11-30-2001

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.	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

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. http://www.atsdr.cdc.gov/toxpro2.html

Francis, B.M. 1989. Relative developmental toxicities of nine diphenyl ethers related to nitrophen. Environ. Toxicol. Chem. 8: 681-688.

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.

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)

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.

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.

U.S. EPA. 1991. Chemical Assessments and Related Activities (CARA). Office of Health and Environmental Assessment, Washington, DC. April.

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.

U.S. EPA. 2000. Drinking Water Regulations and Health Advisories. Office of Water, Washington, DC. Online. http://www.epa.gov/ost/drinking/standards/

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. http://www.epa.gov/iris/

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

11-30-2001

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 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
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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 RfC

Background

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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. http://www.atsdr.cdc.gov/toxpro2.html

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

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

11-30-2001

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
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CERCLA	Comprehensive Environmental Response, Compensation and Liability Act of 1980
CNS	central nervous system
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p-OSF	provisional oral slope factor
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p-RfD	provisional oral reference dose
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RCRA	Resource Conservation and Recovery Act
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SCE	sister chromatid exchange
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TSCA	Toxic Substances Control Act
UF	uncertainty factor
µg	microgram
µmol	micromoles
VOC	volatile organic compound

11-30-2001

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

Background

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Disclaimers

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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 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. http://www.atsdr.cdc.gov/toxpro2.html

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

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11-30-2001

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
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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

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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