

QCAT 2.0 Evaluation:

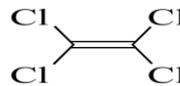
Author: Rolfe Parsloe
Title: Toxics Reduction Specialist
Organization: WA State Dept. Ecology
Date: 9/28/2015

Peer Review:

Reviewer: Alex Stone
Title: Chemist
Organization: WA Dept. of Ecology
Date: 5/5/2016

QCAT for Safer Chemicals Example Chemical Assessment Worksheet

Chemical Name: Tetrachloroethylene
CAS Registry Number: 127-18-4
Also Called: Perc; PERC; Ethylene, tetrachloro-
Identify Applications/Functional Uses: Dry cleaning solvent
Molecular Formula: C₂Cl₄
Molecular Weight: 165.82
Chemical Structure:



Hazard Summary Table:

Human Health Group 1 (HH1)					Human Health Group 2 (HH2)							Ecological			Fate		Physical	
C	M	R	D	E	AT	ST	N	SnS	SnR	IrS	IrE	AA	CA	E _o	P	B	Ex	F
H	M	M	M	M	M							vH			vH	L		

Note: Please see Appendix A for glossary of hazard endpoint acronyms.

Grades		
Initial	Data Gap	Final
F	NA	F

Although data was limited for some hazard endpoints, a level of concern could be assigned to perchloroethylene (PERC) for all nine QCAT hazard endpoints. Based upon this data, PERC was identified as a carcinogen due to listings by a number of authoritative bodies including the US NIH’s Report on Carcinogens, IARC’s identification as a probable carcinogen, appearance on the California EPA’s Prop 65 list as a carcinogen, etc. Using QCAT grading criteria, PERC meets the CMR (carcinogenic, mutagenic or reproductive toxicant) criteria (Grading Criteria F5) and is assigned an Initial Grade F. As no data gaps were identified and a data gap analysis is not required for any chemical assigned an Initial Grade F, PERC was assigned a Final Grade of F.

Human Health Effects – Group I

Carcinogenicity (C) Hazard Level (H, M, L or DG): H

Research Summary: Tetrachloroethylene appears on nine authoritative lists and sources such as the US NIH’s Report on Carcinogens, IARC’s identification as a probably carcinogen, appearance on the California EPA’s Prop 65 list as a carcinogen which equated to a high level of concern. Tetrachloroethylene was assigned a moderate level of concern by three additional authoritative sources. Based upon the determinations by organizations such as IARC, NIH and California EPA and the

QCAT 2.0 Evaluation:

Author: Rolfe Parsloe

Title: Toxics Reduction Specialist

Organization: WA State Dept. Ecology

Date: 9/28/2015

Peer Review:

Reviewer: Alex Stone

Title: Chemist

Organization: WA Dept. of Ecology

Date: 5/5/2016

preponderance of the organizations assigning a high level of concern, perchloroethylene was assigned a **HIGH** level of concern.

References:

Pharos:

High level of concern:

- **US Environmental Protection Agency** *Integrated Risk Information System Database (IRIS)* (2005) Likely to be carcinogenic to humans. This equates to a HIGH level of concern in the QCAT methodology.
- **International Agency for Research on Cancer, World Health Organization** *Monographs On the Evaluation of Carcinogenic Risks to Humans*, Group 2A: Agent is probably carcinogenic to humans. This equates to a HIGH level of concern in the QCAT methodology.
- **US Dept of Health & Human Services** *Report on Carcinogens* Reasonably Anticipated to be Human Carcinogen. This equates to a HIGH level of concern in the QCAT methodology.
- **State of California Environmental Protection Agency** *Chemicals Known to the State to Cause Cancer or Reproductive Toxicity - California Proposition 65 - Safe Drinking Water and Toxic Enforcement Act of 1986* Cancer. This equates to a HIGH level of concern in the QCAT methodology.
- **US Centers for Disease Control** *NIOSH Carcinogen List* Occupational carcinogen. This equates to a HIGH level of concern in the QCAT methodology.
- **New Zealand Environmental Protection Authority** *New Zealand HSNO Chemical Classifications*, 6.7A - Known or presumed human carcinogens. This equates to a HIGH level of concern in the QCAT methodology.
- **Government of Japan** *GHS Classifications* Carcinogenicity - Category 1B
- **US Environmental Protection Agency** *Risk Management Actions & TSCA Work Plans*, Probable human carcinogen - TSCA Criteria met. This equates to a HIGH level of concern in the QCAT methodology.
- **European Commission** *Classification, Labelling and Packaging Regulation (CLP) - Classification and Labelling Inventory – CMRs* Carcinogen Category 2 - Suspected human carcinogen. This equates to a HIGH level of concern in the QCAT methodology

Moderate level of concern:

- **European Commission** *Substances with EU Risk & Safety Phrases (Commission Directive 67-548-EEC)* R40: Limited evidence of a carcinogenic effect. This equates to a MODERATE level of concern in the QCAT methodology.
- **European Commission** *Regulation on the Classification, Labelling and Packaging of Substances and Mixtures (CLP) Annex 6 Table 3-1 - GHS Hazard code criteria H351* Suspected of causing cancer. This equates to a MODERATE level of concern in the QCAT methodology.

QCAT 2.0 Evaluation:

Author: Rolfe Parsloe

Title: Toxics Reduction Specialist

Organization: WA State Dept. Ecology

Date: 9/28/2015

Peer Review:

Reviewer: Alex Stone

Title: Chemist

Organization: WA Dept. of Ecology

Date: 5/5/2016

- **MAK Commission of Germany (Deutsche Forschungsgemeinschaft)** *List of Substances with MAK & BAT Values & Categories* Carcinogen Group 3B - Evidence of carcinogenic effects but not sufficient for classification. This equates to a MODERATE level of concern in the QCAT methodology.

Mutagenicity and Genotoxicity (M) Hazard Level (H, M, L or DG): M

Research Summary: Data on mutagenicity and genotoxicity was limited. The HSDB had numerous references to studies (more than 10) that reported no evidence of mutagenicity or genotoxicity of PERC in mice. Two HSDB studies that did indicate genotoxicity are summarized below. Based upon this information, a **MODERATE** level of concern was assigned for mutagenicity and genotoxicity.

HSDB:

Moderate level of concern:

- HSDB: /GENOTOXICITY/ The clastogenicity of **tetrachloroethylene** (tetra) was detected by means of the micronucleus assay using hepatocytes and reticulocytes from ddY male mice, to understand its effects in upon hepatocellular carcinomas in mice. The frequency of micronucleated hepatocytes of mice that received a single injection of tetra after partial hepatectomy increased to levels that were significantly higher than those of controls treated with solvent. However, the micronucleus assay using peripheral blood reticulocytes from ddY male mice, revealed that tetra did not induce to a statistically significant increase in micronucleus frequency. These results suggested that tetra metabolites have a clastogenic effect in vivo upon mouse liver but not upon bone marrow cells.
[\[Murakami k, Horikawa K; Chemosphere 31 \(7\): 3733-9 \(1995\)\] **PEER REVIEWED**](#)
- /GENOTOXICITY/ Induction of DNA damage in the liver and kidney of male CD1 mice was studied by means of the alkaline Comet assay after oral administration of **tetrachloroethylene** at the doses of 1000 and 2000 mg/kg/day. A statistically significant dose-related increase in tail intensity was established in hepatocytes, indicating that **tetrachloroethylene** induced DNA damage in the liver. No effect on DNA damage was observed in the kidney. The results are in agreement with carcinogenicity data in mice, in which **tetrachloroethylene** induced tumors in the liver but not in the kidney, and support that a genotoxic mode of action might be involved in liver carcinogenicity in mice.
[\[Cederberg H et al; Mutagenesis 25 \(2\): 133-8 \(2010\)\] **PEER REVIEWED** PubMed Abstract](#)

Reproductive Toxicity (R) Hazard Level (H, M, L or DG): M

Research Summary: Data for reproductive toxicity was limited. An assessment by the Japanese METI/MOE assigned a classification of Category 2 to tetrachloroethylene. This equates to a

QCAT 2.0 Evaluation:

Author: Rolfe Parsloe

Title: Toxics Reduction Specialist

Organization: WA State Dept. Ecology

Date: 9/28/2015

Peer Review:

Reviewer: Alex Stone

Title: Chemist

Organization: WA Dept. of Ecology

Date: 5/5/2016

MODERATE level of concern using the QCAT criteria and was used to assign the same level of reproductive concern for tetrachloroethylene.

References:

Japan/METI/MOE:

- GS Classifications, Toxic to reproduction, Category 2.

Development Tox. including Developmental Neurotoxicity (D) Hazard Level (H, M, L or DG): H

Research Summary: Data on developmental toxicity is limited. Tetrachloroethylene is identified by one authoritative source, Grandjean and Landrigan, as a neurodevelopmental toxicant. Based upon this limited information, tetrachloroethylene was assigned a **HIGH** level of concern.

References:

Grandjean & Landrigan, Neurobehavioral effects of developmental toxicity, Lancet Neurol, 2014, 13:330-38.

- Identified as a developmental neurotoxicants.

Endocrine Disruption (E) Hazard Level (H, M, L or DG): M

Research Summary: Two sources of data were identified. One, the European Commission identified a moderate level of concern. The second, TEDX, identified the chemical as a potential endocrine disruptor and added it to the list of chemicals for more review. As the TEDX is more of a screening list, greater emphasis was placed upon the authoritative EC determination; therefore, a **MODERATE** level of concern was assigned to tetrachloroethylene for endocrine disruption.

References:

European Commission:

- *EU Community Strategy for Endocrine Disruptors - Priority List Category 2* - In vitro evidence of biological activity related to endocrine disruption. This equates to a MODERATE level of concern using the QCAT criteria.

The Endocrine Disruption Exchange (TEDX):

- *TEDX List of Potential Endocrine Disruptors* Potential Endocrine Disruptor. This equates to a HIGH level of concern using the QCAT criteria.

Human Health Effects – Group II

Acute Mammalian Toxicity (AT) Hazard Level (VH, H, M, L or DG):

QCAT 2.0 Evaluation:

Author: Rolfe Parsloe

Title: Toxics Reduction Specialist

Organization: WA State Dept. Ecology

Date: 9/28/2015

Peer Review:

Reviewer: Alex Stone

Title: Chemist

Organization: WA Dept. of Ecology

Date: 5/5/2016

Research Summary: Based upon data identified in HSDB, numerous inhalation rat and mouse data and one oral rat study identify a moderate level of concern for acute mammalian toxicity using QCAT chemical ranking criteria. One study reported in both HSDB and RTECs identified an oral rat LD₅₀ of 2,629 mg/kg which equates to a low level of concern using QCAT chemical ranking criteria. As there were numerous inhalation and an additional oral rat study that identified a moderate level of concern and only one study that identified a low level of concern, PERC was assigned a **MODERATE** level of concern for acute mammalian toxicity.

HSDB:

Moderate level of concern:

- LD₅₀ Rat oral 320 mg/kg bw
[European Commission, ESIS; IUCLID Dataset, Tetrachloroethylene (127-18-4) p. 83 (2000 CD-ROM edition). Available from, as of September 23, 2010: <http://esis.jrc.ec.europa.eu/> **PEER REVIEWED**
- LC₅₀ Rat inhalation 4,100 ppm/6 hr
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: <http://monographs.iarc.fr/ENG/Classification/index.php> p. V63 191 (1995)] **PEER REVIEWED**
- LC₅₀ Rat inhalation 5,000 ppm/8 hr
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: <http://monographs.iarc.fr/ENG/Classification/index.php> p. V63 191 (1995)] **PEER REVIEWED**
- LC₅₀ Mouse inhalation 5,200 ppm/4 hr
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: <http://monographs.iarc.fr/ENG/Classification/index.php> p. V63 191 (1995)] **PEER REVIEWED**
- LC₅₀ Mouse inhalation 2,978 ppm/6 hr
[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at:

QCAT 2.0 Evaluation:

Author: Rolfe Parsloe

Title: Toxics Reduction Specialist

Organization: WA State Dept. Ecology

Date: 9/28/2015

Peer Review:

Reviewer: Alex Stone

Title: Chemist

Organization: WA Dept. of Ecology

Date: 5/5/2016

<http://monographs.iarc.fr/ENG/Classification/index.php> p. V63 191 (1995)] ****PEER REVIEWED****

- LC₅₀ Rat inhalation 4,000 ppm/ 4hr
[American Conference of Governmental Industrial Hygienists. Documentation of the TLV's and BEI's with Other World Wide Occupational Exposure Values. CD-ROM Cincinnati, OH 45240-4148 2010.] ****PEER REVIEWED****
- LC₅₀ Rat Inhalation 2,445 ppm/ 4 hr
[National Industrial Chemicals Notification and Assessment Scheme; Tetrachloroethylene (127-18-4) Assessment Report No. 15 p. 46 (June 2001). Available from as of September 29, 2010:<http://www.nicnas.gov.au/Publications/CAR/PEC.asp> ****PEER REVIEWED****

Low level of concern

- LD₅₀ Rat oral 2,629 mg/kg
[Lewis, R.J. Sr. (ed) Sax's Dangerous Properties of Industrial Materials. 11th Edition. Wiley-Interscience, Wiley & Sons, Inc. Hoboken, NJ. 2004., p. 2857] ****PEER REVIEWED****

RTECS:

Low level of concern:

LD₅₀ - Lethal dose, 50 percent kill Oral Rodent - rat 2,629 mg/kg

Environmental Health Effects

Acute Aquatic (AA) Toxicity Hazard Level: (vH, H, M, L or DG): vH

Research Summary: Based upon data identified in Pharos, two sources identified a very high level of concern for acute aquatic toxicity using QCAT chemical ranking criteria. New Zealand had identified the chemical as very ecotoxic in the aquatic environment (9.1A) and Japan NITE as a category 1 aquatic environment toxicant. Pharos also identified a third source. The European Union assigned PERC a risk phrase of R51, toxic to aquatic organisms. This equates to a high level of concern using QCAT chemical ranking criteria. As two of the three sources indicated PERC is very highly toxic to the aquatic environment PERC was assigned a **VERY HIGH** level of concern for acute aquatic toxicity.

References:

Pharos:

Very high level of concern:

- New Zealand – GHS – 9.1A (algal) – Very ecotoxic in the aquatic environment
- Japan – GHS – Hazardous to the aquatic environment (acute) – Category 1

QCAT 2.0 Evaluation:

Author: Rolfe Parsloe

Title: Toxics Reduction Specialist

Organization: WA State Dept. Ecology

Date: 9/28/2015

Peer Review:

Reviewer: Alex Stone

Title: Chemist

Organization: WA Dept. of Ecology

Date: 5/5/2016

High level of concern:

- EU – Risk Phrases: R51, Toxic to aquatic organisms

Environmental Fate

Persistence (P) Hazard Level: (vH, H, M, L, vL or DG): vH

Research Summary: PERC is identified by Environment Canada as persistent which equates to a high level of concern using the QCAT chemical ranking criteria. Data within the HSDB suggests that PERC will degrade in air and water with a half-life of 96 days and 9 months, respectively. Both of these values equate to a very high level of concern using QCAT chemical ranking criteria. Lastly, EPA's PBT Profiler assigns a half-life in water and air, the two media to which 93% of PERC is expected to be found, of 60 and 96 days for a high and very high level of concern, respectively. As several data sources indicate a very high level of concern, PERC is assigned a **VERY HIGH** for persistence.

References:

Pharos:

- Environment Canada-Domestic Substances List: Persistent

HSDB (emphasis added):

- If released to air, a vapor pressure of 18.5 mm Hg at 25 deg C indicates tetrachloroethylene will exist solely as a vapor in the atmosphere. Vapor-phase tetrachloroethylene will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; **the half-life for this reaction in air is estimated to be 96 days.** Hydrolysis is not expected to be an important environmental fate process based on a **hydrolysis half-life of 9 months.** (SRC)

PBT Profiler:

- EPA's PBT Profiler Provided the following results for PERC:

Media	Half-life (days)	% in each medium
- Water	60	47
- Soil	120	7
- Sediment	540	0
- Air	96	46

Bioaccumulation (B) Potential Hazard Level: (vH, H, M, L, vL or DG): L

Research Summary: Three sources identified that PERC had either a very low or low bioaccumulation potential. The HSDB identified BCF values ranging between 26 and 115 which equates to a very low to low level of concern, respectively, using QCAT chemical ranking criteria. The PBT Profiler assigned a BCF of 81 which also equates to a very low level of concern. The Canadian DSL indicated PERC was

QCAT 2.0 Evaluation:

Author: Rolfe Parsloe

Title: Toxics Reduction Specialist

Organization: WA State Dept. Ecology

Date: 9/28/2015

Peer Review:

Reviewer: Alex Stone

Title: Chemist

Organization: WA Dept. of Ecology

Date: 5/5/2016

not bioaccumulative. Based upon these results, PERC was assigned a **LOW** level of concern for bioaccumulation.

References:

HSDB (emphasis added):

- ... Measured **BCF values of 26-115** in fish indicate that bioconcentration in aquatic organisms is low to high. (SRC)

PBT Profiler:

- EPA's PBT Profiler indicated a BCF = 81 for PERC.

Canadian DSL listing:

- Not bioaccumulative.

OCAT 2.0 Evaluation:

Author: Rolfe Parsloe

Title: Toxics Reduction Specialist

Organization: WA State Dept. Ecology

Date: 9/28/2015

Peer Review:

Reviewer: Alex Stone

Title: Chemist

Organization: WA Dept. of Ecology

Date: 5/5/2016

Appendix A:

AA	=	Acute Aquatic Toxicity
AT	=	Acute Mammalian Toxicity
B	=	Bioaccumulation
C	=	Carcinogenicity
CA	=	Chronic Aquatic Toxicity
D	=	Developmental Toxicity (incl. Developmental Neurotoxicity)
E	=	Endocrine Activity
Eo	=	Other Ecotoxicity studies
F	=	Flammability
HH1	=	Human Health Group 1 (C, M, R, D, E)
HH2	=	Human Health Group 2 (AT)
IrE	=	Irritation-Eye
IrS	=	Irritation-Skin
M	=	Mutagenicity & Genotoxicity
N	=	Neurotoxicity
P	=	Persistence
R	=	Reproductive Toxicity
Rd	=	Repeat dose
Rx	=	Reactivity
Sd	=	Single dose
SnR	=	Sensitization-Respiratory
SnS	=	Sensitization-Skin
ST	=	Systemic Toxicity & Organ Effects (incl. Immunotoxicity)