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Provisional Peer-Reviewed Toxicity Values for

1,1,2-Trichloropropane
(CASRN 598-77-6)

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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).

TABLE OF CONTENTS

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 FOR 1,1,2-TRICHLOROPROPANE (CASRN 598-77-6)

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 (http://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

1,1,2-Trichloropropane, CAS No. 598-77-6, is a chlorinated hydrocarbon that is a liquid at room temperature. 1,1,2-Trichloropropane is one of the trichloropropane (TCP) isomers. TCPs are by-products of synthetic processes used to manufacturer propylene chlorohydrins and other propylene derivatives. The molecular formula is $C_3H_5Cl_3$, and the structure is shown in Figure 1. Table 1 provides a list of physicochemical properties.

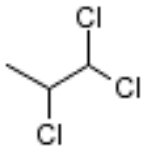

Figure 1. Chemical Structure of 1,1,2-Trichloropropane

Table 1. Physicochemical Properties of 1,1,2-Trichloropropane (CASRN 598-77-6)[a]

Property (unit)	Value
Boiling point (ºC at 760 mmHg)	132
Melting point (ºC)	No data
Density (g/mL at 25°C)	1.305
Vapor pressure (mmHg at 25ºC)	3.1
pH (unitless)	No data
Solubility in water (mg/L at 25ºC)	1900
Relative vapor density (air = 1)	No data
Molecular weight (g/mol)	147.43

[a]ChemID (2010).

The United States Environmental Protection Agency (U.S. EPA) Integrated Risk Information System (IRIS) database (U.S. EPA, 1988a) provides an oral reference dose (RfD) of 5×10^{-3} mg/kg-day based on an oral subchronic study (Villeneuve et al., 1985) in rats. IRIS does not report a chronic inhalation reference concentration (RfC) or cancer assessment (U.S. EPA, 1988a). No RfD, RfC, or cancer assessment for 1,1,2-trichloropropane is included on the Drinking Water Standards and Health Advisories List (U.S. EPA, 2009a). A subchronic RfD value of 5×10^{-3} mg/kg-day is included in the Health Effects Assessment Summary Tables (HEAST) (U.S. EPA, 2011), which was derived from the IRIS RfD, but no RfC is derived. The Chemical Assessments and Related Activities (CARA) list includes a Health and Environmental

Effects Profile (HEEP) for trichloropropanes that, due to inadequate noncancer data, derives no toxicity value for 1,1,2-trichloropropane (U.S. EPA, 1994). The toxicity of 1,1,2-trichloropropane 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 (CalEPA, 2008, 2009) has not derived toxicity values for exposure to 1,1,2-trichloropropane. No occupational exposure limits for 1,1,2-trichloropropane have been recommended or derived by the American Conference of Governmental Industrial Hygienists (ACGIH, 2011), the National Institute of Occupational Safety and Health (NIOSH, 2010), or the Occupational Safety and Health Administration (OSHA, 2006).

The HEAST (U.S. EPA, 2011) does not report any cancer toxicity values or an oral slope factor (OSF) for 1,1,2-trichloropropane. The International Agency for Research on Cancer (IARC, 2011) has not reviewed the carcinogenic potential of 1,1,2-trichloropropane. 1,1,2-Trichloropropane is not included in the *12th Report on Carcinogens* (NTP, 2011). CalEPA (2008) has not derived a quantitative estimate of carcinogenic potential for 1,1,2-trichloropropane.

Literature searches were conducted on sources published from 1900 through August 3, 2011 for studies relevant to the derivation of provisional toxicity values for 1,1,2-trichloropropane, CAS No. 598-77-6. Searches were conducted using U.S. EPA's Health and Environmental Research Online (HERO) database of scientific literature. HERO searches the following databases: AGRICOLA; American Chemical Society; BioOne; Cochrane Library; DOE: Energy Information Administration, Information Bridge, and Energy Citations Database; EBSCO: Academic Search Complete; GeoRef Preview; GPO: Government Printing Office; Informaworld; IngentaConnect; J-STAGE: Japan Science & Technology; JSTOR: Mathematics & Statistics and Life Sciences; NSCEP/NEPIS (EPA publications available through the National Service Center for Environmental Publications [NSCEP] and National Environmental Publications Internet Site [NEPIS] database); PubMed: MEDLINE and CANCERLIT databases; SAGE; Science Direct; Scirus; Scitopia; SpringerLink; TOXNET (Toxicology Data Network): ANEUPL, CCRIS, ChemIDplus, CIS, CRISP, DART, EMIC, EPIDEM, ETICBACK, FEDRIP, GENE-TOX, HAPAB, HEEP, HMTC, HSDB, IRIS, ITER, LactMed, Multi-Database Search, NIOSH, NTIS, PESTAB, PPBIB, RISKLINE, TRI, and TSCATS; Virtual Health Library; Web of Science (searches Current Content database among others); World Health Organization; and Worldwide Science. The following databases outside of HERO were searched for relevant health information: ACGIH, ATSDR, CalEPA, 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)

Table 2 provides an overview of the relevant database for 1,1,2-trichloropropane and includes all potentially relevant repeated short-term-, subchronic-, and chronic-duration studies. Principal studies are identified. The phrase, "statistical significance" used throughout the document, indicates a p-value of <0.05.

Table 2. Summary of Potentially Relevant Data for 1,1,2-Trichloropropane (CASRN 598-77-6)

Category	Number Of Male/Female, Strain, Species, Study Type, Study Duration	Dosimetry[a]	Critical Effects	NOAEL[a]	BMDL/ BMCL[a]	LOAEL[a]	Reference (Comments)	Notes[b]
Human								
1. Oral (mg/kg-d)								
Subchronic	No data							
Chronic	No data							
Developmental	No data							
Reproductive	No data							
Carcinogenicity	No data							
2. Inhalation (mg/m^3)								
Subchronic	No data							
Chronic	No data							
Developmental	No data							
Reproductive	No data							
Carcinogenicity	No data							
Animal								
1. Oral (mg/kg-d)[a]								
Subchronic	**10/10, Sprague-Dawley rat, drinking water, 7 d/wk, 90 d**	**Males: 0, 0.14, 1.4, 14, and 139 (Adjusted)** **Females: 0, 0.15, 1.5, 15, and 152 (Adjusted)**	**Males: mild lesions in liver, kidney, and thyroid at 139 mg/kg-d** **Females: mild lesions in liver, kidney, and thyroid at 152 mg/kg-d**	**14**	**NDr**	**139**	**Villeneuve et al. (1985)**	**IRIS, PS, PR**
Chronic	No data							
Developmental	No data							

Table 2. Summary of Potentially Relevant Data for 1,1,2-Trichloropropane (CASRN 598-77-6)								
Category	**Number Of Male/Female, Strain, Species, Study Type, Study Duration**	**Dosimetry[a]**	**Critical Effects**	**NOAEL[a]**	**BMDL/ BMCL[a]**	**LOAEL[a]**	**Reference (Comments)**	**Notes[b]**
Reproductive	No data							
Carcinogenicity	No data							
2. Inhalation (mg/m^3)								
Subchronic	No data							
Chronic	No data							
Developmental	No data							
Reproductive	No data							
Carcinogenicity	No data							

[a]Dosimetry: NOAEL and LOAEL values from long-term exposure (4 weeks and longer) are converted from a discontinuous to a continuous (weekly) exposure, e.g., NOAELadj = NOAEL × Drinking Water per Day × (1 ÷ Body Weight) × (Days Dosed ÷ Total Days) unless otherwise indicated.
[b]IRIS = Utilized by IRIS, date of last update; NA = not applicable; PS = principal study, PR = Peer Reviewed.

NDr = Not determinable.

HUMAN STUDIES

Oral Exposures

The effects of oral exposure of humans to 1,1,2-trichloropropane have not been evaluated in subchronic-duration, chronic-duration, developmental, reproductive, or carcinogenicity studies.

Inhalation Exposures

The effects of inhalation exposure of humans to 1,1,2-trichloropropane have not been evaluated in subchronic-duration, chronic-duration, developmental, reproductive, or carcinogenicity studies.

ANIMAL STUDIES

Oral Exposures

The effects of oral exposure of animals to 1,1,2-trichloropropane have been evaluated in one subchronic study (Villeneuve et al., 1985). No short-term, chronic, developmental, reproductive, or other studies were identified.

Short-Term Studies

No short-term studies were identified.

Subchronic Studies

The study by Villeneuve et al. (1985) is selected as the principal study for the derivation of the subchronic p-RfD. In a peer-reviewed study, Villeneuve et al. (1985) administered 1-, 10-, 100-, or 1000-mg/L 1,1,2-trichloropropane (Columbia Organic Chemicals, Columbia, SC; purity >99%; solubilized in 0.5% Emulphor) in drinking water to young adult Sprague-Dawley rats (10/sex/treatment) for 90 days. Additionally, two control groups were used, one using tap water alone, while the other control group was given tap water with 0.5% Emulphor. Because body weights and water intake were not reported for 1,1,2-trichloropropane-dosed animals, adjusted daily doses are calculated as 0, 0.14, 1.4, 14, and 139 mg/kg-day for males and 0, 0.15, 1.5, 15, and 152 mg/kg-day for females using default values for body weight (0.267 and 0.204 kg for males and females, respectively) and drinking water consumption rate (0.037 and 0.031 L/day for males and females, respectively) (U.S. EPA, 1988b). Animals weighed between 60−70 g at study initiation. Food and water were provided ad libitum. Animals were examined for clinical signs of toxicity daily. Body-weight changes and water intake were also monitored throughout the study. GLP compliance was not reported by the study authors.

At the end of treatment, animals were sacrificed, and the brain, liver, kidney, heart, and spleen were weighed and histologically examined (Villeneuve et al., 1985). Hematological analysis (hemoglobin, packed cell volume, mean corpuscular hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin concentration, total erythrocytes, and total and differential counts of leukocytes) was conducted following sacrifice. Serum biochemical analysis conducted following sacrifice included measurement of sodium, potassium, inorganic phosphorus, total protein, calcium, cholesterol, glutamic oxaloacetic transaminase, total bilirubin, alkaline phosphatase, glucose, uric acid, lactate dehydrogenase, and serum sorbitol dehydrogenase activity. Hepatic mixed function oxidase activities (aniline hydroxylase, aminopyrine demethylase, and ethoxyresorufin deethylase) were measured as indicators of liver function. The study authors performed statistical analysis using one-way analysis of variance

followed by Duncan's Multiple Range Test to determine significant differences ($p \leq 0.05$) between treated and control groups.

One female from the 15-mg/kg-day dose group and one male from the 139-mg/kg-day group died during the study, but the cause of death was not determined (Villeneuve et al., 1985). However, the study authors did not consider these deaths treatment-related. There were no statistically significant differences in body-weight gain, water intake, or absolute organ weights in any of the treatment or control groups (quantitative data not provided). Relative liver weight was statistically significantly increased in males treated with 139 mg/kg-day (reportedly, 4% of body weight compared to 3.7% in both the vehicle and water controls; values for the other dose groups are not provided). In high-dose females (152 mg/kg-day), serum cholesterol levels were statistically significantly increased compared to both vehicle (135%) and water controls (139%) (96 nmol HCHO/mg protein/hour compared to 71 in the vehicle and 69 in the water controls; values for the other dose groups were not provided). The study authors reported no other dose-related effects on clinical, organ weight, biochemical, hematological, or hepatic mixed function oxidase activities (quantitative data not provided).

Villeneuve et al. (1985) described histological effects in the liver, kidneys, and thyroid of treated animals. High-dose males (139 mg/kg-day) and females (152 mg/kg-day) exhibited changes in the liver described as "mild but significant" by the study authors. These changes included anisokaryosis, accentuated zonation, and occasional fatty vacuolation (quantitative data not provided). Mild changes in kidney histopathology were also noted at the high dose in both sexes of rats and included eosinophilic inclusions, pyknosis, nuclear displacement, fine glomerular adhesions, interstitial reactions, and histologic proteinuria (quantitative data not provided). Mild thyroid changes in the high-dose groups of both sexes included angular collapse of some follicles, reduction in colloid density, and increased epithelial height (quantitative data not provided). The study authors reported that these effects were more prevalent and more severe in treated males as compared to treated females (quantitative data not provided). No other histological effects were described by the study authors.

Based on histological lesions reported in the liver, kidneys, and thyroid of high-dose males and females, with the males acknowledged by the study authors as the more sensitive sex, a LOAEL of 139 mg/kg-day is identified, with a corresponding NOAEL of 14 mg/kg-day.

Chronic Studies
No chronic studies were identified.

Developmental Studies
No developmental toxicity studies were identified in the literature.

Reproductive Studies
No reproductive toxicity studies were identified.

Other Studies
No other toxicity studies on 1,1,2-trichloropropane were identified.

Inhalation Exposures

No inhalation exposure studies were identified.

OTHER DATA (ACUTE STUDIES, OTHER EXAMINATIONS)

No studies were identified that examined the genotoxic potential of 1,1,2-trichloropropane in vitro or in vivo. One acute dermal toxicity study, two acute inhalation toxicity studies, and one acute oral toxicity study that examined the effects of 1,1,2-trichloropropane were identified (Hazleton Labs, 1992; Smyth et al., 1954). These studies are summarized in Table 3 and discussed further below.

Table 3. Other 1,1,2-Trichloropropane (CASRN 598-77-6) Studies

Test	Materials and Methods	Results	Conclusions	References
Carcinogenicity (exposures other than oral or inhalation)	No data			
Acute studies	5 male Carworth-Wistar rats/dose, gavage exposure followed by 14-d observation period LD_{50} calculated using the method of Thompson (1947) using the tables of Weil (1952)	LD_{50} 1.23 g/kg (0.94−1.62)[a]	Death following exposure (mechanism unreported)	Smyth et al. (1954)
Acute studies	Sprague-Dawley Rat (6 males/6 females), acute inhalation, 6 hr exposure; 3500 ppm (21,000 mg/m^3)	100% mortality during the 6-hr exposure apparently caused by central nervous system depression; ataxia and incoordination; congested lungs, liver, and kidneys; poorly differentiated kidneys and purple lungs observed in males; pale kidneys observed in 1/6 females	Death, possibly from central nervous system depression, following exposure	Hazleton Labs (1992; unpublished)
Acute studies	6 male albino rats, 4 hr inhalation exposure followed by a 14 d observation period; 2000 ppm (12,000 mg/m^3)	3/6 rats died within the 14 d following a 4 hr inhalation exposure to 12,000 mg/m^3	Death following exposure (mechanism unreported)	Smyth et al. (1954)
Acute studies	4 male New Zealand giant albino rabbits, dermal exposure to clipped skin occluded with plastic film for 24 hr;14-d observation period LD_{50} calculated using the method of Thompson (1947) using the tables of Weil (1952)	Dermal LD_{50} 14.1 mL/kg (8.8−22.9)[a]	Death following exposure (mechanism unreported)	Smyth et al. (1954)
Metabolism/ toxicokinetic	No data			
Mode of action/ mechanistic	No data			
Immunotoxicity	No data			
Neurotoxicity	No data			

[a]Values represent calculated means with parentheses noting the limits of ±1.96 standard deviations.

Tests Evaluating Carcinogenicity, Genotoxicity, and/or Mutagenicity

The carcinogenicity, genotoxicity, and mutagenicity potential of 1,1,2-trichloropropane have not been evaluated.

Acute Studies

One acute oral toxicity study in rats (Smyth et al., 1954), two acute inhalation toxicity studies in rats (Hazleton Labs 1992; Smyth et al., 1954), and one acute dermal toxicity study in rabbits (Smyth et al., 1954) were identified.

Smyth et al. (1954) performed one oral acute study in which five male Carworth-Wistar rats/dose (weighing 90−120 g) were administered a single dose of 1,1,2-trichloropropane and observed for mortality for up to 14 days. The study authors tested a range of doses spaced in a logarithmic series, although the exact doses used were not reported. An oral LD_{50} of 1.23 g/kg was calculated using the method of Thompson (1947) and the tables of Weil (1952). The study authors reported no other effects.

Hazleton Labs (1992) conducted an unpublished, acute inhalation toxicity study in which 6 male and 6 female Sprague-Dawley rats (average weights: 295 and 204 g, respectively) were exposed to 3500-ppm 1,1,2-trichloropropane for 6 hours. This exposure is converted to 21,000 mg/m^3 by multiplying 3500 ppm by the molecular weight of 1,2,2-trichloropropane (147.43 g/mol) and dividing the value by the standard molar volume of an ideal gas (24.45). No air controls were reported. Ataxia and effects on coordination were observed within 45 minutes after beginning exposure to 1,1,2-trichloropropane. After 2 hours of exposure all animals were prostrate, and after 3 hours of exposure some animals stopped breathing. All animals died prior to termination of the 6-hour exposure period. The study authors stated that the apparent cause of mortality was central nervous system depression. Autopsy revealed that the lungs, liver, and kidneys of all animals were congested. In males, kidneys were poorly differentiated, and lungs had a purple appearance. Pale kidneys were observed in one female. Authors observed similar effects in animals exposed to four other chlorinated hydrocarbons (3500 ppm of 1,2,2-trichloropropane, 1,1,2-trichloropropene-1, 1,1,1-trichloropropane, and ethyltrichloroethylene) and no effects from another chlorinated hydrocarbon (3500 ppm of 2,2-dichloropropane). Of the chemicals tested, the effects of 1,1,2-trichloropropane were noted to be most severe (quantitative data not provided).

Smyth et al. (1954) exposed 6 male albino rats to inhaled concentrations of 2000-ppm 1,1,2-trichloropropane for 4 hours. This exposure is converted to 12,000 mg/m^3 by multiplying 2000 ppm by the molecular weight of 1,1,2-trichloropropane (147.43 g/mol) and dividing the value by the standard molar volume of an ideal gas (24.45). Animals were observed for mortality for 14 days following the exposure period, during which 3 of the 6 rats had died. No other details were provided in the study report.

Smyth et al. (1954) also assessed dermal penetration in 4 male New Zealand giant albino rabbits weighing 2.5−3.5 kg using the one-day cuff method. Fur was clipped closely to the skin and the test site was occluded with plastic film for the 24-hour exposure period. Effects were assessed up to 14 days after exposure. An acute dermal LD_{50} value was calculated using a similar method to that reported for oral exposure in rats (Smyth et al., 1954). The study authors

calculated a dermal LD_{50} of 14.1 mL/kg for rabbits, indicating dermal penetration. No other effects were described.

Metabolism/Toxicokinetic Studies
No metabolism or toxicokinetic studies were identified.

MOA/Mechanistic Studies
No MOA or mechanistic studies were identified.

Immunotoxicity
No immunotoxicity studies were identified.

Neurotoxicity
No neurotoxicity studies were identified.

Other
In parallel to the Villeneuve et al. (1985) investigation of the subchronic oral administration of 1,1,2-trichloropropane in rats, a similar investigation using the same methods was conducted using 1,2,3-trichloropropane. 1,2,3-Trichloropropane led to effects to the liver, kidney, and thyroid (Villeneuve et al., 1985). The histological effects observed after 1,2,3-trichloropropane exposure were similar to those in the 1,1,2-trichloropropane study. Lesions observed in the livers, kidneys, and thyroid of rats exposed to 1000-mg/L 1,1,2-trichloropropane were also observed in rats exposed to 1000-mg/L 1,2,3-trichloropropane, though effects were generally more prevalent and more severe in rats exposed to 1,2,3-trichloropropane. In addition to the lesions reported with 1,1,2-trichloropropane exposure, female rats exposed to 1000-mg/L 1,2,3-trichloropropane demonstrated biliary hyperplasia.

Additional differences indicated that the response to 1,2,3-trichloropropane may be more severe than to 1,1,2-trichloropropane. Both chemicals led to increased relative liver weights in males; however, the effect was also observed in females treated with 1,2,3-trichloropropane. Additionally, relative kidney and brain weights were elevated in 1,2,3-trichloropropane-exposed rats, but were unaffected by 1,1,2-trichloropropane exposure. 1,2,3-trichloropropane decreased body-weight gains and daily water intake; these changes may be responsible for the changes in relative—but not absolute—organ weights. Serum cholesterol levels (females only), hepatic aminopyrine demethylase activity (males and females), and aniline hydroxylase activity (males only) were increased compared to both vehicle and water controls in animals treated with 1000-mg/L 1,2,3-trichloropropane. Although they share a NOAEL (100 mg/L) and LOAEL (1000 mg/L) in this study, 1,2,3-trichloropropane is reported to be more toxic than 1,1,2-trichloropropane on the basis of more numerous and severe effects at the LOAEL.

DERIVATION OF PROVISIONAL VALUES

Tables 4 and 5 present a summary of noncancer and cancer reference values, respectively.

Table 4. Summary of Noncancer Reference Values for 1,1,2-Trichloropropane (CASRN 598-77-6)

Toxicity Type (units)	Species/Sex	Critical Effect	p-Reference Value	POD Method	POD	UF_C	Principal Study
Subchronic p-RfD (mg/kg-d)	Rat/M	Mild lesions in liver, kidney, and thyroid	1×10^{-2}	NOAEL	14[a]	1000	Villeneuve et al. (1985)
RfD (mg/kg-d) IRIS (U.S. EPA, 1988a)	Rat/M+F	Mild lesions in liver, kidney, and thyroid	5×10^{-3}	NOAEL	15[a]	3000[b]	Villeneuve et al. (1985)
Subchronic p-RfC (mg/m^3)	NDr	NDr	NDr	NDr	NDr	NDr	NDr
Chronic p-RfC (mg/m^3)	NDr	NDr	NDr	NDr	NDr	NDr	NDr

[a]Villeneuve et al. (1985) reported within the study that intake at the NOAEL dose of 100 mg/L was 15−20 mg/kg-d. U.S. EPA (1988a) used the lower value, 15 mg/kg-d, to derive a chronic RfD. The same effect was used to derive a subchronic p-RfD; however, the dose is slightly altered in following current guidance for dosimetric adjustments (U.S. EPA, 1988a).

[b]U.S. EPA (1988b) applied an uncertainty factor of 3000 based on a UF_A of 10, a UF_S of 10, a UF_H of 10, and a UF_D of 3 (note: a UF_D of 10 is applied to the subchronic p-RfD derived in this PPRTV document following current practice to account for lack of data on reproductive and developmental effects).

NDr = Not determined.

Table 5. Summary of Cancer Values for 1,1,2-Trichloropropane (CASRN 598-77-6)

Toxicity Type	Species/Sex	Tumor Type	Cancer Value	Principal Study
p-OSF	NDr	NDr	NDr	NDr
p-IUR	NDr	NDr	NDr	NDr

NDr = Not determined.

DERIVATION OF ORAL REFERENCE DOSES

Derivation of Subchronic Provisional RfD (Subchronic p-RfD)

The Villeneuve et al. (1985) study is selected as the critical study for the derivation of a subchronic p-RfD. This study is a published, peer-reviewed study and meets the standards of study design and performance with numbers of animals, examination of potential toxicity endpoints, and presentation of information. Furthermore, this is the only study of subchronic duration located in the literature. The critical endpoints are an increased incidence of mild lesions in the liver, kidneys, and thyroid observed in male and female rats exposed to 1,1,2-trichloropropane in drinking water for 90 days, with males reported as the most sensitive sex. The same study was used by IRIS (U.S. EPA, 1988a) to derive a chronic RfD. The critical endpoint is supported by similar effects described by Villeneuve et al. (1985) following oral exposure to the related chemical, 1,2,3-trichloropropane. Further details of the study on 1,2.3-trichloropropane are provided in the "Other Data" section of this document. Details of the 1,1,2-trichloropropane study are provided in the "Review of Potentially Relevant Data" section of this document. The point of departure (POD) from this study is a NOAEL (14 mg/kg-day for mild liver, kidney, and thyroid lesions in male rats). Benchmark dose (BMD) analysis cannot be performed on these data because quantitative data for the critical effects are not provided in the study report.

The following dosimetric adjustments were made for each dose in the principal study for the water treatment.

$$\begin{aligned} \mathbf{NOAEL_{ADJ}} &= \mathbf{NOAEL \times Water\ Consumption\ per\ Day \times (1 \div Body\ Weight) \times (Days\ Dosed \div Total\ Days)} \\ &= 100\ \text{mg/L} \times 0.037\ \text{L/day} \times (1 \div 0.267\ \text{kg}) \times (90\ \text{days dosed} \div 90\ \text{total days}) \\ &= 100\ \text{mg/L} \times 0.037\ \text{L/day} \times 3.75\ \text{kg}^{-1} \times 1 \\ &= \mathbf{14\ mg/kg\text{-}day} \end{aligned}$$

The subchronic p-RfD based on a NOAEL of 14 mg/kg-day for mild liver, kidney, and thyroid lesions in the male rat (Villeneuve et al., 1985) is derived as follows:

$$\begin{aligned} \mathbf{Subchronic\ p\text{-}RfD} &= \mathbf{NOAEL \div UF_C} \\ &= 14\ \text{mg/kg-day} \div 1000 \\ &= \mathbf{1 \times 10^{-2}\ mg/kg\text{-}day} \end{aligned}$$

Table 6 summarizes the uncertainty factors for the subchronic p-RfD of 1,1,2-trichloropropane.

Table 6. Uncertainty Factors for Subchronic p-RfD of 1,1,2-Trichloropropane (CASRN 598-77-6)

UF	Value	Justification
UF_A	10	A UF_A of 10 is applied for interspecies extrapolation to account for potential toxicokinetic and toxicodynamic differences between rats and humans.
UF_D	10	A UF_D of 10 is applied because there are no acceptable two-generation reproduction studies or developmental studies by this route of exposure.
UF_H	10	A UF_H of 10 is applied for intraspecies differences to account for potentially susceptible individuals in the absence of information on the variability of response to humans.
UF_L	1	A UF_L of 1 is applied for using a POD based on a NOAEL.
UF_S	1	A UF_S of 1 is applied because a subchronic-duration study was utilized as the critical study.
UF_C	1000	Product of UF_A, UF_D, UF_H, UF_L, and UF_S.

The confidence of the subchronic p-RfD for 1,1,2-trichloropropane is low as explained in Table 7 below.

Table 7. Confidence Descriptors for Subchronic p-RfD for 1,1,2-Trichloropropane (CASRN 598-77-6)

Confidence Categories	Designation[a]	Rationale
Confidence in study	M	The confidence in the study is medium. Villeneuve et al. (1985) examined most—but not all—of the appropriate subchronic endpoints. The study was peer reviewed. The study included multiple effect levels, and both a NOAEL and LOAEL were identified. The study by Villeneuve et al. (1985) was also used to derive a chronic RfD by IRIS (U.S. EPA, 1988a).
Confidence in database	L	The confidence in the database is low because the database for subchronic oral exposure includes only the single study by Villeneuve et al. (1985). The database does not include any acceptable reproduction or development studies.
Confidence in subchronic p-RfD	L	The overall confidence in the subchronic p-RfD is low. The overall confidence cannot be greater than lowest entry in table.

[a]L = Low, M = Medium, H = High.

Derivation of Chronic Provisional RfD (Chronic p-RfD)

A chronic RfD of 5×10^{-3} mg/kg-day is available on IRIS (U.S. EPA, 1988a), based on increased incidence of mild lesions in the liver, kidney, and thyroid reported in rats exposed to 1000 mg/L 1,1,2-trichloropropane (adjusted to 150 mg/kg-day) via drinking water for 90 days, with a NOAEL of 100 mg/L (adjusted to 15 mg/kg-day) (Villeneuve et al., 1985). The principal study used by IRIS is also utilized in this document for a subchronic p-RfD. The IRIS database should be checked to determine if any changes have been made.

DERIVATION OF INHALATION REFERENCE CONCENTRATIONS

Derivation of Subchronic Provisional RfC (Subchronic p-RfC)

No inhalation exposure studies on 1,1,2-trichloropropane were identified.

Derivation of Chronic Provisional RfC (Chronic p-RfC)

No inhalation exposure studies on 1,1,2-trichloropropane were identified.

CANCER WEIGHT-OF-EVIDENCE DESCRIPTOR

Table 8 identifies the cancer weight-of-evidence (WOE) descriptor for 1,1,2-trichloropropane.

Table 8. Cancer WOE Descriptor for 1,1,2-Trichloropropane (CASRN 598-77-6)

Possible WOE Descriptor	Designation	Route of Entry (oral, inhalation, or both)	Comments
"Carcinogenic to Humans"	NA	NA	No human cancer studies are available.
"Likely to Be Carcinogenic to Humans"	NA	NA	No animal cancer data are available.
"Suggestive Evidence of Carcinogenic Potential"	NA	NA	No evidence assessing carcinogenicity is available.
"Inadequate Information to Assess Carcinogenic Potential"	**Selected**	**Both**	**No evidence assessing carcinogenicity via the oral or inhalation route is available in the literature.**
"Not Likely to Be Carcinogenic to Humans"	NA	NA	No strong evidence of noncarcinogenicity in humans is available.

NA = not applicable.

While there is no evidence assessing the carcinogenicity of 1,1,2-trichloropropane via either the oral or the inhalation route of exposure, the related compound, 1,2,3-trichloropropane, is a likely human carcinogen via the oral route of exposure (U.S. EPA, 2009b) based on evidence of genotoxicity and occurrence of tumors at multiple sites in both rats and mice. Additionally, halogenated propanes have been generally found to be positive in assays testing for mutagenicity (Låg et al., 1994; Ratpan and Plaumann, 1988). This indicates a need for future studies addressing the carcinogenic potential of 1,1,2-trichloropropane.

DERIVATION OF PROVISIONAL CANCER POTENCY VALUES

Derivation of Provisional Oral Slope Factor (p-OSF)

No oral carcinogenicity studies on 1,1,2-trichloropropane were identified.

Derivation of Provisional Inhalation Unit Risk (p-IUR)

No inhalation carcinogenicity studies on 1,1,2-trichloropropane were identified.

APPENDIX A. PROVISIONAL SCREENING VALUES

No screening values are presented.

APPENDIX B. DATA TABLES

No data tables are presented.

APPENDIX C. BMD OUTPUTS

No BMD outputs are presented.

APPENDIX D. REFERENCES

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