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Provisional Peer-Reviewed Toxicity Values for

2,2-Dichloropropane
(CASRN 594-20-7)

Superfund Health Risk Technical Support Center
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Questions regarding the contents of this document may be directed to the U.S. EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center (513-569-7300).

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COMMONLY USED ABBREVIATIONS

BMC	benchmark concentration
BMCL	benchmark concentration lower bound 95% confidence interval
BMD	benchmark dose
BMDL	benchmark dose lower bound 95% confidence interval
HEC	human equivalent concentration
HED	human equivalent dose
IUR	inhalation unit risk
LOAEL	lowest-observed-adverse-effect level
$LOAEL_{ADJ}$	LOAEL adjusted to continuous exposure duration
$LOAEL_{HEC}$	LOAEL adjusted for dosimetric differences across species to a human
NOAEL	no-observed-adverse-effect level
$NOAEL_{ADJ}$	NOAEL adjusted to continuous exposure duration
$NOAEL_{HEC}$	NOAEL adjusted for dosimetric differences across species to a human
NOEL	no-observed-effect level
OSF	oral slope factor
p-IUR	provisional inhalation unit risk
POD	point of departure
p-OSF	provisional oral slope factor
p-RfC	provisional reference concentration (inhalation)
p-RfD	provisional reference dose (oral)
RfC	reference concentration (inhalation)
RfD	reference dose (oral)
UF	uncertainty factor
UF_A	animal-to-human uncertainty factor
UF_C	composite uncertainty factor
UF_D	incomplete-to-complete database uncertainty factor
UF_H	interhuman uncertainty factor
UF_L	LOAEL-to-NOAEL uncertainty factor
UF_S	subchronic-to-chronic uncertainty factor
WOE	weight of evidence

PROVISIONAL PEER-REVIEWED TOXICITY VALUES
2,2-DICHLOROPROPANE (CASRN 594-20-7)

BACKGROUND

A Provisional Peer-Reviewed Toxicity Value (PPRTV) is defined as a toxicity value derived for use in the Superfund Program. PPRTVs are derived after a review of the relevant scientific literature using established Agency guidance on human health toxicity value derivations. All PPRTV assessments receive internal review by a standing panel of National Center for Environment Assessment (NCEA) scientists and an independent external peer review by three scientific experts.

The purpose of this document is to provide support for the hazard and dose-response assessment pertaining to chronic and subchronic exposures to substances of concern, to present the major conclusions reached in the hazard identification and derivation of the PPRTVs, and to characterize the overall confidence in these conclusions and toxicity values. It is not intended to be a comprehensive treatise on the chemical or toxicological nature of this substance.

The PPRTV review process provides needed toxicity values in a quick turnaround timeframe while maintaining scientific quality. PPRTV assessments are updated approximately on a 5-year cycle for new data or methodologies that might impact the toxicity values or characterization of potential for adverse human health effects and are revised as appropriate. It is important to utilize the PPRTV database (http://hhpprtv.ornl.gov) to obtain the current information available. When a final Integrated Risk Information System (IRIS) assessment is made publicly available on the Internet (www.epa.gov/iris), the respective PPRTVs are removed from the database.

DISCLAIMERS

The PPRTV document provides toxicity values and information about the adverse effects of the chemical and the evidence on which the value is based, including the strengths and limitations of the data. All users are advised to review the information provided in this document to ensure that the PPRTV used is appropriate for the types of exposures and circumstances at the site in question and the risk management decision that would be supported by the risk assessment.

Other U.S. Environmental Protection Agency (EPA) programs or external parties who may choose to use PPRTVs are advised that Superfund resources will not generally be used to respond to challenges, if any, of PPRTVs used in a context outside of the Superfund program.

QUESTIONS REGARDING PPRTVS

Questions regarding the contents and appropriate use of this PPRTV assessment should be directed to the EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center (513-569-7300).

INTRODUCTION

2,2-Dichloropropane (2,2-DCP; synonyms: acetone dichloride; isopropylidene chloride; dichlorodimethylmethane; dimethyldichloromethane) CAS No. 594-20-7, is a chloroalkane. Chloroalkanes are used as industrial solvents, for degreasing of metals, as fumigants or substitutes for terpenes, in dry cleaning, for soil sterilization, and as weed killers (Freitag et al., 1994). Based on its high vapor pressure, 2,2-DCP is volatile. A table of physicochemical properties for 2,2-DCP is provided below (see Table 1). The molecular formula of 2,2-DCP is $C_3H_6C_{12}$ and the chemical structure is shown in Figure 1.

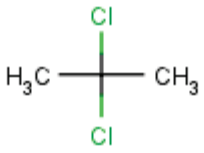

Figure 1. Structure of 2,2-DCP (NLM, 2011)

Table 1. Physicochemical Properties of 2,2-DCP (CASRN 594-20-7)[a]

Property (unit)	Value
Boiling point (ºC)	69.3
Melting point (ºC)	−35.0
Density (g/mL) (25ºC)	1.082
Vapor pressure (atm at 25ºC)	1.78×10^{-1}
pH (unitless)	ND
Solubility in water (mg/L at 25ºC)	391 (slightly soluble in water)
Relative vapor density (air = 1)	ND
Molecular weight (g/mol)	112.99

[a]ChemIDplusLite (2011); U.S. EPA (2007); Wolfram Mathematica (2011).
ND = no data.

No reference dose (RfD), reference concentration (RfC), or cancer assessment for 2,2,-DCP is included in the U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS) (U.S. EPA, 2011b) or on the Drinking Water Standards and Health Advisories List (U.S. EPA, 2011a). No RfD or RfC values are reported in the Health Effects Assessment Summary Tables (HEAST) (U.S. EPA, 2003). The Chemical Assessments and Related Activities (CARA) database does not include a Health and Environmental Effects Profile (HEEP) for 2,2,-DCP (U.S. EPA, 1994). The toxicity of 2,2,-DCP has not been reviewed by the Agency for Toxic Substances and Disease Registry (ATSDR, 2011) or the World Health Organization (WHO, 2011). The California Environmental Protection Agency (Cal EPA, 2011, 2008) has not derived toxicity values for exposure to 2,2-DCP. No occupational exposure limits for 2,2,-DCP have been derived or recommended by the American Conference of Governmental Industrial Hygienists (ACGIH, 2011), the National Institute for Occupational Safety and Health (NIOSH, 2007), or the Occupational Safety and Health Administration (OSHA, 2006).

The HEAST (U.S. EPA, 2003) does not report any values. The International Agency for Research on Cancer (IARC, 2011) has not reviewed the carcinogenic potential of 2,2,-DCP. 2,2,-DCP is not included in the *12th Report on Carcinogens* (NTP, 2011). Cal EPA (2009) has not prepared a quantitative estimate of the carcinogenic potential of 2,2,-DCP.

Literature searches were conducted on sources published from 1900 through May 2012 for studies relevant to the derivation of provisional toxicity values for 2,2-DCP, CAS No. 594-20-7. The following databases were searched by chemical name, synonyms, or CAS No.: ACGIH, ANEUPL, ATSDR, BIOSIS, Cal EPA, CCRIS, CDAT, ChemIDplus, CIS, CRISP, DART, EMIC, EPIDEM, ETICBACK, FEDRIP, GENE-TOX, HAPAB, HERO, HMTC, HSDB, IARC, INCHEM IPCS, IPA, ITER, IUCLID, LactMed, NIOSH, NTIS, NTP, OSHA, OPP/RED, PESTAB, PPBIB, PPRTV, PubMed (toxicology subset), RISKLINE, RTECS, TOXLINE, TRI, U.S. EPA IRIS, U.S. EPA HEAST, U.S. EPA HEEP, U.S. EPA OW, and U.S. EPA TSCATS/TSCATS2. The following databases were searched for toxicity values or exposure limits: ACGIH, ATSDR, Cal EPA, U.S. EPA IRIS, U.S. EPA HEAST, U.S. EPA HEEP, U.S. EPA OW, U.S. EPA TSCATS/TSCATS2, NIOSH, NTP, OSHA, and RTECS.

REVIEW OF POTENTIALLY RELEVANT DATA (CANCER AND NONCANCER)

No information is available regarding repeat-dose oral or inhalation exposure of humans or animals to 2,2-DCP. An in vitro study by Tornero-Velez et al. (2004) investigated the metabolism rates of 2,2-DCP and 1,3-DCP in rat liver microsomes and cytosol based on P450 and GST pathways in clearance and activation using gas chromatography. No metabolism of 2,2-DCP via a GSH-dependent conjugation pathway was observed, and the study authors observed only a minor level of clearance via the P450 pathway (7×10^{-4} L/h/mg microsomal protein). 2,2-DCP was not mutagenic in various strains of *Salmonella*, including those containing GSTT1-1, indicating that GSTT1-1 does not produce mutagenic metabolites (Torne-Velez et al., 2004). Frietag et al. (1994) reported structural configurations and potential influence on the toxicity of chloroalkanes including 2,2-DCP; however, the available data are insufficient to perform a toxicity assessment of 2,2-DCP. Additionally, a preliminary structure-activity relationship (SAR) analysis for this chemical did not suggest a reliable surrogate chemical at this time.

DERIVATION OF PROVISIONAL VALUES

Limitations in the available data preclude development of both cancer and noncancer toxicity values.

CANCER WEIGHT-OF-EVIDENCE (WOE) DESCRIPTOR

Limitations in the available data preclude development of a WOE descriptor.

MODE-OF-ACTION (MOA) DISCUSSION

Limitations in the available data preclude determination of a MOA discussion.

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