

## Provisional Peer Reviewed Toxicity Values for

4-Bromodiphenyl ether (CASRN 101-55-3)

Derivation of an Oral RfD

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

## 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. intravenouskg kilogramL 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

## PROVISIONAL PEER REVIEWED TOXICITY VALUES FOR 4-BROMODIPHENYL ETHER (CASRN 101-55-3) Derivation of an Oral RfD

## **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.

#### INTRODUCTION

IRIS (U.S. EPA, 2001) does not contain an RfD for 4-bromodiphenyl ether (4-bromophenyl phenyl ether). 4-Bromodiphenyl ether is not included in the Drinking Water Standards and Health Advisory list (U.S. EPA, 2000). The HEAST (U.S. EPA, 1997) reports that data were inadequate for risk assessment for 4-bromodiphenyl ether, based on a 1986 HEEP (U.S. EPA, 1986). Besides the 1986 HEEP on 4-bromodiphenyl ether, the CARA list (U.S. EPA, 1991, 1994) includes a 1983 HEEP on brominated diphenyl ethers as a class (U.S. EPA, 1983). Neither document contains any relevant toxicity information for 4-bromodiphenyl ether. ATSDR (2000) has not published a toxicological profile for 4-bromodiphenyl ether, nor has this chemical been the subject of an IARC monograph (IARC, 2000). The World Health Organization (WHO, 1994) has published an Environmental Health Criteria document for Brominated Diphenyl Ethers that includes a discussion of 4-bromodiphenyl ether. The NTP status report (NTP, 2000) was also searched to identify relevant data for the derivation of a provisional RfD for 4-bromodiphenyl ether. Update literature searches were conducted from

1985 to June 2000 for data relevant to RfD derivation. The databases searched were: TOXLINE, TSCATS, MEDLINE, GENETOX, HSDB, EMIC/EMICBACK, DART/ETICBACK, and RTECS.

## REVIEW OF THE PERTINENT LITERATURE

#### **Human Studies**

No studies were located regarding oral exposure of humans to 4-bromodiphenyl ether.

#### **Animal Studies**

No oral animal studies suitable for use in the derivation of an RfD for 4-bromodiphenyl ether were located. Available data were limited to a single developmental toxicity study that found no evidence of maternal or developmental effects produced by 4-bromodiphenyl ether at doses up to 1000 mg/kg-day (Francis, 1989). In this study, groups of 20-21 pregnant Swiss mice were treated with 4-bromodiphenyl ether at doses of 100 or 1000 mg/kg-day by gavage in corn oil on days 5-14 of gestation. There was no effect on maternal weight gain during gestation, production of litters, litter size, pup survival through weaning, pup body weights through weaning (except for a slight statistically significant increase in the low dose group on day 21 only), or pup organ weights at post-weaning sacrifice.

# FEASIBILITY OF DERIVING A PROVISIONAL RfD FOR 4-BROMODIPHENYL ETHER

A provisional RfD for 4-bromodiphenyl ether cannot be derived due to lack of suitable human and animal data.

### **REFERENCES**

ATSDR (Agency for Toxicological Substances Disease Registry). 2000. Toxicological Profile Information Sheet. U.S. Department of Health and Human Services, Public Health Service, Atlanta, GA. Online. <a href="http://www.atsdr.cdc.gov/toxpro2.html">http://www.atsdr.cdc.gov/toxpro2.html</a>

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NTP (National Toxicology Program). 2000. Management Status Report. Examined August, 2000. Online.

http://ntp-server.niehs.nih.gov/cgi/iH Indexes/Res Stat/iH Res Stat Frames.html)

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U.S. EPA. 1986. Health and Environmental Effects Profile for 4-Bromophenyl phenyl ether. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

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U.S. EPA. 1994. Chemical Assessments and Related Activities (CARA). Office of Health and Environmental Assessment, Washington, DC. December.

U.S. EPA. 1997. Health Effects Assessment Summary Tables. FY-1997 Update. Prepared by the Office of Research and Development, National Center for Environmental Assessment, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC. July, 1997. EPA/540/R-97/036. NTIS PB 97-921199.

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U.S. EPA. 2001. Integrated Risk Information System (IRIS). Office of Research and Development, National Center for Environmental Assessment, Washington, DC. Examined August, 2000. Online. <a href="http://www.epa.gov/iris/">http://www.epa.gov/iris/</a>

WHO (World Health Organization). 1994. Environmental Health Criteria Monograph on Brominated Diphenyl Ethers. Monograph 162. International Programme on Chemical Safety, Geneva, Switzerland.

## Provisional Peer Reviewed Toxicity Values for

4-Bromodiphenyl ether (CASRN 101-55-3)

Derivation of an Inhalation RfC

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

## Acronyms and Abbreviations

bw body weight

cc cubic centimeters
CD Caesarean Delivered

CERCLA Comprehensive Environmental Response, Compensation and Liability Act

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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)

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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

## PROVISIONAL PEER REVIEWED TOXICITY VALUES FOR 4-BROMODIPHENYL ETHER (CASRN 101-55-3) Derivation of an Inhalation RfC

## **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).
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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**

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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.

#### INTRODUCTION

IRIS (U.S. EPA, 2001) does not contain an RfC for 4-bromodiphenyl ether (4-bromophenyl phenyl ether). The HEAST (U.S. EPA, 1997) reports that data were inadequate for risk assessment for 4-bromodiphenyl ether, based on a 1986 HEEP (U.S. EPA, 1986). Besides the 1986 HEEP on 4-bromodiphenyl ether, the CARA list (U.S. EPA, 1991, 1994) includes a 1983 HEEP on brominated diphenyl ethers as a class (U.S. EPA, 1983). Neither document contains any relevant toxicity information for 4-bromodiphenyl ether. ATSDR (2000) has not published a toxicological profile for 4-bromodiphenyl ether, nor has this chemical been the subject of an IARC monograph (IARC, 2000). Occupational exposure limits for 4-bromodiphenyl ether have not been established by the ACGIH (2000), OSHA (2000), or NIOSH (2000). The World Health Organization (WHO, 1994) has published an Environmental Health Criteria document for Brominated Diphenyl Ethers that includes a discussion of 4-bromodiphenyl ether. The NTP status report (NTP, 2000) was also searched to identify relevant data for the derivation of a provisional RfC for 4-bromodiphenyl ether. Update literature

searches were conducted from 1985 to June 2000 for data relevant to RfC derivation. The databases searched were: TOXLINE, TSCATS, MEDLINE, GENETOX, HSDB, EMIC/EMICBACK, DART/ETICBACK, and RTECS.

#### REVIEW OF THE PERTINENT LITERATURE

#### **Human Studies**

No studies were located regarding inhalation exposure of humans to 4-bromodiphenyl ether.

#### **Animal Studies**

No studies were located regarding inhalation exposure of animals to 4-bromodiphenyl ether.

# FEASIBILITY OF DERIVING A PROVISIONAL RfC FOR 4-BROMODIPHENYL ETHER

A provisional RfC for 4-bromodiphenyl ether cannot be derived due to lack of suitable human and animal data.

#### REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). 2000. TLVs® and BEIs®: Threshold Limit Values for Chemical Substances and Physical Agents, Biological Exposure Indices. ACGIH, Cincinnati, OH.

ATSDR (Agency for Toxicological Substances Disease Registry). 2000. Toxicological Profile Information Sheet. U.S. Department of Health and Human Services, Public Health Service, Atlanta, GA. Online. <a href="http://www.atsdr.cdc.gov/toxpro2.html">http://www.atsdr.cdc.gov/toxpro2.html</a>

IARC (International Agency for Research on Cancer). 2000. Cumulative cross index to IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. IARC Monographs. 75: 459-491.

NIOSH (National Institute for Occupational Safety and Health). 2000. NIOSH Pocket Guide to Chemical Hazards. Index by CASRN. Examined August, 2000. Online. http://www.cdc.gov/niosh/npg/npgdcas.html

NTP (National Toxicology Program). 2000. Management Status Report. Online. http://ntp-server.niehs.nih.gov/cgi/iH Indexes/Res Stat/iH Res Stat Frames.html

OSHA (Occupational Safety and Health Administration). 2000. OSHA Standard 1915.1000 for Air Contaminants. Part Z, Toxic and Hazardous Substances. Examined August, 2000. Online. http://www.osha-slc.gov/OshStd\_data/1915\_1000.html

U.S. EPA. 1983. Health and Environmental Effects Profile for Brominated Diphenyl Ethers. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

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## Provisional Peer Reviewed Toxicity Values for

4-Bromodiphenyl ether (CASRN 101-55-3)

Derivation of an Oral Slope Factor

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

## Acronyms and Abbreviations

bw body weight

cc cubic centimeters
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sq.cm. square centimeters

TSCA Toxic Substances Control Act

UF uncertainty factor

μg microgram μmol micromoles

VOC volatile organic compound

## PROVISIONAL PEER REVIEWED TOXICITY VALUES FOR 4-BROMODIPHENYL ETHER (CASRN 101-55-3) Derivation of an Oral Slope Factor

## **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:

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#### INTRODUCTION

IRIS (U.S. EPA, 2001) reports a cancer classification for 4-bromodiphenyl ether (4-bromophenyl phenyl ether) of group D - not classifiable as to human carcinogenicity, based on no human data and inadequate animal data (one short-term injection study). Due to the absence of appropriate data, an oral slope factor was not derived. This assessment, verified on 06/15/90, was based on a 1986 HEEP (U.S. EPA, 1986). 4-Bromodiphenyl ether is not listed in the Drinking Water Standards and Health Advisory list (U.S. EPA, 2000) or the HEAST (U.S. EPA, 1997). Besides the 1986 HEEP on 4-bromodiphenyl ether, the CARA list (U.S. EPA, 1991, 1994) includes a 1983 HEEP on brominated diphenyl ethers as a class (U.S. EPA, 1983). ATSDR (2000) has not published a toxicological profile for 4-bromodiphenyl ether, nor has 4-bromodiphenyl ether been discussed in an IARC monograph (IARC, 2000). The World Health Organization (WHO, 1994) has published an Environmental Health Criteria document for Brominated Diphenyl Ethers that includes a discussion of 4-bromodiphenyl ether. The NTP status report (NTP, 2000) was also searched to identify relevant data for the derivation of a slope

factor for 4-bromodiphenyl ether. Update literature searches were conducted from 1985 to June 2000 for data relevant to derivation of an oral slope factor. The databases searched were: TOXLINE, TSCATS, MEDLINE, GENETOX, HSDB, EMIC/EMICBACK, DART/ETICBACK, and RTECS.

## REVIEW OF THE PERTINENT LITERATURE

## **Human Studies**

No studies were located regarding oral exposure of humans to 4-bromodiphenyl ether.

#### **Animal Studies**

No oral animal studies suitable for derivation of an oral slope factor for 4-bromodiphenyl ether were located.

## **Other Studies**

4-Bromodiphenyl ether was negative in a short-term *in vivo* screening assay for pulmonary adenoma in strain A/ST mice that received between 17 and 24 injections of doses ranging from 40 to 200 mg/kg per injection (Theiss et al., 1977) and for sister chromatid exchange *in vivo* in CD-1 mice treated by gavage at doses up to 579 mg/kg-day for 14 days (Borzelleca, 1983).

## FEASIBILITY OF DERIVING A PROVISIONAL ORAL SLOPE FACTOR FOR 4-BROMODIPHENYL ETHER

A provisional oral slope factor for 4-bromodiphenyl ether cannot be derived due to lack of suitable human and animal data.

### **REFERENCES**

ATSDR (Agency for Toxicological Substances Disease Registry). 2000. Toxicological Profile Information Sheet. U.S. Department of Health and Human Services, Public Health Service, Atlanta, GA. Online. <a href="http://www.atsdr.cdc.gov/toxpro2.html">http://www.atsdr.cdc.gov/toxpro2.html</a>

Borzelleca, J.F. 1983. A review of volatile organic contaminant data. Proc. AWWA Water Qual. Tech. Conf. p. 225-244.

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Thiess, J.C., G.D. Stoner, M.B. Shimkin and E.K. Weisburger. 1977. Test for carcinogenicity of organic contaminants of United States drinking waters by pulmonary tumor response in Strain A mice. Cancer Res. 37: 2717-2720.

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## Provisional Peer Reviewed Toxicity Values for

4-Bromodiphenyl ether (CASRN 101-55-3)

Derivation of an Inhalation Unit Risk

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

## 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. intravenouskg kilogramL 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

## PROVISIONAL PEER REVIEWED TOXICITY VALUES FOR 4-BROMODIPHENYL ETHER (CASRN 101-55-3) Derivation of an Inhalation Unit Risk

## **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.

#### INTRODUCTION

IRIS (U.S. EPA, 2001) reports a cancer classification for 4-bromodiphenyl ether (4-bromophenyl phenyl ether) of group D - not classifiable as to human carcinogenicity, based on no human data and inadequate animal data (one short-term injection study). Due to the absence of appropriate data, an inhalation unit risk was not derived. This assessment, verified 06/15/90, was based on a 1986 HEEP (U.S. EPA, 1986). 4-Bromodiphenyl ether is not listed in the HEAST cancer table (U.S. EPA, 1997). Besides the 1986 HEEP on 4-bromodiphenyl ether, the CARA list (U.S. EPA, 1991, 1994) includes a 1983 HEEP on brominated diphenyl ethers as a class (U.S. EPA, 1983). ATSDR (2000) has not published a toxicological profile for 4-bromodiphenyl ether, nor has 4-bromodiphenyl ether been discussed in an IARC monograph (IARC, 2000). The World Health Organization (WHO, 1994) has published an Environmental Health Criteria document for Brominated Diphenyl Ethers that includes a discussion of 4-bromodiphenyl ether. The NTP status report (NTP, 2000) was also searched to identify relevant data for the derivation of an inhalation unit risk for 4-bromodiphenyl ether. Update literature searches were conducted

from 1985 to June 2000 for data relevant to derivation of an inhalation unit risk. The databases searched were: TOXLINE, TSCATS, MEDLINE, GENETOX, HSDB, EMIC/EMICBACK, DART/ETICBACK, and RTECS.

#### REVIEW OF THE PERTINENT LITERATURE

#### **Human Studies**

No studies were located regarding inhalation exposure of humans to 4-bromodiphenyl ether.

#### **Animal Studies**

No studies were located regarding inhalation exposure of animals to 4-bromodiphenyl ether.

## **Other Studies**

4-Bromodiphenyl ether was negative in a short-term *in vivo* screening assay for pulmonary adenoma in strain A/ST mice that received between 17 and 24 injections of doses ranging from 40 to 200 mg/kg per injection (Theiss et al., 1977) and for sister chromatid exchange *in vivo* in CD-1 mice treated by gavage at doses up to 579 mg/kg-day for 14 days (Borzelleca, 1983).

# FEASIBILITY OF DERIVING A PROVISIONAL INHALATION UNIT RISK FOR 4-BROMODIPHENYL ETHER

A provisional inhalation unit risk for 4-bromodiphenyl ether cannot be derived due to lack of suitable human and animal data.

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