lithium is based as well on data taken from the routine long-term treatment of bipolar disorder. The lithium NOAEL oral is calculated from the administered oral dose for long-term treatment of bipolar disorder: 84 to 169 mg lithium / day (corresponding to the desired sustained concentrations of 0.5 -1 mmole lithium/L in blood/serum). Dividing the oral doses (84 to 169 mg lithium / day) to 70 kg, these values are obtained: 1.2 to 2.4 mg/kg bw/day. Using 60 kg, the values are 1.4 to 2.8 mg/kg bw/day, representing the optional NOAEL values for lithium for the oral route. As a worst-case value, a NOAEL repeated dose toxicity oral of 1.2 mg lithium/kg bw was chosen.</p> <p>Other Tier 3: No value is available at this time from these Tier 3 sources/databases: HEAST, NTP ROC, health and environmental agencies of California, Massachusetts, Minnesota, New Jersey, New York, and Texas, WHO (IARC), WHO (IPCS/INCHEM), Canada, The Netherlands (RIVM) and OECD HPV.</p>		
Inhalation Unit Risk Factor (IURF) (($\mu\text{g}/\text{m}^3$) ⁻¹)	--	NA	MDEQ, 2015	
IURF details	NA	<p>Carcinogen Weight-of-Evidence (WOE) Class: "data are inadequate for an assessment of human carcinogenic potential"</p> <p>Tier 1 and 2 Sources:</p> <p>IRIS: No IRIS file available at this time.</p>		Complete



	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
		PPRTV: Per PPRTV (6/12/2008), no value at this time. MRL: NA; MRLs are for non-cancer effects only Tier 3 Source: MDEQ: Per DEQ-CCD, no value 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	YES-oral Yes-inhalation, the RfD and RfC are based on reproductive-developmental effects. Oral Exposure Pathways- Single Exposure Inhalation Exposure Pathways- Full Term Exposure	MDEQ, 2015	
Developmental or Reproductive Toxicity Details	--	RfD Critical effect: adverse effects in several organs and systems and developmental effects, primarily involving the heart. RfC Critical effect: significant increase in neonate birth weight (macrosomia).		
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, 2015		
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		

	Part 201 Value	Updated Value	Source/Reference/ Date	Comments/Notes /Issues
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, 2004	
ABS _{gi} details		RAGS E (USEPA, 2004) Default Value		
Skin absorption efficiency value (AE _d)	---	0.01	MDEQ, 2015	
AE _d details				
Ingestion Absorption Efficiency (AE _i)		0.5	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)	440
Updated GSI value (µg/L)	440
Rule 57 Drinking Water Value (µg/L)	720

	Rule 57 Value (µg/L)	Verification Date
Human Non-cancer Values- Drinking water source (HNV-drink)	720	2/2006
Human Non-Cancer Values- Non-drinking water sources (HNV-Non-drink)	58,000	2/2006
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)	440	6/2008
Aquatic maximum value (AMV)	910	6/2008
Final Acute Value (FAV)	1,800	6/2008

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 ($\mu\text{g}/\text{kg}$)	400	MDEQ, 2015
Target Detection Limit – Water ($\mu\text{g}/\text{L}$)	10	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