FINAL
8-27-2013

Provisional Peer-Reviewed Toxicity Values for

3,4-Dichlorobenzotrifluoride
(CASRN 328-84-7)

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

AUTHORS, CONTRIBUTORS, AND REVIEWERS

CHEMICAL MANAGER

Jeff Swartout
National Center for Environmental Assessment, Cincinnati, OH

DRAFT DOCUMENT PREPARED BY

ICF International
9300 Lee Highway
Fairfax, VA 22031

PRIMARY INTERNAL REVIEWERS

Audrey Galizia, DrPH
National Center for Environmental Assessment, Washington, DC

Q. Jay Zhao, PhD, MPH, DABT
National Center for Environmental Assessment, Cincinnati, OH

This document was externally peer reviewed under contract to
Eastern Research Group, Inc.
110 Hartwell Avenue
Lexington, MA 02421-3136

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 confidence limit
BMD	benchmark dose
BMDL	benchmark dose lower confidence limit
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 inhalation reference concentration
p-RfD	provisional oral reference dose
RfC	inhalation reference concentration
RfD	oral reference dose
UF	uncertainty factor
UF_A	interspecies uncertainty factor
UF_C	composite uncertainty factor
UF_D	database uncertainty factor
UF_H	intraspecies 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 3,4-DICHLOROBENZOTRIFLUORIDE (CASRN 328-84-7)

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 U.S. EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center (513-569-7300).

INTRODUCTION

3,4-Dichlorobenzotrifluoride (3,4-DCBTF; CASRN 328-84-7; also known as 1,2-dichloro-4-[trifluoromethyl]-benzene) is a clear liquid solvent used as an intermediate in the preparation of diphenyl ether herbicides such as acifluorfen and oxyfluorfen (U.S. EPA, 1987; Yih and Swithenbank, 1975). It may also be used as a single-phase fluid in industrial cleaning applications (Chen and Lindrose, 2000). The empirical formula for 3,4-DCBTF is $C_7H_3Cl_2F_3$, and its structure is shown in Figure 1, and the physicochemical properties of 3,4-DCBTF are provided below in Table 1.

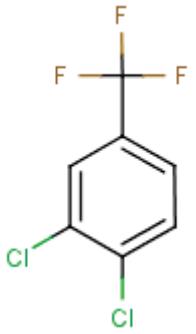

Figure 1. Structure of 3,4-Dichlorobenzotrifluoride

Table 1. Physicochemical Properties of 3,4-Dichlorobenzotrifluoride (1,2-dichloro-4-[trifluoromethyl]-benzene); CASRN 328-84-7[a]

Property (unit)	Value
Boiling point (ºC)	173.5°C
Melting point (ºC)	-12
Density (g/cm^3)	1.478
Vapor pressure (mm Hg at 20ºC)	1.6 mm Hg
pH (unitless)	ND
Solubility in water (ml/L at 23°C)	11.6
Relative vapor density (air = 1)	ND
Molecular weight (g/mol)	214.9993
Flash point (°C)	77
Octanol/water partition coefficient (unitless)	ND

[a]Values from U.S. EPA (2005) and (ChemBlink).

ND = no data.

A summary of available toxicity values for 3,4-DCBTF from U.S. EPA and other agencies/organizations is provided in Table 2.

Table 2. Summary of Available Toxicity Values for 3,4-Dichlorobenzotrifluoride

Source/Parameter[a]	Value (Applicability)	Notes	Reference	Date Accessed
Noncancer				
ACGIH	NV	NA	(ACGIH, 2013)	NA
ATSDR	NV	NA	(ATSDR, 2013)	NA
Cal/EPA	NV	NA	(Cal/EPA, 2012b)	NA
NIOSH	NV	NA	(NIOSH, 2010)	NA
OSHA	NV	NA	(OSHA, 2011, 2006)	NA
IRIS	NV	NA	U.S. EPA	8-1-2013
Drinking water	NV	NA	(U.S. EPA, 2011a)	NA
HEAST	NV	NA	(U.S. EPA, 2011b)	NA
CARA HEEP	NV	NA	(U.S. EPA, 1994)	NA
WHO	NV	NA	WHO	8-1-2013
Cancer				
IRIS	NV	NA	U.S. EPA	8-1-2013
HEAST	NV	NA	(U.S. EPA, 2011b)	NA
IARC	NV	NA	IARC	8-1-2013
NTP	NV	NA	(NTP, 2011)	NA
Cal/EPA	NV	NA	(Cal/EPA, 2012a, b, 2009)	NA

[a]Sources: American Conference of Governmental Industrial Hygienists (ACGIH); Agency for Toxic Substances and Disease Registry (ATSDR); California Environmental Protection Agency (Cal/EPA); National Institute for Occupational Safety and Health (NIOSH); Occupational Safety and Health Administration (OSHA); Chemical Assessments and Related Activities (CARA); Health and Environmental Effects Profile (HEEP); World Health Organization (WHO); Integrated Risk Information System (IRIS); Health Effects Assessment Summary Tables (HEAST); International Agency for Research on Cancer (IARC); National Toxicology Program (NTP).

NA = not applicable; NV = not available.

Literature searches were conducted on sources published from 1900 through August 2013, for studies relevant to the derivation of provisional toxicity values for 3,4-DCBTF, CAS No. 328-84-7. 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 (U.S. 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 3 provides an overview of the relevant database for 3,4-DCBTF 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 3. Summary of Potentially Relevant Data for 3,4-Dichlorobenzotrifluoride (CASRN 328-84-7)

Category	Number of Male/Female Strain, Species, Study Type, and Study Duration	Dosimetry	Critical effects	NOAEL	BMDL/ BMCL	LOAEL	Reference (Comments)	Notes
Human								
1. Oral (mg/kg-d)								
Subchronic	ND							
Chronic	ND							
Developmental	ND							
Reproductive	ND							
Carcinogenicity	ND							
2. Inhalation (mg/m^3)								
Subchronic	ND							
Chronic	ND							
Developmental	ND							
Reproductive	ND							
Carcinogenicity	ND							
Animal								
1. Oral								
Short-Term	5/5, S-D, rat, diet, 28 d	0; 2; 20; 200; 2,000 ppm in feed (nominal)	Reduced feed consumption (12−16%) at highest dose. No other treatment-related effects. Study considered invalid by the study authors because of compound volatility in feed stock; also two unidentified contaminants present in blood and urine samples at high levels and in stock preparation at lower levels.	NDr	DU	NDr	Raltech Scientific Services, Inc. (1978; as cited in U.S. EPA, 2005)	NPR

Table 3. Summary of Potentially Relevant Data for 3,4-Dichlorobenzotrifluoride (CASRN 328-84-7)

Category	Number of Male/Female Strain, Species, Study Type, and Study Duration	Dosimetry	Critical effects	NOAEL	BMDL/ BMCL	LOAEL	Reference (Comments)	Notes
Short-Term	15/15, S-D, rat, diet, 5 wk	0;125; 500; 2,000 ppm in feed (nominal)	No treatment-related effects at any dose. Study suspended early; considered invalid by the study authors because of compound volatility in feed. Impurities likely in test compound preparation.	NDr	DU	NDr	Raltech Scientific Services, Inc. (1979)	NPR
	3/3, S-D rat, gavage, 7 d/wk, 14 d	0, 7.5, 15, 30, 60, 120 mg/kg-d	Effects in mean liver weights and liver/body-weight ratio (dose groups not specified, magnitude not specified but not statistically significant); no other treatment-related effects observed.	NDr	DU	NDr	Elars Bioresearch Laboratories, Inc. (1980; as cited in U.S. EPA, 2005)	NPR
	5/5, albino CD rat, gavage, 7 d/wk, 14 d	**0, 7.5, 15, 30, 60, 120 mg/kg-d**	**Hyaline droplet degeneration of tubular epithelium within the renal cortex of kidneys in 3 male rats at the highest dose; no other kidney effects observed; increased liver weight of unspecified magnitude at highest dose. Possible impurities in test compound preparation.**	**60**	**DU**	**120**	**Raltech Scientific Services, Inc. (1980; as cited in U.S. EPA, 2005)**	**PS, NPR**
Chronic	ND							
Developmental	ND							
Reproductive	ND							
Carcinogenicity	ND							
2. Inhalation								
Subchronic	NA							
Chronic	ND							
Developmental	ND							
Reproductive	ND							
Carcinogenicity	ND							

DU = data unsuitable; NA = not applicable; ND = no data; NDr = not determined; NPR = not peer reviewed; PS = principal study; S-D = Sprague-Dawley.

HUMAN STUDIES

No data on the effects of 3,4-DCBTF in humans following inhalation or oral exposure were identified. It was speculated by one source (ITC, 1983) that overexposure to vapors may cause irritation of the nose and throat (HSDB, 2011).

ANIMAL STUDIES

Oral Exposure

Short-Term Studies

Four unpublished (non-peer-reviewed) short-term oral studies in rats were identified in the literature.

Raltech Scientific Services, Inc. (1978; as cited in U.S. EPA, 2005); 28-day rat feeding study

In a 28-day, Good Laboratory Practice (GLP), range-finding study in Sprague-Dawley rats, five animals per sex per dose group were fed 0; 2; 20; 200; or 2,000 ppm 3,4-DCBTF (unknown purity) in the diet. The actual measured exposures were reported to be 2; 20; 211; or 2,440 ppm in the diet (timing of measurements not specified). However, the study authors subsequently amended the report with a note stating that the study was considered to be invalid because of the compound stability issue in feed as reported in Raltech Scientific Services, Inc. (1979). In addition, in the original report (Raltech Scientific Services, 1978), the study authors reported the presence of two unknown compounds in blood and urine from the treated animals at levels approximately equal to 3,4-DCBTF itself. These same two compounds were found in the stock 3,4-DCBTF preparation at levels up to 15% of the total mixture; it was unclear whether the 15% was representative of the total amount of impurities or each impurity. Although the study authors stated that the two impurities could have contributed to the toxicity of the mixture (Raltech Scientific Services, 1978), they concluded that the impurities were probably isomers of 3,4-DCBTF, perhaps of lower chlorination, but did not attempt to further identify or quantify these components.

Individual body weights and total weekly feed consumption were measured weekly on Days 7, 14, 21, and 28. Blood and urine samples were collected prior to the complete necropsy conducted on each animal. No treatment-related deaths were reported. Gross pathology demonstrated normal organ and tissue appearance in all rats, and the study authors stated that lesions were found in the lung and lymph nodes but were not considered to be treatment-related. There were no treatment-related effects on feed consumption, body weights, or body-weight gains for females. However, there was a slight dose- and duration-dependent reduction of body weights for males, although not statistically significant. Average male rat body weights at 4 weeks were reduced by 3-9%, with the largest reductions in the two highest dose groups. Average male body weights in the highest dose group for the previous 3 weeks were consistently lower than controls by about 5%. Body weights in previous weeks for all other treatment groups were the same as controls. Also, body-weight gains for males were reduced by 11-20% from control levels in all treatment groups in Week 4, with a 16% reduction at the lowest dose. A slight dose- and duration-dependent reduction in total weekly feed consumption for males was observed, culminating in reductions of 12 and 16% at 4 weeks in the two highest dose groups, respectively. Also, relative feed consumption (as a fraction of body weight) at 4 weeks was reduced by 5.6 and 7.4% for the two highest dose groups, respectively.

Although not statistically significant at the tested level ($p < 0.05$), reductions in feed consumption, body-weight gain, and body weight for treated males at 4 weeks are apparent and may have been treatment related. Actual exposures are difficult to quantify. Average daily oral exposures would have been lower but perhaps as high as 70% of nominal doses, given approximately a 10% average daily loss of 3,4-DCBTF from feed (based on the two reported weekly recovery measures of 9 and 52%). Inhalation exposures could also have been present. In addition, exposures to the two unidentified impurities, which might have been structurally-similar isomers, could have contributed to the outcomes. No effects on feed consumption or body weight were observed for 3,4-DCBTF after 4 weeks in the Raltech Scientific Services, Inc. (1979) study at higher exposure levels (see following). The combined uncertainties preclude the identification of a NOAEL or LOAEL for 3,4-DCBTF.

Raltech Scientific Services, Inc. (1979); 5-week rat feeding study

In a study originally designed to be 90 days in length, 15 male and 15 female Sprague-Dawley rats were dosed with 0; 125; 500; or 2,000 ppm (unknown purity) in an oil suspension in their feed, although dosages were not considered reliable as the compound was subsequently found to be unstable in feed by the study authors (see following). The study was conducted under GLP. The study was suspended after 5 weeks because 7-day stability studies indicated that the compound was rapidly lost from the feed within 24 hours after the initial assay, with only 9-52% remaining after 1 week from repeat studies. By this time, the animals had progressed through the first week of mating in the reproduction part of the study but apparently had been receiving a much lower dose than the protocol indicated (Raltech Scientific Services, 1979). Group mean weekly body weights and total feed consumption for the first 4 weeks were given in the report. For this assessment, U.S. EPA calculated average daily feed consumptions as fractions of body weight of 0.06 for males and 0.07 for females, with little variation across treatment groups. Nominal adjusted average intakes over the first 4 weeks were 0, 7.5, 30, and 120 mg/kg-day for males and 0, 8.8, 35, and 140 mg/kg-day for females.

The animals were observed twice a day, and individual body weights and feed consumption were measured on Days 7, 14, 21, and 28 of the test. Blood and urine samples were collected prior to terminal sacrifice, and all animals sacrificed were subjected to gross postmortem examinations. Body-weight gains were normal for all groups of animals and at necropsy, and all animals were "essentially normal." Five animals had congested lungs or lungs with pinpoint red foci, and four animals had uteri that were distended with fluid; the treatment groups in which these effects were observed were not specified. One animal had an enlarged thyroid, and another had an enlarged area in the mesenteric lymph nodes. The study authors considered none of these lesions to be treatment related.

The study authors (Raltech Scientific Services, 1979) stated that the study was considered invalid because of uncertainties regarding feed stability. In addition, U.S. EPA considers that the purity of the test compound was likely compromised considering the presence of two unidentified contaminants in the stock 3,4-DCBTF preparation for the previous 28-day range-finding study (Raltech Scientific Services, 1978); the study authors did not comment on this issue. As for the 28-day study (Raltech Scientific Services, 1979), significant inhalation exposure may have occurred. Because of the considerable uncertainties, a NOAEL or LOAEL cannot be identified for this study.

Elars Bioresearch Laboratories (1980; as cited in U.S. EPA, 2005); 14-day rat gavage study

In a 14-day range-finding study in Sprague-Dawley rats, three animals per sex per dose group were given 0, 7.5, 15, 30, 60, or 120 mg/kg-day of 3,4-DCBTF (95% purity) via daily gavage (Elars Bioresearch Laboratories, 1980; as cited in U.S. EPA, 2005). This study was conducted under GLP but was not peer reviewed. Corn oil was used as the diluent and vehicle control. Clinical pathology was performed on one animal per sex per dose group prior to terminal sacrifice. U.S. EPA (2005) stated that no treatment-related gross pathology or any other abnormalities were observed. Mean liver weights and liver-to-body-weight ratios were increased in treated groups and controls, but these were not statistically significant; the magnitude of the liver-weight changes and the dose groups in which they occurred were not reported in the secondary source (U.S. EPA, 2005). Original study results and statistical analyses are not available for review, so the magnitude of the liver-weight changes cannot be evaluated for establishing a LOAEL. Because of the lack of detail on liver weight, neither a NOAEL or LOAEL can be identified from this study.

Raltech Scientific Services, Inc. (1980; as cited in U.S. EPA, 2005); 14-day rat gavage study

Raltech Scientific Services, Inc. (1980; as cited in U.S. EPA, 2005)[1] is selected as the principal study for the derivation of screening provisional subchronic RfD. In a 14-day range-finding study in albino CD rats, 5 animals per sex per dose group were given 0, 7.5, 15, 30, 60, or 120 mg/kg-day of 3,4-DCBTF (unknown purity) via gavage (Raltech Scientific Services, Inc., 1980; as cited in U.S. EPA, 2005). Corn oil was used as the diluent and vehicle control. Compound stability is not an issue for this study because of gavage administration. Individual body weights were measured daily, and feed consumption was measured each week. Necropsy was performed on lungs, liver, and kidneys. In addition, erythrocyte count, total and differential leukocyte count, hemoglobin, and hematocrit were determined. Terminal absolute and relative liver weights in males at the highest dose, and "mean weight" at 30 mg/kg-day, were significantly increased compared to the control group; no details on the magnitude of the increases were provided. It is unclear from the study summary whether the "mean weight" increase at 30 mg/kg-day refers to body weight or organ weight increase, and in which sex this was observed. Gross pathology revealed a higher frequency of lung lesions in treated male rats overall, and increased treatment-related incidence of liver and kidney lesions. Histopathologic examination of the liver and kidney was performed. There was no dose-related pattern for observed liver lesions, and no correlation could be made between increase in liver weight and the number of liver lesions. According to the secondary source, U.S. EPA (2005), the changes in the liver were of low incidence and were not toxicologically significant. In the kidney, hyaline droplet degeneration of the tubular epithelium within the renal cortex occurred in five male rats, three of whom were in the high-dose group. According to U.S. EPA (2005), this lesion occurs spontaneously in the glomerulonephritis syndrome in rats but is infrequent in animals of this age. Therefore, U.S. EPA (2005) concluded that the degenerative changes found in the kidney may be test related.

Hyaline droplet accumulation in the renal proximal tubule epithelium in male rats could be an indicator of alpha-2 urinary globulin accumulation, which does not occur in humans. For a diagnosis of alpha-2 urinary globulin accumulation, a sequence of tubule epithelial cell necrosis,

[1]The original study report is not available.

granular cast formation, and medullary mineralization would need to be observed in the dose response (U.S. EPA, 1991). Because the primary source is no longer available for this study and U.S. EPA (2005) does not provide sufficient detail on the hyaline droplet accumulation, it is not known whether the kidney changes are indicative of alpha-2 urinary globulin accumulation, and, therefore, this possibility cannot be excluded from consideration. There was no evidence of other kidney pathology. Other kidney effects such as varying degrees of congestion were observed, but these were noted to be of low incidence and judged to be "not clearly dose-related" by U.S. EPA (2005). No data are available from the original study, which was neither peer-reviewed nor conducted under GLP. In addition, this study was conducted in the same laboratory as the Raltech Scientific Services, Inc. (1979, 1978), so there is a probability that impurities were present in the test compound stock preparation (at levels up to 15% of the total mixture). However, because compound stability in feed and inhalation coexposure are not concerns for this study, U.S. EPA has defined a NOAEL of 60 mg/kg-day and a LOAEL of 120 mg/kg-day based on the kidney effects observed in male rats in this study.

Elars Bioresearch Laboratories (1981)

This study was summarized in the Toxic Substances Control Act Test Submissions (SRC, 2010) database as a modified 90-day reproduction study in rats exposed to para-chlorobenzotrifluoride (PCBTF). However, the original report stated that both 3,4-DCBTF and PCBTF were tested but gave results only for PCBTF. The study was a 90-day reproduction study, in which 20 male and 20 female Sprague-Dawley rats per group were treated daily with either 0, 5, 15, or 45 mg/kg-day PCBTF (95% purity) via gavage for 4 weeks prior to mating. Parental rats were dosed until the F1 litters were born and weaned at 21 days of age (for a total of 76 to 83 days of dosing), and weanling rats were dosed daily for at least 90 days. Weekly body weight and feed consumption, clinical pathology, urinalysis, and gross necropsy were performed. This study was conducted under GLP but does not appear to be peer-reviewed. Increased absolute and relative liver weights were reported at the two highest doses, and increased absolute kidney weights were reported at the highest dose. No gross or microscopic lesions were observed in either organ. This study is only of interest with respect to the finding of increased kidney weights following exposure to a structurally-similar compound, and it supports the kidney effects reported in the principal study chosen for the screening subchronic p-RfD (Raltech Scientific Services, Inc.,1980; as cited inU.S. EPA, 2005). Otherwise, this study is not informative as to 3,4-DCBTF toxicity.

Inhalation Exposure

No studies were identified.

OTHER DATA

The genotoxicity and mutagenicity of 3,4-DCBTF has been tested in several in vitro studies (see Table 4) and one in vivo test system (see Table 5) with generally negative results. All of the genotoxicity/mutagenicity study results were obtained from secondary sources (listed in Table 5), and no original sources were available for review.

Table 4. Genotoxicity and Mutagenicity Studies of 3,4-Dichlorobenzotrifluoride In Vitro

Test System	Endpoint	Test Conditions	Results[a]		Dose[c]	Reference
			Without Activation	With Activation[b]		
Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538	Reverse mutation	Plate incorporation assay	–	–	10 µL/plate	Litton Bionetics, Inc. (1978; as cited in U.S. EPA, 2005)
Saccharomyces cerevisiae D4	Reverse mutation	Plate incorporation assay	–	–	10 µL/plate	Litton Bionetics, Inc (1978a; as cited in U.S. EPA, 2005)
Escherichia coli W3110/polA$^+$, P3478/polA$^-$	DNA Repair test	Plate incorporation assay	–	–	10 µL/plate	Litton Bionetics, Inc. (1978a; as cited in U.S. EPA, 2005)
Mouse lymphoma L5178Y cell lines	Forward mutation assay	4-hr exposure, total test 24 hr	–	–	31,300 µL/mL (nonactivation); 62,500 µL/mL (activation)	Litton Bionetics, Inc. (1978b; as cited in SRC, 2010)
Mouse lymphoma L5178Y cell lines	Sister chromatid exchange (SCE)	4-hr exposure	–	+	20 µL/mL	Stetka and Brusick (1979; as cited in U.S. EPA, 2005)
Human heteroploid EUE fibroblast cells	Induction of unscheduled DNA synthesis	Unknown	+?	+?	Unknown	ITC (1983; as cited in HSDB, 2011)
Mouse fibroblast BALB/3T3 cells	Cell transformation	Unknown	–?	–?	Unknown	ITC (1983; as cited in HSDB, 2011)

[a]+ = positive, – = negative, ± = equivocal, ND = no data, ? = positive or negative results identified, but activation status unknown.
[b]Exogenous metabolic activation used.
[c]Lowest effective dose for positive results, highest dose tested for negative or equivocal results.

Table 5. Mutagenicity Studies of 3,4-Dichlorobenzotrifluoride In Vivo

Test System	Endpoint	Test Conditions	Results[a]	Dose[b]	Reference
Mouse (CD-1 males)	Mouse Urine Assay	Mice given 50, 167, and 500 mg/kg by gavage once/d for 2 d. Urine samples collected and tested for mutagenicity. No details provided.	–	500 mg/kg	Litton Bionetics, Inc. (1979; as cited in U.S. EPA, 2005)

[a]+ = positive, – = negative.
[b]Lowest effective dose for positive results, highest dose tested for negative or equivocal results.

DERIVATION OF PROVISIONAL VALUES

Tables 6 and 7 present a summary of noncancer and cancer reference values, respectively. IRIS data are indicated in the table, if available.

Table 6. Summary of Noncancer Reference Values for 3,4-Dichlorobenzotrifluoride (CASRN 328-84-7)

Toxicity Type (units)	Species/Sex	Critical Effect	p-Reference Value	POD Method	POD_{HED}	UF_C	Principal Study
Screening subchronic p-RfD (mg/kg-d)	Rat/M	Kidney lesions	5×10^{-2}	NOAEL	14.4	300	Raltech Scientific Services, Inc. (1980; as cited in U.S. EPA, 2005)
Screening chronic p-RfD (mg/kg-d)	NDr						
Subchronic p-RfC (mg/m^3)	NDr						
Chronic p-RfC (mg/m^3)	NDr						

NDr = Not determined.

Table 7. Summary of Cancer Values for 3,4-Dichlorobenzotrifluoride (CASRN 328-84-7)

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

NDr = Not determined.

DERIVATION OF ORAL REFERENCE DOSES

Derivation of Subchronic Provisional RfD (Subchronic p-RfD)

Four studies were evaluated for deriving a screening subchronic p-RfD for 3,4-DCBTF. Two short-term feeding studies (Raltech Scientific Services, 1979, 1978) were excluded because of test compound volatility in feed, resulting in highly uncertain oral exposures and potential secondary inhalation exposures of unknown magnitude. In addition, two unidentified contaminants at relatively high levels in blood and urine samples in the treated animals further complicated the interpretation of the results. A 14-day rat gavage study (Raltech Scientific Services, 1980; as cited in U.S. EPA, 2005) was also discounted because details on reported increases in liver weight were lacking. The original study report for the remaining 14-day gavage study in rats (Raltech Scientific Services, Inc., 1980; as cited in U.S. EPA, 2005) was not available, so this study was also deemed inadequate for the derivation of a subchronic p-RfD. However, the (Raltech Scientific Services, Inc., 1980; as cited in U.S. EPA, 2005) 14-day gavage study in rats is used as the principal study to derive a screening subchronic p-RfD provided in Appendix A of this document.

Derivation of Chronic Provisional RfD (Chronic p-RfD)

There were no chronic studies located regarding the toxicity of oral exposure to 3,4-DCBTF and, as stated above, the existing data are similarly insufficient for derivation of a chronic p-RfD. Therefore, no chronic p-RfD is derived. In addition, no screening chronic p-RfD is derived because the two unpublished 14-day studies (Elars Bioresearch Laboratories, 1980; as cited in U.S. EPA, 2005; Raltech Scientific Services, Inc., 1980; as cited in U.S. EPA, 2005) are deemed to be of inadequate duration for extrapolation to chronic exposure duration.

DERIVATION OF INHALATION REFERENCE CONCENTRATIONS

There are no relevant inhalation studies for evaluating subchronic or chronic toxicity from 3,4-DCBTF exposure. The only inhalation study found was an acute lethality study in rats (Duckworth, 1979; as cited in U.S. EPA, 2005) and is not suitable for consideration as the basis for any provisional value from inhalation exposure to 3,4-DCBTF.

Derivation of Subchronic Provisional RfC (Subchronic p-RfC)

A subchronic p-RfC cannot be derived for 3,4-DCBTF because no subchronic inhalation data are available.

Derivation of Chronic Provisional RfC (Chronic p-RfC)

A chronic p-RfC cannot be derived for 3,4-DCBTF because no chronic inhalation data are available.

CANCER WEIGHT-OF-EVIDENCE (WOE) DESCRIPTOR

There are no human or animal data available on the carcinogenicity of 3,4-DCBTF. U.S. EPA has not classified 3,4-DCBTF for carcinogenicity, and no other agencies have reviewed or classified the carcinogenic potential of the chemical (IARC, 2010; Cal/EPA, 2008; NTP, 2005). The cancer WOE descriptor for 3,4-DCBTF is *"Inadequate Information to Assess Carcinogenic Potential"* (see Table 8).

Table 8. Cancer WOE Descriptor for 3,4-Dichlorobenzotrifluoride			
Possible WOE Descriptor	**Designation**	**Route of Entry**	**Comments**
"Carcinogenic to Humans"	NA	NA	No human carcinogenicity studies were identified.
"Likely to Be Carcinogenic to Humans"	NA	NA	No animal carcinogenicity studies were identified.
"Suggestive Evidence of Carcinogenic Potential"	NA	NA	No animal carcinogenicity studies were identified.
"Inadequate Information to Assess Carcinogenic Potential"	**Selected**	**Both**	**Selected due to the lack of any data on carcinogenicity.**
"Not Likely to Be Carcinogenic to Humans"	NA	NA	There are no data to indicate that 3,4-dichlorobenzotrifluoride is not likely to be carcinogenic to humans.

Mutagenicity studies for 3,4-DCBTF have demonstrated generally negative results. Results of the Ames test in *Salmonella typhimurium*, yeast, and *E. coli* were negative, as were the fibroblast cell transformation assay, the forward mutation assay, and an in vivo urine mutagenicity assay (ITC, 1983; as cited in HSDB, 2011; Litton Bionetics, Inc., 1978b; as cited in SRC, 2010; Litton Bionetics, Inc., 1978a, 1979, as cited in U.S. EPA, 2005). Positive results were noted in a sister chromatid exchange assay (Stetka and Brusick, 1979; as cited in U.S. EPA, 2005), and 3,4-DCBTF induced unscheduled DNA synthesis in EUE cells (ITC, 1983; as cited in HSDB, 2011). In the absence of epidemiological or rodent carcinogenicity studies, there is inadequate information to assess the carcinogenic potential of 3,4-DCBTF.

DERIVATION OF PROVISIONAL CANCER POTENCY VALUES

Derivation of Provisional Oral Slope Factor (p-OSF)

No p-OSF can be derived for 3,4-DCBTF because no carcinogenicity data are available by the oral route of exposure.

Derivation of Provisional Inhalation Unit Risk (p-IUR)

No p-IUR can be derived for 3,4-DCBTF because no carcinogenicity data are available by the inhalation route of exposure.

APPENDIX A. PROVISIONAL SCREENING VALUES

For reasons noted in the main PPRTV document, it is inappropriate to derive provisional subchronic or chronic p-RfDs for 3,4-DCBTF. 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.

DERIVATION OF SCREENING PROVISIONAL ORAL REFERENCES DOSES

Derivation of Screening Subchronic Provisional RfD (Screening Subchronic p-RfD)

Four studies were evaluated for deriving a screening subchronic p-RfD for 3,4-DCBTF. Two short-term feeding studies (Raltech Scientific Services, 1979, 1978) were excluded because of test compound volatility in feed, resulting in highly uncertain oral exposures and potential secondary inhalation exposures of unknown magnitude. In addition, two unidentified contaminants at relatively high levels in blood and urine samples in the treated animals further complicated the interpretation of the results. A 14-day rat gavage study (Raltech Scientific Services, 1980) was also discounted because details on reported increases in liver weight were lacking. A single 14-day study was deemed adequate for the determination of a screening subchronic p-RfD (Raltech Scientific Services, Inc., 1980; as cited in U.S. EPA, 2005). The original study report is not available for review; the results were summarized in U.S. EPA's High Production Volume Information System (2005). This secondary source (U.S. EPA, 2005) is not considered a peer-reviewed document. For this reason, use of this study as a principal study is restricted to derivation of a screening value.

The selected principal study (Raltech Scientific Services, Inc., 1980; as cited in U.S. EPA, 2005) was a 14-day range-finding study using albino CD rats given 0, 7.5, 15, 30, 60, or 120 mg/kg-day of 3,4-DCBTF (unknown purity) via gavage. This study was not conducted according to GLP (U.S. EPA, 2005). The study used five animals of each sex per dose group, and only liver and kidney effects were examined. Hyaline droplet degeneration of tubular epithelium in the renal cortex of the kidneys in male rats was observed. Because the primary study was not available, it is not possible to determine whether the hyaline droplet degeneration of tubular epithelium in the renal cortex of the kidneys in male rats was indicative of alpha 2u-globulin accumulation. Consequently, the observed kidney lesions are considered relevant to humans (U.S. EPA, 1991). No other kidney effects were reported. The Elars Bioresearch Laboratories (1981) study of the structurally related PCBTF isomer in rats reported increased kidney weights at the highest dose (although no kidney lesions were observed), supporting the kidney as a target for 3,4-DCBTF toxicity . Liver lesions were also reported in the (Raltech Scientific Services, Inc., 1980; as cited in U.S. EPA, 2005), but no correlation could be made between increase in liver weight and the number of liver lesions. According to U.S. EPA (2005), the changes in the liver were of low incidence and were not toxicologically significant. A

NOAEL of 60 mg/kg-day and a LOAEL of 120 mg/kg-day based on the kidney effects were identified for Raltech Scientific Services, Inc. (1980; as cited in U.S. EPA, 2005). Although the increase in absolute and relative liver weights in males at 120 mg/kg-day could be considered a possible co-critical effect, the incidence and magnitude of these increases were not reported in the secondary source (U.S. EPA, 2005). Therefore, the kidney lesions are considered as the primary critical effect, and the NOAEL of 60 mg/kg-day was selected as the point of departure (POD) for derivation of the screening subchronic p-RfD.

In U.S. EPA's *Recommended Use of Body Weight$^{3/4}$ as the Default Method in Derivation of the Oral Reference Dose* (U.S. EPA, 2011c), the Agency endorses a hierarchy of approaches to derive human equivalent oral exposures from data from laboratory animal species, with the preferred approach being physiologically based toxicokinetic (PBTK) modeling. Other approaches may include using some chemical-specific information, without a complete PBTK model. In lieu of chemical-specific models or data to inform the derivation of human equivalent oral exposures, U.S. EPA endorses body weight (BW) scaling to the 3/4 power (i.e., $BW^{3/4}$) as a default to extrapolate toxicologically equivalent doses of orally administered agents from all laboratory animals to humans for the purpose of deriving an RfD under certain exposure conditions. More specifically, the use of $BW^{3/4}$ scaling for deriving a RfD is recommended when the observed effects are associated with the parent compound or a stable metabolite but not for portal-of-entry effects or developmental endpoints.

A PBTK model for 3,4-DCBTF is not available for use in extrapolating doses from animals to humans. The critical effect (kidney lesions) is not a portal-of-entry or developmental effect and is presumed to be associated with the parent compound or a stable metabolite. Therefore, scaling by $BW^{3/4}$ is relevant for deriving human equivalent doses (HEDs) for these effects.

Following U.S. EPA (2011c) guidance, the POD for kidney effects in adult animals is converted to an HED through application of a dosimetric adjustment factor (DAF)[2] derived as follows:

$$DAF = (BW_a^{1/4} \div BW_h^{1/4})$$

Where:

DAF = dosimetric adjustment factor
BW_a = animal body weight
BW_h = human body weight

Using a BW_a of 0.25 kg for rats and a BW_h of 70 kg for humans (U.S. EPA, 1988), the resulting DAF is 0.24. Applying this DAF to the NOAEL, identified for the critical effect in mature rats yields a $NOAEL_{HED}$ as follows:

[2]As described in detail in *Recommended Use of Body Weight$^{3/4}$ as the Default Method in Derivation of the Oral Reference Dose* (U.S. EPA, 2011c), rate-related processes scale across species in a manner related to both the direct ($BW^{1/1}$) and allometric scaling ($BW^{3/4}$) aspects such that $BW^{3/4} \div BW^{1/1} = BW^{-1/4}$, converted to a $DAF = BW_a^{1/4} \div BW_h^{1/4}$.

$NOAEL_{HED}$ = NOAEL (mg/kg-day) × DAF
= 60 mg/kg-day × 0.24
= 14.4 mg/kg-day

The screening subchronic p-RfD for 3,4-DCBTF is derived as follows:

Screening Subchronic p-RfD = $NOAEL_{HED}$ ÷ UF
= 14.4 mg/kg-day ÷ 300
= **5×10^{-2} mg/kg-day**

The composite UF of 300 is estimated, as presented in Table A.1.

Table A.1. Uncertainty Factors for Screening Subchronic p-RfD of 3,4-Dichlorobenzotrifluoride

UF	Value	Justification
UF_A	3	A UF_A of 3 ($10^{0.5}$) has been applied to account for uncertainty in characterizing the toxicodynamic differences between rats and humans following oral 3,4-DCBTF exposure. The toxicokinetic uncertainty has been accounted for by calculation of a human equivalent dose (HED) through application of a dosimetric adjustment factor (DAF) as outlined in the U.S. EPA's *Recommended Use of Body Weight$^{3/4}$ as the Default Method in Derivation of the Oral Reference Dose*(U.S. EPA, 2011c).
UF_D	10	A UF_D of 10 has been applied because there are no acceptable two-generation reproductive toxicity or developmental toxicity studies.
UF_H	10	A UF_H of 10 has been applied for inter-individual variability to account for human-to-human variability in susceptibility in the absence of quantitative information to assess the toxicokinetics and toxicodynamics of 3,4-DCBTF in humans.
UF_L	1	A UF_L of 1 has been applied for LOAEL-to-NOAEL extrapolation because the POD is a NOAEL.
UF_S	1	Although the duration of the principal study (Raltech Scientific Services, Inc., 1980; as cited in U.S. EPA, 2005) is less than subchronic at 14 days, a UF_S of 1 has been applied.
UF_C	300	

Derivation of Screening Chronic Provisional RfD (Screening Chronic p-RfD)

The 14-day study used is deemed to be of inadequate duration for extrapolation to chronic exposure durations. Therefore, no screening chronic p-RfD is derived.

APPENDIX B. DATA TABLES

No data tables are presented.

APPENDIX C. BMD MODELING OUTPUTS

No BMD modeling was performed.

APPENDIX D. REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). (2013). 2013 TLVs and BEIs. Based on documentation of the threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH.

ATSDR (Agency for Toxic Substances and Disease Registry). (2013). Minimal risk levels (MRLs) for hazardous substances. Atlanta, GA. Retrieved from http://www.atsdr.cdc.gov/mrls/mrllist.aspID - 2

Cal/EPA (California Environmental Protection Agency). (2008). Cal/EPA - OEHHA toxicity criteria database. Sacramento, CA: Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/risk/ChemicalDB/index.asp

Cal/EPA (California Environmental Protection Agency). (2009). Appendix A: Hot spots unit risk and cancer potency values. Sacramento, CA: Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/air/hot_spots/2009/AppendixA.pdf

Cal/EPA (California Environmental Protection Agency). (2012a). All OEHHA acute, 8-hour and chronic reference exposure levels (chRELs) as on February 2012. Sacramento, CA: Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/air/allrels.html

Cal/EPA (California Environmental Protection Agency). (2012b). OEHHA toxicity criteria database. Sacramento, CA: Office of Environmental Health Hazard Assessment. http://www.oehha.ca.gov/tcdb/

ChemBlink. 3,4 Dichlorobenzotrifluoride [Database]. Retrieved from http://www.chemblink.com/products/328-84-7.htm

Chen, HCB; Lindrose, M. Single phase cleaning fluid, (Occidental Chemical Corporation2000). http://patents.justia.com/2000/06020299.html

Elars Bioresearch Labs (Elars Bioresearch Laboratories Inc.). (1981). Modified 90 day gavage and reproduction study in rats: 3,4-DCBTF. (408188012). Niagara Falls, NY: Hooker Chemical Company.

HSDB (Hazardous Substances Data Bank). (2011). 3,4-Dichlorobenzotrifluoride (CASRN: 328-84-7). Washington, DC: National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+328-84-7

IARC (International Agency for Research on Cancer). IARC Monographs on the evaluation of carcinogenic risk to humans. Available online at http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php. Accessed 8-1-2013.

IARC (International Agency for Research on Cancer). (2010). Ingested nitrate and nitrite and cyanobacterial peptide toxins. Lyon, France. http://monographs.iarc.fr/ENG/Monographs/vol94/mono94.pdf

ITC (TSCA Interagency Testing Committee). (1983). 3,4-dichlorobenzotrifluoride: Information review #346 (draft) [EPA Report]. (EPA 560/ITC/83-0264). Washington, DC: U.S. Environmental Protection Agency.

NIOSH (National Institute for Occupational Safety and Health). (2010). NIOSH pocket guide to chemical hazards. Index of chemical abstracts service registry numbers (CAS No.). Atlanta, GA: Center for Disease Control and Prevention, U.S. Department of Health, Education and Welfare. http://www.cdc.gov/niosh/npg/npgdcas.html

NTP (National Toxicology Program). (2005). Report on carcinogens, eleventh edition. Research Triangle Park, NC. http://ntp.niehs.nih.gov/index.cfm?objectid=32BA9724-F1F6-975E-7FCE50709CB4C932

NTP (National Toxicology Program). (2011). Report on carcinogens: Twelfth edition (12th ed.). Research Triangle Park, NC. http://ntp.niehs.nih.gov/ntp/roc/twelfth/roc12.pdf

OSHA (Occupational Safety & Health Administration). (2006). Table Z-1 limits for air contaminants. Occupational Safety and Health Administration. http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=9992

OSHA (Occupational Safety & Health Administration). (2011). Air contaminants: occupational safety and health standards for shipyard employment, subpart Z, toxic and hazardous substances. (OSHA Standard 1915.1000). Washington, DC: U.S. Department of Labor. http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10286

Raltech Scientific Services (Raltech Scientific Services Inc.). (1978). 3,4-Dichlorobenzotrifluoride 28-day Feeding Study in Rats. (OTS0526723; EPA Doc # 40-7888046). Madison, WI: Raltech Scientific Services, Inc. http://www.ntis.gov/search/product.aspx?ABBR=OTS0526723

Raltech Scientific Services (Raltech Scientific Services Inc.). (1979). Analytical data on 3,4-DCBTF in feed and animal data through termination of 90-day feeding and reproduction study. (40-7988050; OTS0526731). Niagra Falls, NY: Hooker Chemical and Plastics Company. http://www.ntis.gov/search/product.aspx?ABBR=OTS0526731

Raltech Scientific Services (Raltech Scientific Services Inc.). (1980). 3,4-DCBTF 14-day range feeding and reproduction study in rats. (Study No. 79508-B). Raltech Scientific Services, Madison WI for Hooker Chemicals and Plastics Corporation, Niagara Falls, NY. (As cited in U.S. EPA 2005).

SRC (Syracuse Research Corporation). (2010). 3,4 dichlorobenzotrifluoride [Database]. Syracuse, NY: TSCATS; SRC. Retrieved from http://www.syrres.com/esc/tscats.htm

U.S. EPA (U.S. Environmental Protection Agency). Integrated risk information system (IRIS). Available online at http://dx.doi.org/10.1177/1091581812466418. Accessed on 8-1-2013.

U.S. EPA (U.S. Environmental Protection Agency). (1987). Testing consent order on 3,4-dichlorobenzotrifluoride and response to the Interagency Testing Committee: Final rule. Fed Reg 52: 23547-23548.

U.S. EPA (U.S. Environmental Protection Agency). (1988). Recommendations for and documentation of biological values for use in risk assessment [EPA Report]. (EPA/600/6-87/008). Cincinnati, OH. http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=34855

U.S. EPA (U.S. Environmental Protection Agency). (1991). Alpha-2u-globulin: Association with chemically induced renal toxicity and neoplasia in the male rat [EPA Report]. (EPA/625/3-91/019F). Washington, DC. http://www.ntis.gov/search/product.aspx?ABBR=PB92143668

U.S. EPA (U.S. Environmental Protection Agency). (1994). Chemical assessments and related activities (CARA) [EPA Report]. (600R94904; OHEA-I-127). Washington, DC. http://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=60001G8L.txt

U.S. EPA (U.S. Environmental Protection Agency). (2005). High Production Volume Information System (HPVIS) - Chemical name: Benzene, 1,2 dichloro 4-(trifluoromethyl)- CAS Number: 328-84-7 [EPA Report]. http://iaspub.epa.gov/oppthpv/quicksearch.display?pChem=101941

U.S. EPA (U.S. Environmental Protection Agency). (2011a). 2011 Edition of the drinking water standards and health advisories [EPA Report]. (EPA 820-R-11-002). Washington, DC. http://water.epa.gov/action/advisories/drinking/upload/dwstandards2011.pdf

U.S. EPA (U.S. Environmental Protection Agency). (2011b). Health Effects Assessment Summary Tables (HEAST). Available online at http://epa-heast.ornl.gov/

U.S. EPA (U.S. Environmental Protection Agency). (2011c). Recommended use of body weight 3/4 as the default method in derivation of the oral reference dose [EPA Report]. (EPA/100/R11/0001). Washington, DC. http://www.epa.gov/raf/publications/interspecies-extrapolation.htm

WHO (World Health Organization). Online catalog for the Environmental Health Criteria Series. Available online at http://www.who.int/ipcs/publications/ehc/en/. Accessed on 8-1-2013.

Yih, RY; Swithenbank, C. (1975). New potent diphenyl ether herbicides. J Agric Food Chem 23: 592-593.