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Provisional Peer-Reviewed Toxicity Values for

1,2,3-Trichloropropene
(CASRN 96-19-5)

Superfund Health Risk Technical Support Center
National Center for Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency
Cincinnati, OH 45268

COMMONLY USED ABBREVIATIONS

BMD	Benchmark Dose
IRIS	Integrated Risk Information System
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
p-OSF	provisional oral slope factor
p-RfC	provisional inhalation reference concentration
p-RfD	provisional oral reference dose
RfC	inhalation reference concentration
RfD	oral reference dose
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

PROVISIONAL PEER-REVIEWED TOXICITY VALUES FOR 1,2,3-TRICHLOROPROPENE (CASRN 96-19-5)

Background

On December 5, 2003, the U.S. Environmental Protection Agency's (U.S. EPA's) Office of Superfund Remediation and Technology Innovation (OSRTI) revised its hierarchy of human health toxicity values for Superfund risk assessments, establishing the following three tiers as the new hierarchy:

1. U.S. EPA's Integrated Risk Information System (IRIS).
2. Provisional Peer-Reviewed Toxicity Values (PPRTVs) used in U.S. EPA's Superfund Program.
3. Other (peer-reviewed) toxicity values, including:
   - Minimal Risk Levels produced by the Agency for Toxic Substances and Disease Registry (ATSDR),
   - California Environmental Protection Agency (CalEPA) values, and
   - EPA Health Effects Assessment Summary Table (HEAST) values.

A PPRTV is defined as a toxicity value derived for use in the Superfund Program when such a value is not available in U.S. EPA's IRIS. PPRTVs are developed according to a Standard Operating Procedure (SOP) and are derived after a review of the relevant scientific literature using the same methods, sources of data, and Agency guidance for value derivation generally used by the U.S. EPA IRIS Program. All provisional toxicity values receive internal review by two U.S. EPA scientists and external peer review by three independently selected scientific experts. PPRTVs differ from IRIS values in that PPRTVs do not receive the multiprogram consensus review provided for IRIS values. This is because IRIS values are generally intended to be used in all U.S. EPA programs, while PPRTVs are developed specifically for the Superfund Program.

Because new information becomes available and scientific methods improve over time, PPRTVs are reviewed on a 5-year basis and updated into the active database. Once an IRIS value for a specific chemical becomes available for Agency review, the analogous PPRTV for that same chemical is retired. It should also be noted that some PPRTV documents conclude that a PPRTV cannot be derived based on inadequate data.

Disclaimers

Users of this document should first check to see if any IRIS values exist for the chemical of concern before proceeding to use a PPRTV. If no IRIS value is available, staff in the regional Superfund and Resource Conservation and Recovery Act (RCRA) program offices are advised to carefully review the information provided in this document to ensure that the PPRTVs used are appropriate for the types of exposures and circumstances at the Superfund site or RCRA facility in question. PPRTVs are periodically updated; therefore, users should ensure that the values contained in the PPRTV are current at the time of use.

It is important to remember that a provisional value alone tells very little about the adverse effects of a chemical or the quality of evidence on which the value is based. Therefore, users are strongly encouraged to read the entire PPRTV document and understand the strengths and limitations of the derived provisional values. PPRTVs are developed by the U.S. EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center for OSRTI. Other U.S. EPA programs or external parties who may choose of their own initiative to use these PPRTVs are advised that Superfund resources will not generally be used to respond to challenges of PPRTVs used in a context outside of the Superfund Program.

Questions Regarding PPRTVs

Questions regarding the contents of the PPRTVs and their appropriate use (e.g., on chemicals not covered, or whether chemicals have pending IRIS toxicity values) 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), or OSRTI.

INTRODUCTION

No RfD, RfC, or carcinogenicity assessment for 1,2,3-trichloropropene is available on IRIS (U.S. EPA, 2009). The HEAST (U.S. EPA, 1997) lists subchronic and chronic oral RfD values of 5E-3 mg/kg-day for 1,2,3-trichloropropene based on route-to-route extrapolation from a subchronic inhalation study in dogs (McKenna et al., 1978). The assessment was based on a NOAEL of 18 mg/m^3 for eye irritation and included application of an oral absorption factor of 0.5 and an uncertainty factor of 100 (10 for extrapolation from dogs to humans and 10 to protect sensitive individuals). The source document for this derivation was a Health and Environmental Effects Profile (HEEP) for Chloropropenes (U.S. EPA, 1983). The HEAST and source HEEP do not include RfC or cancer assessments for 1,2,3-trichloropropene. The Drinking Water Standards and Health Advisories list (U.S. EPA, 2006) does not include 1,2,3-trichloropropene. The CARA (U.S. EPA, 1991, 1994) lists only the previously mentioned HEEP (U.S. EPA, 1983) for Chloropropenes. ATSDR (2008) has not produced a Toxicological Profile for 1,2,3-trichloropropene, and no Environmental Health Criteria Document is available (WHO, 2009). The carcinogenicity of 1,2,3-trichloropropene has not been assessed by IARC (2009) or NTP (2005, 2009). ACGIH (2007), OSHA (2008), and NIOSH (2008) have not established occupational health standards for 1,2,3-trichloropropene.

Literature searches were conducted from 1960s through May 2008 for studies relevant to the derivation of provisional toxicity values for 1,2,3-trichloropropene. Databases searched included MEDLINE, TOXLINE (Special), BIOSIS, TSCATS 1/TSCATS 2, CCRIS, DART/ETIC, GENETOX, HSDB, RTECS, and Current Contents (previous 6 months). A final search of the literature was conducted for the period from May 2008 thru April 2009.

REVIEW OF PERTINENT DATA

Human Studies

No data were located regarding the effects of 1,2,3-trichloropropene in humans following inhalation or oral exposure.

Animal Studies

Oral Exposure

Only one oral study was located. Groups of five Charles River CD rats/sex were administered 1,2,3-trichloropropene (96% pure) by gavage in corn oil at doses of 0, 3, 10, 30, 100, or 300 mg/kg-day daily for 4 weeks (Johannsen et al., 1991a). Rats were monitored for clinical signs and mortality throughout the study, and body weight and food consumption were recorded weekly. Blood for clinical chemistry analysis was collected prior to sacrifice. Rats were examined grossly, but only the liver was examined for histopathology (all dose groups). All high-dose males and females died within the first week (most within 48 hours). Clinical signs preceding death included labored breathing, decreased activity, and impaired hind limb function. Pathological findings in these animals included congestion in various organs (lungs, thymus, stomach, liver), and slight-to-moderate fatty change in the liver (10/10). No mortality was observed at the lower doses.

The only effects observed at the lower doses were excessive salivation following dosing in some of the rats treated with 100 mg/kg-day, and a 9% decrease in mean body weight in the males from the same dose group after 4 weeks (data shown graphically; statistical significance not reported) (Johannsen et al., 1991a). The study authors considered the decreased body weight gain to be treatment-related. There were no discernible treatment-related effects on body weight in females. Food consumption was reported by the researchers to be similar to controls in the treated rats. There were no treatment-related effects on clinical chemistry variables (data not shown). No gross pathological changes or microscopic changes in the liver of rats surviving to the end of the study were observed by the study authors. Because the body-weight data show marginal changes after only 4 weeks of exposure, it is possible that the change in body weight could have increased with increasing exposure duration. This change in body weight can be used to assign a NOAEL of 30 mg/kg-day and a LOAEL of 100 mg/kg-day for 1,2,3-trichloropropene in this study. The 300 mg/kg-day dose is a FEL for lethality.

Inhalation Exposure

Johannsen et al. (1991b) conducted subchronic inhalation toxicity and reproductive experiments in rats exposed to 1,2,3-trichloropropene.

Subchronic Studies—In a range-finding study, groups of five male and five female Sprague-Dawley (S-D) rats were exposed to 0, 5, 20, or 100 ppm (0, 30, 119, or 590 mg/m^3) of 1,2,3-trichloropropene vapor (whole-body exposure) 6 hours/day, 5 days/week, for 4 weeks (Johannsen et al., 1991b). The protocol for this study was not reported by the authors, and the only other details regarding the study were reported as follows. All rats exposed to 100 ppm died. Rats in the 20 ppm group (and the 100 ppm group prior to death) showed signs of irritation (droopy eyelids, alopecia, lacrimation, red nasal and/or anal discharge) and reduced mean body

weights (primarily in the females; magnitudes not reported). No effects were reported at 5 ppm. The LOAEL for this study is 20 ppm (119 mg/m^3) on the basis of nasal irritation, and the NOAEL is 5 ppm (30 mg/m^3).

Following the range-finding study, groups of 15 S-D rats of each sex were exposed to 0, 1, 5, or 15 ppm (corresponding to mean analytical concentrations of 0, 2.8, 5.5, 14.9 ppm or 0, 17, 33, 89 mg/m^3) of 1,2,3-trichloropropene vapor (whole-body exposure) 6 hours/day, 5 days/week, for 13 weeks (Johannsen et al., 1991b). Toxicological variables evaluated included survival, body weight, hematology, serum chemistry, urinalysis, organ weights, and gross and microscopic examination of major organs and tissues from the control and high-dose groups. No respiratory tract tissues or structures other than lungs were evaluated microscopically. All rats survived the duration of the study, and no abnormal behavioral reactions were observed. Red nasal discharge (not characterized further) and yellow staining of the anogenital fur were observed, but not quantified, in the high-dose (15 ppm) group, and a 9% decrease in body-weight gain was reported at the end of the study in females of the same dose group (data not shown). The study authors considered the reduced weight gain to be treatment-related. Conversely, no treatment-related changes in clinical chemistry analytes, hematology, urinalysis, organ weights, or gross or microscopic pathology were observed (data not shown). The high concentration of 15 ppm (89 mg/m^3) in this study is a LOAEL for nasal irritation (presumed bloody discharge). The NOAEL is 5 ppm (33 mg/m^3).

A previous inhalation study was reported only as an abstract. Groups (numbers unspecified) of male and female S-D rats, Golden Syrian hamsters, and Beagle dogs (males only) were exposed to 0, 3, 10, or 25 ppm (0, 18, 59, or 149 mg/m^3) of 1,2,3-trichloropropene vapor (presumed whole-body exposure) 6 hours/day, 5 days/week, for approximately 90 days (McKenna et al., 1978). The toxicological variables evaluated included clinical signs, body weight, urinalysis, clinical hematology and chemistry analytes, gross and microscopic pathology, and organ weights. Hepatic nonprotein sulfhydryl (NPSH) assays were conducted on additional groups of rats and hamsters following single or subchronic exposure. Eye irritation was observed in dogs exposed at the 10- and 25-ppm levels, while other adverse effects were reported only in the animals of the 25-ppm group. These adverse effects included eye irritation in rats, upper respiratory irritation in hamsters, decreased body weight in rats and male hamsters, elevated serum ALT (SGPT) levels in rats and decreased liver cell size in male hamsters (data not shown). The NPSH concentrations showed a dose-related decrease as a result of single inhalation exposures in rats and hamsters, but this effect was not seen following subchronic exposure. Based on limited reporting in the available abstract, the NOAEL for this study appears to be 3 ppm (18 mg/m^3). The LOAEL appears to be 10 ppm (59 mg/m^3) for eye irritation in dogs.

Reproductive/Developmental Studies—Groups of 10 male and 20 female S-D rats were exposed to 0, 1, or 5 ppm (0, 6, or 30 mg/m^3) of 1,2,3-trichloropropene vapor (whole-body exposure) 6 hours/day, 5 days/week, for a 10-week premating period, a mating period of up to 30 days, and (females only) from day 0 to day 14 of gestation (Johannsen et al., 1991b). Adult male rats were sacrificed at the completion of the 30-day mating period. Mated females were allowed to deliver litters, and both the dams and pups were sacrificed at weaning on Day 21 of lactation. Toxicological variables evaluated in the adult rats included: clinical signs, body weight, necropsy, organ weight, and microscopic examination of the reproductive tract. Pup survival and body weight were monitored throughout lactation, and dead pups were necropsied.

No effects were found on parental body weights (data not shown), mating and fertility indices, gestational length, fetal viability at birth, litter size, pup growth and survival (data not shown), organ weights and gross and microscopic pathology in parents (data not shown), or gross pathology in pups (data not shown; Johannsen et al., 1991b). Nasal irritation or other clinical signs were not mentioned by the study authors. The NOAEL for reproductive toxicity in this study is 5 ppm (30 mg/m^3), the highest concentration tested.

Other Studies

Genotoxicity

Studies in *Salmonella typhimurium* demonstrated that 1,2,3-trichloropropene is mutagenic in bacteria (Stolzenberg and Hine, 1980; Neudecker and Henschler, 1986; Monsanto Co., 1982a,b, 1984a). Although reversion frequency was increased both with and without metabolic activation, the effect was far greater in the presence of a metabolic-activating system. Studies in other test systems have not indicated genotoxicity. 1,2,3-Trichloropropene produced negative results in an assay for unscheduled DNA synthesis in rat hepatocytes (Williams et al., 1989). Acute exposure to vapor concentrations up to 1248 mg/m^3 of trichloropropene did not produce clastogenic effects in rat bone marrow cells in vivo (Monsanto Co., 1984b).

DERIVATION OF PROVISIONAL SUBCHRONIC AND CHRONIC ORAL RfD VALUES FOR 1,2,3-TRICHLOROPROPENE

Subchronic p-RfD

There are no human studies and no studies of subchronic duration (e.g., 13 weeks) that can be used to derive a subchronic p-RfD for 1,2,3-trichloropropene. A NOAEL of 30 and LOAEL of 100 mg/kg-day can be derived from the 4-week gavage study by Johannsen et al. (1991a) based on decreased body weight in male rats. Although the observed decrease was marginal after 4 weeks, it is possible that a further decrease could occur with increased exposure duration. In this study, the high dose of 300 mg/kg-day was a FEL that killed all animals within 1 week, and it also produced mild target organ effects on the liver within that time. Due to the absence of clearly reported body-weight data for the study, benchmark dose modeling (BMD) cannot be used to determine a point of departure (POD). As such, the NOAEL of 30 mg/kg-day is used as the POD for the derivation of subchronic and chronic p-RfD values.

A **subchronic p-RfD** is derived by applying a composite UF of 1000 to the NOAEL of 30 mg/kg-day as follows:

Subchronic p-RfD = NOAEL/UF
= 30 mg/kg-day/1000
= **0.03 mg/kg-day or 3 × 10^{-2} mg/kg-day**

The composite UF of 1000 is composed of the following:

- A full UF of 10 is applied for interspecies extrapolation to account for potential pharmacokinetic and pharmacodynamic differences between rats and humans.
- A full UF of 10 for intraspecies differences is applied to account for potentially susceptible individuals in the absence of information on the variability of response in humans.
- A full database UF of 10 is applied to account for database deficiencies. It lacks reproductive and developmental toxicity studies.

A UF for extrapolating from a subchronic to a chronic exposure is not applied because a subchronic study is available, and a UF for extrapolating from a LOAEL to a NOAEL is not applied because a NOAEL is available.

Confidence in the key study is low. The study employed small group sizes and a short exposure duration. A limited number of endpoints were studied, and histopathological examination was restricted to the liver. Confidence in the database is low, as no supporting studies were located. Low confidence in the subchronic p-RfD value follows.

Chronic p-RfD

There are no human studies and no chronic studies that can be used as the basis for a chronic p-RfD for 1,2,3-trichloropropene. However, the Appendix of this document contains a Screening Value based on a composite uncertainty factor of 10,000 that may be useful in certain instances. Please see the attached Appendix for details.

DERIVATION OF PROVISIONAL SUBCHRONIC AND CHRONIC INHALATION RfC VALUES FOR 1,2,3-TRICHLOROPROPENE

The limited database for 1,2,3-trichloropropene supports irritant effects as critical for inhalation exposure. A NOAEL of 5 ppm (33 mg/m^3 as measured) and LOAEL of 15 ppm (89 mg/m^3) were identified from the subchronic rat inhalation study conducted by Johannsen et al. (1991b) based on nasal irritation. The importance of irritant effects for this chemical is supported by the results of the 4-week range-finding study conducted by the same researchers, which reported nasal and eye irritant effects at 20 and 100 ppm (119 and 590 mg/m^3). Reduced body weight (at 20 ppm) and death (at 100 ppm) were the only other effects observed in these studies. The study by McKenna et al. (1978) found some evidence for target effects on the liver in rats and hamsters—but only at concentrations producing irritant effects and reductions in body weight in these animals. The principal effect in this study was eye irritation in dogs, which defined an apparent NOAEL of 3 ppm and LOAEL of 10 ppm (18 and 59 mg/m^3). These results are consistent with Johannsen et al. (1991b). The reproduction study by Johannsen et al. (1991b) showed that 1,2,3-trichloropropene does not produce reproductive effects at nonirritant concentrations (i.e., the NOAEL for reproductive effects was 5 ppm [30 mg/m^3]).

Subchronic and chronic p-RfC values for 1,2,3-trichloropropene can be derived based on the critical effect of nasal irritation in the subchronic rat inhalation study by Johannsen et al. (1991b). Data for this effect are not reported by the study authors, and, therefore, BMD modeling cannot be used to determine a POD. However, the NOAEL of 5 ppm (33 mg/m^3 as measured) from the study can be used to derive a $NOAEL_{HEC}$ that, in turn, can be used as a POD for the derivation of subchronic and chronic RfC values. Due to irritant effects, 1,2,3-trichloropropene is treated as a Class 1 gas. A $NOAEL_{HEC}$ is calculated for a Class 1 respiratory effect in the extrathoracic region as follows (U.S. EPA, 1994b):

$$NOAEL_{ADJ} = 33\ mg/m^3 \times 6\ hours \div 24\ hours \times 5\ days \div 7\ days = 5.8\ mg/m^3$$
$$NOAEL_{HEC} = NOAEL_{ADJ} \times RGDR_{ET}$$
$$RGDR_{ET} = (V_E/SA_{ET})_A \div (V_E/SA_{ET})_H$$

where

$RGDR_{ET}$ = regional gas deposition ratio in the extrathoracic region
V_E = minute volume (mL/min)
SA_{ET} = surface area of extrathoracic region (cm^2)
A,H = subscripts denoting laboratory animal and human, respectively
$(V_E)_A$ = 0.27 m^3/day (U.S. EPA, 1988) (subchronic, S-D male rats)
$(V_E)_H$ = 20 m^3/day (U.S. EPA, 1988)
$(SA_{ET})_A$ = 15 cm^2 (U.S. EPA, 1994b)
$(SA_{ET})_H$ = 200 cm^2 (U.S. EPA, 1994b)
$RGDR_{ET}$ = (0.27 m^3/day/15 cm^2)/(20 m^3/day/200 cm^2) = 0.18

$$NOAEL_{HEC} = NOAEL_{ADJ} \times RGDR_{ET}$$
$$= 5.8\ mg/m^3 \times 0.18$$
$$= 1.05\ mg/m^3 \approx 1\ mg/m^3$$

Subchronic p-RfC

A **subchronic p-RfC** is derived by applying to the $NOAEL_{HEC}$ of 1 mg/m^3 a composite UF of 300 as follows:

$$\textbf{Subchronic p-RfC} = NOAEL_{HEC}/UF$$
$$= 1\ mg/m^3/300$$
$$= \mathbf{0.003\ mg/m^3\ or\ 3 \times 10^{-3}\ mg/m^3}$$

The composite UF of 300 is composed of the following factors:

- A partial UF of 3 ($10^{0.5}$) is applied for interspecies extrapolation to account for potential pharmacodynamic differences between rats and humans. Converting the rat data to human-equivalent concentrations by the dosimetric equations accounts for pharmacokinetic differences between rats and humans; thus, a full UF of 10 for interspecies extrapolation was not used.
- A full UF of 10 for intraspecies differences is applied to account for potentially susceptible individuals in the absence of information on the variability of response in humans.

- A full UF of 10 is applied to account for deficiencies in the database. The database includes a subchronic study in rats, supported by 4-week and one-generation reproduction studies in rats but lacks a two-generation reproduction study and a developmental toxicity study.

A UF for extrapolating from a subchronic to a chronic exposure is not applied because a subchronic study was available, and a UF for extrapolating from a LOAEL to a NOAEL is not applied because a NOAEL was available.

Confidence in the critical study is medium. The study utilized an appropriate number of animals and exposure levels, and it includes a variety of relevant endpoints. The critical effect was identified, but no quantitative data regarding this effect or other endpoints studied are presented. Confidence in the database is medium. The critical study is supported by the 4-week range-finding study presented in the same paper and another subchronic inhalation study that was available only as an abstract. A single-generation reproduction study showed no effects on reproduction, but developmental effects have not been studied. Medium confidence in the subchronic p-RfC values follows.

Chronic p-RfC

A **chronic p-RfC** is derived by applying to the $NOAEL_{HEC}$ of 1 mg/m^3 a composite UF of 3000 as follows:

$$\begin{aligned} \textbf{Chronic p-RfC} &= NOAEL_{HEC}/UF \\ &= 1\ mg/m^3/3000 \\ &= \mathbf{0.0003\ mg/m^3\ or\ 3 \times 10^{-4}\ mg/m^3} \end{aligned}$$

The composite UF of 100 is composed of the following factors:

- A partial UF of 3 ($10^{0.5}$) is applied for interspecies extrapolation to account for potential pharmacodynamic differences between rats and humans. Converting the rat data to human-equivalent concentrations by the dosimetric equations accounts for pharmacokinetic differences between rats and humans; thus, a full UF of 10 for interspecies extrapolation is not used.
- A full UF of 10 is applied to account for extrapolating from a subchronic study to approximate chronic exposure.
- A full UF of 10 for intraspecies differences is applied to account for potentially susceptible individuals in the absence of information on the variability of response in humans.
- A full UF of 10 is applied to account for deficiencies in the database. The database includes a subchronic study in rats, supported by 4-week and one-generation reproduction studies in rats, but lacks a two-generation reproduction study and a developmental toxicity study.

A UF for extrapolating from a LOAEL to a NOAEL is not applied because a NOAEL is available.

As discussed for the subchronic p-RfC, confidence in the critical study is medium. Confidence in the database, in support of a chronic p-RfC, is low. The critical study is supported by the 4-week range-finding study presented in the same paper and another subchronic inhalation

study that was available only as an abstract. A single-generation reproduction study showed no effects on reproduction, but developmental effects have not been studied. Low confidence in the chronic p-RfC values follows.

PROVISIONAL CARCINOGENICITY ASSESSMENT FOR 1,2,3-TRICHLOROPROPENE

Weight-of-Evidence Descriptor

There are no human or animal carcinogenicity data for 1,2,3-trichloropropene. Genotoxicity data indicate that this chemical is mutagenic in bacteria (especially with activation), but studies in mammalian test systems for unscheduled DNA synthesis in rat hepatocytes in vitro and clastogenicity in rat bone marrow in vivo were negative. Under the current U.S. EPA cancer guidelines (U.S. EPA, 2005), there is "*Inadequate Information to Assess the Human Carcinogenic Potential*" of 1,2,3-trichloropropene. However, there is concern that this compound may have carcinogenic activity, based on the genetic toxicity data (i.e., strongly positive results in the *Salmonella* reverse mutation assay) and structure-activity comparisons. The NTP (2005), in the Eleventh Report on Carcinogens, noted positive carcinogenicity in the following compounds that are structurally-related to 1,2,3-trichloropropene:

- 1,2-dichloroethane
- 1,2-dibromo-3-chloropropane
- 1,3-dichloropropene
- 3-chloro-2-methylpropene

Quantitative Estimates of Carcinogenic Risk

Derivation of quantitative estimates of cancer risk for 1,2,3-trichloropropene is precluded by the lack of suitable data.

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APPENDIX A. DERIVATION OF A SCREENING VALUE FOR 1,2,3-TRICHLOROPROPENE

For reasons noted in the main PPRTV document, it is inappropriate to derive provisional toxicity values for 1,2,3-trichlorpropene. However, information is available for this chemical which, although insufficient to support derivation of a provisional toxicity value, under current guidelines, may be of limited use to risk assessors. In such cases, the Superfund Health Risk Technical Support Center summarizes available information in an Appendix and develops a "Screening Value." Appendices receive the same level of internal and external scientific peer review as the PPRTV documents to ensure their appropriateness within the limitations detailed in the document. Users of screening toxicity values in an appendix to a PPRTV assessment should understand that there is considerably more uncertainty associated with the derivation of an appendix screening toxicity value than for a value presented in the body of the assessment. Questions or concerns about the appropriate use of Screening Values should be directed to the Superfund Health Risk Technical Support Center.

There are no human studies and no chronic studies that can be used as the basis for a chronic p-RfD for 1,2,3-trichloropropene. However, a **chronic screening RfD** can be derived from the 4-week study by Johannsen et al. (1991a) by applying to the NOAEL of 30 mg/kg-day a composite UF of 10,000 as follows:

Chronic Screening RfD = NOAEL/UF
= 30 mg/kg-day/10,000
= **0.003 mg/kg-day or 3×10^{-3} mg/kg-day**

The composite UF of 10,000 is composed of the following:

- A full UF of 10 is applied for interspecies extrapolation to account for potential pharmacokinetic and pharmacodynamic differences between rats and humans.
- A full UF of 10 for intraspecies differences is applied to account for potentially susceptible individuals in the absence of information on the variability of response in humans.
- A full UF of 10 is applied for using a subchronic study to approximate chronic exposure.
- A full database UF of 10 is applied to account for deficiencies in the data base. The toxicological database for oral exposure to 1,2,3-trichloropropene lacks a chronic study, as well as reproductive and developmental toxicity studies.

A UF for extrapolating from a LOAEL to a NOAEL is not applied because a NOAEL was available.

Confidence in the key study is low. The study employed small group sizes and a short exposure duration. A limited number of endpoints were studied, and histopathological examination was restricted to the liver. Confidence in the database is low, as no supporting studies were located. Low confidence in the chronic screening RfD value follows.