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Provisional Peer Reviewed Toxicity Values for

Dibenzofuran
(CASRN 132-64-9)

Superfund Health Risk Technical Support Center
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U.S. Environmental Protection Agency
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Acronyms and Abbreviations

bw	body weight
cc	cubic centimeters
CD	Caesarean Delivered
CERCLA	Comprehensive Environmental Response, Compensation and Liability Act of 1980
CNS	central nervous system
cu.m	cubic meter
DWEL	Drinking Water Equivalent Level
FEL	frank-effect level
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
g	grams
GI	gastrointestinal
HEC	human equivalent concentration
Hgb	hemoglobin
i.m.	intramuscular
i.p.	intraperitoneal
IRIS	Integrated Risk Information System
IUR	inhalation unit risk
i.v.	intravenous
kg	kilogram
L	liter
LEL	lowest-effect level
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
m	meter
MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MF	modifying factor
mg	milligram
mg/kg	milligrams per kilogram
mg/L	milligrams per liter
MRL	minimal risk level
MTD	maximum tolerated dose
MTL	median threshold limit
NAAQS	National Ambient Air Quality Standards
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
PBPK	physiologically based pharmacokinetic
ppb	parts per billion
ppm	parts per million
PPRTV	Provisional Peer Reviewed Toxicity Value
RBC	red blood cell(s)
RCRA	Resource Conservation and Recovery Act
RDDR	Regional deposited dose ratio (for the indicated lung region)
REL	relative exposure level
RfC	inhalation reference concentration
RfD	oral reference dose
RGDR	Regional gas dose ratio (for the indicated lung region)
s.c.	subcutaneous
SCE	sister chromatid exchange
SDWA	Safe Drinking Water Act
sq.cm.	square centimeters
TSCA	Toxic Substances Control Act
UF	uncertainty factor
µg	microgram
µmol	micromoles
VOC	volatile organic compound

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PROVISIONAL PEER REVIEWED TOXICITY VALUES FOR DIBENZOFURAN (CASRN 132-64-9)

Background

On December 5, 2003, the U.S. Environmental Protection Agency'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. EPA's Integrated Risk Information System (IRIS).

2. Provisional Peer-Reviewed Toxicity Values (PPRTV) used in 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 EPA's Integrated Risk Information System (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 EPA IRIS Program. All provisional toxicity values receive internal review by two EPA scientists and external peer review by three independently selected scientific experts. PPRTVs differ from IRIS values in that PPRTVs do not receive the multi-program consensus review provided for IRIS values. This is because IRIS values are generally intended to be used in all 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 five-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 manuscripts 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 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 manuscript and understand the strengths and limitations of the derived provisional values. PPRTVs are developed by the EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center for OSRTI. Other 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 EPA Office of Research and Development's National Center for Environmental Assessment, Superfund Health Risk Technical Support Center (513-569-7300), or OSRTI.

This document has passed the STSC quality review and peer review evaluation indicating that the quality is consistent with the SOPs and standards of the STSC and is suitable for use by registered users of the PPRTV system.

INTRODUCTION

RfD and RfC values for dibenzofuran (DBF) were not available on IRIS (U.S. EPA, 2007) or in the HEAST (U.S. EPA, 1997). There is a Class D cancer assessment on IRIS (U.S. EPA, 2007). Dibenzofuran was included in a Drinking Water Toxicity Profile from 1992 (U.S. EPA, 1992), although no oral toxicity value was listed. The Office of Water did not include dibenzofuran on the latest Drinking Water Regulations (U.S. EPA, 2006a) or the Drinking Water Contaminant Candidate List (U.S. EPA, 2006b). The CARA list (U.S. EPA, 1991, 1994)

included a Health Effects Assessment (HEA) (U.S. EPA, 1987) and a Reportable Quantity Document (U.S. EPA, 1989) for Dibenzofuran. The HEA concluded that additional toxicity testing was necessary and did not derive a toxicity value due to the lack of data (U.S. EPA, 1987). The 1987 HEA for Dibenzofuran neither identified nor included discussion of Thomas et al. (1940), the primary source of data used in this PPRTV document. By contrast, the 1989 Reportable Quantity Document for Dibenzofuran (U.S. EPA, 1989) used Thomas et al. (1940) as the basis for derivation of composite scores and the corresponding reportable quantities for dibenzofuran.

ATSDR had not published a Toxicological Profile for dibenzofuran (ATSDR, 2006). NTP did not study the toxicity of dibenzofuran (NTP, 2006). WHO (2006) provided no relevant information. Available data on carcinogenicity, mutagenicity, metabolism, and other biological effects were summarized for dibenzofuran by the National Cancer Institute (NCI, 2000). Data on the adverse health effects of various halogenated dibenzofurans were available; however, the biological activity varies greatly among these congeners. U.S. EPA (1986a) did not recommend risk assessment by analogy to any of these more widely studied chemicals. NCI (2000) reported that the most structurally related chemical was dibenzo-p-dioxin. NCI (1979) reported that no excess tumors were induced in rats or mice fed dibenzo-p-dioxin up to 10,000 ppm in the diet.

Updated literature searches for noncancer and cancer data were conducted for data available through April 2006. The databases searched included: TOXLINE, MEDLINE, CANCERLIT, CCRIS, TSCATS, HSDB, RTECS, GENETOX, DART/ETICBACK, and EMIC/EMICBACK. Inhalation RfC values were not derived for dibenzofuran, because no human or animal inhalation data were found and the marginal ingestion data seemed inadequate to consider for inter-route extrapolation. However, a subchronic oral p-RfD value was derived, based on a LOAEL point of departure (POD) in Thomas et al. (1940). Chronic toxicity of dibenzofuran is discussed in the appendix. No data were identified from which to derive cancer risk values.

REVIEW OF PERTINENT DATA

Human Studies

Two cross-sectional studies of exposed workers were identified in the OPPT TSCATS database (Koppers 1980a,b). However, these studies reported exposures to dibenzofuran only in complex mixtures of coal tar products. Neither report noted adverse health effects that could be attributed to dibenzofuran exposure. Existing review documents and a detailed literature search identified no other data regarding the toxicity of dibenzofuran in humans.

Animal Studies

The only long-term toxicity data available for dibenzofuran were from a 200-day rat feeding study reported by Thomas et al. (1940). However, this document also will address the NCI (1979) data for dibenzo-p-dioxin, which NCI (2000) considered to be the chemical most structurally related to dibenzofuran.

NCI (1979) reported that unsubstituted dibenzo-p-dioxin, a structural analog of dibenzofuran, exhibited very low toxicity and no evidence of carcinogenicity in Osborne-Mendel rats and B6C3F1 mice, even when the maximum tolerated dose was approached (10,000 ppm in diet). Groups of 35 rats of each gender ingested dibenzo-p-dioxin at 5000 or 10,000 ppm in diet for 110 weeks. Groups of 50 mice of each gender ingested the same doses for 87 or 90 weeks. Controls consisted of groups of 35 untreated rats of each gender and 50 untreated mice of each gender. Mean body weights of the dosed male and female rats and mice were lower than those of the corresponding controls; the depression in the amount of weight gained in the dosed male mice was, however, relatively slight. Except for the male rats, survival at the end of the bioassay was lower in the dosed groups of both rats and mice than in the corresponding control groups. At week 90, at least 57% of the rats and 54% of the mice were still alive. In some male and female rats there was a dose-related increase in the incidence of hepatotoxic alterations characterized by fatty metamorphosis or necrosis. Also in mice, toxic hepatic lesions including liver degeneration, necrosis, fibrosis and/or cirrhosis were observed in slightly increased numbers in the dosed mice ─ particularly in the high-dose females. No tumors were induced in rats or mice of either gender at incidences that were significantly higher in the dosed groups than in the corresponding control groups. The authors concluded that unsubstituted dibenzo-p-dioxin exhibited very low toxicity and was noncarcinogenic in Osborne-Mendel rats and B6C3F1 mice, even when the maximum tolerated dose was approached (10,000 ppm in diet).

The Thomas et al. (1940) report consisted of two studies, a primary 200-day dibenzofuran feeding study and a follow-up 78-day study. In the primary study, groups of five female albino rats (strain not specified), approximately 30 days old, consumed 0, 250, 500, 1000, 2000, or 4000 ppm of dibenzofuran in their food for 200 days. In addition, two female rats consumed 8000 ppm of dibenzofuran in their diet for a shorter period (approximately 100 days). According to the authors, none of the animals exhibited any abnormal activity or behavior, nor was food intake appreciably altered by dibenzofuran administration, although it was noted that the rats receiving dibenzofuran tended to consume more water than controls. The authors also reported no effect on body weight gain at any dose during the exposure period; however, decreases in body length and absolute organ weights were observed in all dibenzofuran-exposed groups at necropsy. The authors also reported that the treated animals had unusually large amounts of abdominal fat, which they interpreted as accounting for the lack of effect on body weight gain. Quantitative data were not provided to support the assertions of no appreciable

changes in food intake or body weight gain, decreases in organ weight and overall length, and excess abdominal fat. In addition, the authors did not report whether a dose-response effect was observed for changes in body length or organ weight, or for excess abdominal fat.

Histological examination of the liver, kidney, spleen, heart, and adrenals was performed in rats exposed to dibenzofuran at 500 ppm and higher, and in the control animals (Thomas et al., 1940). The low dose group (250 ppm) apparently was not examined for histopathology. In the kidney, histological examination of rats exposed to concentrations of 500 ppm and higher revealed fine, brown-pigmented granules in the epithelial cells of proximal convoluted tubules in the deeper parts of the renal cortex. This effect was noted among all rats receiving dibenzofuran, and both the amount of pigmented material within cells and the frequency of occurrence among cells increased with dose of dibenzofuran. In addition, the two rats fed diet containing 8000 ppm dibenzofuran exhibited prominent, irregular dilatation of the collecting tubules with coagulated material resembling protein; other tubules in these two rats were slightly dilated and contained more granular and amorphous material than controls. These effects were reported as occurring without cellular degeneration or glomerular abnormalities. Some (frequency not specified) of the kidneys from rats receiving 4000 ppm showed similar, but less severe, changes. These lesions were not reported among rats fed the lower doses of dibenzofuran. However, quantitative data were not reported. In the spleen, slight hyperplasia of the Malpighian bodies was reported among several rats (frequency not given) in the 4000 and 8000 ppm groups. No alterations, other than reduced organ weight, were noted in the liver, heart, or adrenals of the treated rats.

In the follow-up study to determine whether dietary dibenzofuran affected water balance, an effect noted qualitatively (increased water consumption) in female rats receiving dibenzofuran in their food, Thomas et al. (1940) exposed groups of five male rats (average initial body weight 255 grams) to 0 or 5000 ppm of dibenzofuran in the diet for 78 days. Treated rats exhibited greater water consumption and urine output than controls, suggesting that dibenzofuran altered water balance. The excess in urine output was greater than the excess in water consumption in the treated group, suggesting a slight dehydration of tissues. The authors reported that no alterations in hematological parameters were observed (hemoglobin and erythrocyte, leukocyte, and reticulocyte counts). Tables 1 and 2 have summarized the hematological data reported in the 78-day study.

TABLE 1. Blood cell types in rats exposed to DBF in normal diet for 78 days

Dose	Rats "N"	Hemoglobin	Erythrocytes	Reticulocytes	White cells
0	10	16.3%	8.12×10^6	3.0%	1.44×10^4
5000 ppm	5	16.6%	9.07×10^6	2.35%	1.65×10^4

TABLE 2. Average differential white blood cell counts in 78-day exposed rats vs. "normal rat blood"

Dose	Rats "N"	Lymphocytes	Polymorphonuclear nutrophils	Monocytes	Basophiles	Eosinophils
"Normal"	---	67.9%	27%	5.3%	0.77%	2.1%
5000 ppm	5	63.8%	33.5%	1.18%	0.64%	0.94%

In contrast to qualitative observations reported among the female rats exposed to similar concentrations in the 200-day primary study, the male rats treated for 78 days tended to consume less food than the controls and had a slightly lower rate of body weight gain than the control group. These data and water consumption data are summarized in Table 3. The authors noted that the odor and taste of dibenzofuran at 5000 ppm in the food was distinctly noticeable and may have contributed to this effect. Histological examination was not performed on tissues from these rats.

TABLE 3. Weight gain in male albino rats fed DBF for 78 days vs. controls

Dose	Rats "N"	Weight gain	Food ingestion	Water ingestion
0	5	321 g	6108 g	9652 cc
5000 ppm	5	243 g	5482 g	10,316 cc
Difference	- - - - -	78 g (24%)	626 g (10%)	664 cc (6.9%)

The literature search revealed additional, peripheral data for dibenzofuran, including those for soil nitrification organisms (Sverdrup et al., 2002), drought resistance of certain insects (Sjursen et al., 2001), plant seedling growth (Sverdrup et al., 2003), fungi-specific enzyme systems (Kurihara et al., 2002), and a study of human intellectual effects of exposure (Schantz, 2001) that mistakenly refered to unhalogenated dibenzofuran. Abstracts for these studies reported the following conclusions.

- 75 mg DBF/kg (soil) NOEL for soil nitrification and no effects on soil bacterial diversity (Sverdrup et al., 2002)

- No dose-related decrease in drought tolerance in adult soil-dwelling insects, *Folsomia fimetaria* (Sjursen et al., 2001)
- 20% reduction in plant seedling weight when exposed to 43-93 mg DBF /kg soil (Sverdrup et al., 2003)
- No change in expression of NADH-ubiquinone oxidoreductase (NUO) among DBF-exposed fungus, *Phanerochaete chrysosporium* (Kurihara et al., 2002)

DERIVATION OF A PROVISIONAL SUBCHRONIC ORAL RfD VALUE FOR DIBENZOFURAN

The only subchronic or chronic toxicity data available for dibenzofuran were from the 200-day and 78-day feeding studies described by Thomas et al. (1940). These studies, though of apparently high quality for their era, had a number of major short comings, including the following:

- only qualitative data were reported for most endpoints
- only five organs were examined in the pathology
- the lowest dose group was not subjected to pathology examinations

No pertinent developmental or reproductive data were found for dibenzofuran. The LOAEL data from the Thomas et al. (1940) 200-day feeding study provided the POD for this derivation, because no NOAEL was reported. Data from the 78-day study were used to confirm food ingestion rates estimated using default rates in U.S. EPA, 1986b. Benchmark dose modeling was considered infeasible because adverse effects and the dose-response nature of the response were reported only qualitatively.

The lowest dose tested in the 200-day Thomas et al., 1940 study, 250 ppm in diet, was selected as the LOAEL POD for the aggregate critical effects of reduced length and organ weight, and excess abdominal fat. Ingestion data from the 78-day study was used to estimate the actual doses to the animals treated at the LOAEL, as follows. The 78-day feeding study was conducted under the same conditions as the 200-day primary study. This estimation made the following assumptions.

- Data from the 78-day study (Thomas et al., 1940) were more likely to represent actual food intakes than the default reference food factor from U.S. EPA, 1986b
- Rats in the 200-day study (Thomas et al., 1940) eating a diet treated with 250 ppm dibenzofuran consumed quantities of food closer to the control amounts (6108 g/diet/5 rats) than to the quantities of food treated with 5000 ppm dibenzofuran (5482 g/5 rats) in the 78-day study

- Growth of rats eating the 250 ppm diet in the 200-day study (Thomas et al., 1940) more closely approximated controls than those eating 5000 ppm, and that the 78-day weight provided a reasonable average weight for the 200 day study period.

In the 78-day study, Thomas et al. (1940) reported that a group of 5 control rats ingested a total of 6108 grams of food over the 78 days and grew from 1.273 kg to 1.594 kg/group, while experimental rats ingested 5482 g of food treated with 5000 ppm dibenzofuran and grew from 1.274 kg to 1.517 kg/group of 5 treated rats. The following calculations used food consumption data from the 78-day study to estimate dibenzofuran consumption in the 200-day study at the POD (250 ppm) for the critical effect of reduced length and organ weight, and excess abdominal fat among the exposed rats.

(6108 g diet/5 rats) / 78 days = 78.3 g/diet/5 rats/day

(78.3 g/5 rats/day) x $(250/10^6)$ = 0.0196 g DBF/5 rats/day = 19.6 mg/5 rats/day

19.6 mg DBF/5 rats/day / (1.594 kg/5 rats) = 12.3 mg DBF/kg/day

The estimated dibenzofuran dose of 12.3 g/kg/day was essentially the same as the dose of 12.5 g/kg/day calculated using the EPA default reference food factor (U.S. EPA, 1986b).

Based on the data available, the following uncertainty factors were applied to derive a subchronic oral p-RfD.

- 10 for variability in human susceptibility
- 10 for the uncertainty in animal-to-human extrapolation
- 1 for using data from a 200-day study (in rats) to derive a subchronic p-RfD
- 3 ($10^{0.5}$) for using a minimal LOAEL instead of a NOAEL
- 10 for deficiencies in the database, including the lack of reproductive and developmental data, and the minimal data details reported in the key study

The uncertainty factors noted above provide a composite UF of 3000 ($10^{3.5}$).

In the absence of a NOAEL, a LOAEL could be several orders of magnitude above the actual no adverse effect dose, since it merely represents the lowest dose tested. Nevertheless, the uncertainty factor for using a minimal LOAEL instead of a NOAEL was reduced from 10 to 3 ($10^{0.5}$) because the following findings suggested that the smaller uncertainty factor would be more appropriate in this case. While many of the dose levels tested and the organism effects considered in the following reports would be difficult to relate to humans, together they seem to

emphasize the relatively low toxicity and mild effects of dibenzofuran across a variety of species.

- The Thomas et. al (1940) study noted relatively minor effects in rats, even at very high doses, up to thirty times the LOAEL dose selected as the POD
- Peripheral data in other species indicated very minor effects or no effects among organisms exposed to dibenzofuran
    - 75 mg DBF/kg (soil) NOEL for soil nitrification and for soil bacterial diversity (Sverdrup et al., 2002)
    - No dose-related decrease in drought tolerance in the adult soil-dwelling insects, *Folsomia fimetaria* (Sjursen et al., 2001)
    - 20% reduction in plant seedling weight when exposed to 43-93 mg DBF /kg soil (Sverdrup et al., 2003)
    - No change in expression of NADH-ubiquinone oxidoreductase (NUO) among DBF-exposed *Phanerochaete chrysosporium* fungi (Kurihara et al., 2002)
- NCI (1979) reported no tumors and relatively low toxicity among rats and mice fed diets containing 5000 ppm and 10,000 ppm dibenzo-p-dioxin, a structural analog to dibenzofuran. Effects reported were hepatic lesions, slight reductions in weight gain and nephropathy (in male rats)

Applying the composite UF of $10^{3.5}$ (~3000) to the dietary LOAEL POD of 12.3 mg DBF/kg-day for the combined critical effects of reduced length and organ weight and excess abdominal fat observed in female albino rats allowed the following calculation of the subchronic p-RfD.

Subchronic oral p-RfD = LOAEL / (UF x MF)
= (12.3 mg/kg/day) / ($10^{3.5}$ x 1)
= **$4x10^{-3}$ mg/kg-day**
= 4 µg dibenzofuran/kg-day

The data were insufficient to derive a chronic oral p-RfD value using an acceptable composite uncertainty. However, the Appendix of this document contains a Screening Value that may be useful in certain instances. Please see the attached Appendix for details.

DERIVATION OF PROVISIONAL INHALATION RfC VALUES FOR DIBENZOFURAN

Provisional inhalation RfC values were not derived for dibenzofuran because no useful inhalation exposure data were identified and data were insufficient to attempt inter-route extrapolation from the marginal ingestion data.

STATEMENT OF CONFIDENCE

Confidence in the principal study is low. Thomas et al. (1940) examined a number of endpoints, including histological examination of several major organs. The study had an adequate number of dose groups, but was limited by inclusion of only five rats in each group. Although only female rats were used for the 200-day portion of the study, male rats were used for the shorter water balance study (78 days). Thomas et al. (1940) did not report whether the critical effect selected displayed a dose-response relationship. However, the reductions in growth and organ weights, and the increase in abdominal fat were supported by histological changes noted in the kidney and impairment of water balance at higher doses. Because the critical effects were observed among rats receiving the lowest dose tested, one cannot be certain that the effects noted at 250 ppm (12.5 mg/kg-day), would not have been present at lower doses. Thus, it is uncertain whether 250 ppm is a true LOAEL. Confidence in the database and the resulting RfDs is low because of the limited toxicity data base for dibenzofuran, including lack of human studies and chronic, developmental, or reproductive oral animal studies. However, some confidence is gained from the relatively low toxicity and lack of tumors among rats and mice fed high doses of dibenzo-p-dioxin (NCI, 1979), the chemical identified by NCI (2000) as most structurally related to dibenzofuran. Nevertheless, risk managers are advised to consider any other available data before applying this p-RfD.

Suppliers and users of dibenzofuran should be encouraged to conduct toxicology studies, such as that initiated by EPA in 1978 (NCI, 2000) but then terminated because of lack of funding. The absence of inhalation, toxicokinetic, and metabolic data would justify especially encouraging studies to seek such information.

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APPENDIX

DERIVATION OF A SCREENING VALUE FOR DIBENZOFURAN

For reasons noted in the main PPRTV document, it is inappropriate to derive provisional toxicity values for Dibenzofuran, chronic RfD. 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. In the OSRTI hierarchy, Screening Values are considered to be below Tier 3, "Other (Peer-Reviewed) Toxicity Values."

Screening Values are intended for use in limited circumstances when no Tier 1, 2, or 3 values are available. Screening Values may be used, for example, to rank relative risks of individual chemicals present at a site to determine if the risk developed from the associated exposure at the specific site is likely to be a significant concern in the overall cleanup decision. Screening Values are not defensible as the primary drivers in making cleanup decisions because they are based on limited information. Questions or concerns about the appropriate use of Screening Values should be directed to the Superfund Health Risk Technical Support Center.

The Thomas et al. (1940) study provided insufficient data to derive a chronic oral p-RfD value with uncertainty in an acceptable range. The 200-day rat minimal LOAEL POD of 12.3 mg/kg-day was considered to derive a **screening chronic oral reference dose** by applying a composite uncertainty factor of 10,000 (10^4), including 10 for variability in human susceptibility, 10 for animal-to-human extrapolation, 3 ($10^{0.5}$) for extrapolating from 200-day rat data to a chronic screening value, 3 ($10^{0.5}$) for using a minimal LOAEL instead of a NOAEL, and 10 for deficiencies in the database, including the lack of developmental data and the minimal data details reported in the key study.

Applying the minimal LOAEL dietary POD of 12.3 mg DBF/kg-day and the composite uncertainty factor of 10,000 (10^4) allowed the following calculation:

Screening chronic oral p-RfD = LOAEL/UF
= (12.3 mg/kg-day)/10^4
= **$\underline{1x10^{-3}\ mg/kg\text{-}day}$**
= 1 μg dibenzofuran/kg-day

Confidence in the key study was low, because of the lack of detail on the critical effects and other deficiencies noted in this document. Given the lack of additional studies, confidence in the database also was low, leading to low overall confidence in the screening toxicity value. Users are advised to consider any other available data and to consult with the STSC before using this screening p-RfD.