

Provisional Peer-Reviewed Toxicity Values for

Tris(3-chloro-1-propyl)phosphate
CASRN 1067-98-7

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

Alan Weinrich, National Center for Environmental Assessment, Cincinnati, OH

DRAFT DOCUMENT PREPARED BY

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	iii
BACKGROUND	4
DISCLAIMERS	4
QUESTIONS REGARDING PPRTVS	4
INTRODUCTION	5
REVIEW OF POTENTIALLY RELEVANT DATA (CANCER AND NONCANCER).....	7
DERIVATION OF PROVISIONAL VALUES	7
CANCER WOE DESCRIPTOR.....	7
MODE-OF-ACTION (MOA) DISCUSSION	7
REFERENCES	7

COMMONLY USED ABBREVIATIONS

BMC	benchmark concentration
BMD	benchmark dose
BMCL	benchmark concentration lower bound 95% confidence interval
BMDL	benchmark dose lower bound 95% confidence interval
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
p-OSF	provisional oral slope factor
p-RfC	provisional reference concentration (inhalation)
p-RfD	provisional reference dose (oral)
POD	point of departure
RfC	reference concentration (inhalation)
RfD	reference dose (oral)
UF	uncertainty factor
UF _A	animal-to-human uncertainty factor
UF _C	composite uncertainty factor
UF _D	incomplete-to-complete database uncertainty factor
UF _H	interhuman uncertainty factor
UF _L	LOAEL-to-NOAEL uncertainty factor
UF _S	subchronic-to-chronic uncertainty factor
WOE	weight of evidence

PROVISIONAL PEER-REVIEWED TOXICITY VALUES FOR TRIS(3-CHLORO-1-PROPYL)PHOSPHATE (CASRN 1067-98-7)

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

INTRODUCTION

Tris(3-chloro-1-propyl)phosphate, CAS No. 1067-98-7, belongs to the class of compounds known as chlorinated alkyl phosphate esters (NRC, 2000). Chemicals in this class generally are used as flame retardants and plasticizers. Tris(1-chloro-2-propyl) phosphate (TCPP), CAS No. 13674-84-5, is an isomer of this compound (NRC, 2000); its toxicology is under review by the Agency for Toxic Substances and Disease Registry (ASTDR, 2009), whereas tris(3-chloro-1-propyl)phosphate has not been reviewed. Figure 1 shows the chemical structure of tris(3-chloro-1-propyl)phosphate, and Table 1 lists the physicochemical properties of both tris(3-chloro-1-propyl)phosphate and TCPP.

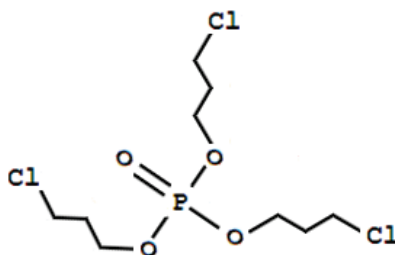


Figure 1. Tris(3-chloro-1-propyl)phosphate Structure

Table 1. Physicochemical Properties for Tris(3-chloro-1-propyl)phosphate and TCPP^a		
Property (unit)	Estimated Value for Tris(3-chloro-1-propyl)phosphate^b	Value for Tris(1-Chloro-2-Propyl) Phosphate
Boiling point (°C)	Not available	235–248
Melting point (°C)	84	380
Density (g/cm ³)	Not available	1.29
Vapor pressure (Pa at 25°C)	0.0006	<266.6
pH	Not available	Not available
Solubility in water (g/100 mL at 25°C)	0.0019	0.11–0.12
Relative vapor density (air = 1)	Not available	Not available
Molecular weight (g/mol)	327.57 ^c	327.59

^aData specific to tris(3-chloro-1-propyl)phosphate often were not available; however, the physicochemical properties of TCPP are presented when available (NRC, 2000).

^bEstimated values from Episuite software using PBT Profiler (www.pbtprofiler.net).

^chttp://lb.chemie.uni-hamburg.de/static/RN/1_1016-82-6%20...%201070-89-9.php?content=120/hxaHikLm.

No reference dose (RfD), reference concentration (RfC), or cancer assessment for tris(3-chloro-1-propyl)phosphate is included in the IRIS database (U.S. EPA, 2011a) or on the Drinking Water Standards and Health Advisories List (U.S. EPA, 2009). The HEAST does not report RfD or RfC values (U.S. EPA, 2011b). The Chemical Assessments and Related Activities (CARA) list (U.S. EPA, 1994) does not include a Health and Environmental Effects Profile (HEEP) for tris(3-chloro-1-propyl)phosphate. The toxicity of tris(3-chloro-1-propyl)phosphate has not been reviewed by ATSDR (2011) or the World Health Organization (WHO, 2011). ATSDR (2009) has reviewed the toxicity of several phosphate ester flame retardants but not tris(3-chloro-1-propyl)phosphate. The California Environmental Protection Agency (CalEPA, 2008, 2009) has not derived toxicity values for exposure to tris(3-chloro-1-propyl)phosphate. No occupational exposure limits for tris(3-chloro-1-propyl)phosphate have been derived by the American Conference of Governmental Industrial Hygienists (ACGIH, 2011), the National Institute of Occupational Safety and Health (NIOSH, 2010), or the Occupational Safety and Health Administration (OSHA, 2010).

The HEAST (U.S. EPA, 2011b) does not report any cancer weight-of-evidence (WOE) or oral slope factor values for tris(3-chloro-1-propyl)phosphate. The International Agency for Research on Cancer (IARC, 2011) has not reviewed the carcinogenic potential of tris(3-chloro-1-propyl)phosphate. Tris(3-chloro-1-propyl)phosphate is not included in the *11th Report on Carcinogens* (NTP, 2005). CalEPA (2008) has not prepared a quantitative estimate of carcinogenic potential for tris(3-chloro-1-propyl)phosphate.

Literature searches were conducted on sources published from 1900 through March 8, 2011 for studies relevant to the derivation of provisional toxicity values for tris(3-chloro-1-propyl)phosphate, CAS No. 1067-98-7. Searches were conducted using 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 (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 risk assessment values: ACGIH, ATSDR, CalEPA, EPA IRIS, EPA HEAST, EPA HEEP, EPA OW, EPA TSCATS/TSCATS2, NIOSH, NTP, OSHA, and RTECS.

REVIEW OF POTENTIALLY RELEVANT DATA (CANCER AND NONCANCER)

The literature search revealed no human or animal studies (acute-, short-term-, or chronic duration), for tris(3-chloro-1-propyl)phosphate. Neither the NICNAS (2001) review of the triphosphates nor the NAS (2000) or ATSDR (2009) reviews of flame-retardant chemicals included relevant information on tris-3-chloropropylphosphate. Nakamura et al. (1979) found that tris(3-chloro-1-propyl)phosphate generally was not mutagenic when tested against *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, or TA1538, with and without rat liver in vitro metabolic activation. Because the database for tris-3-chloropropylphosphate does not include even an LD₅₀, there are insufficient data to indicate whether the toxicology of tris-3-chloropropylphosphate is similar to that for tris(1-chloro-2-propyl) phosphate or other isomers.

DERIVATION OF PROVISIONAL VALUES

Limitations in the available data preclude development of cancer or noncancer toxicity values.

CANCER WOE DESCRIPTOR

Limitations in the available data preclude development of a WOE descriptor.

MODE-OF-ACTION (MOA) DISCUSSION

Limitations in the available data preclude determination of a MOA discussion.

REFERENCES

ACGIH (American Conference of Governmental Industrial Hygienists). (2011) Threshold limit values for chemical substances and physical agents and biological exposure indices. ACGIH, Cincinnati, OH. Available online by subscription at <http://www.acgih.org/ChemSearch/index.cfm>. Accessed on June 15, 2011.

ATSDR (Agency for Toxic Substances and Disease Registry). (2009) Draft Toxicological profile for Phosphate ester flame retardants. U.S. Department of Health and Human Services, Public Health Service, Atlanta, GA. Available online at <http://www.atsdr.cdc.gov/toxprofiles/tp202.pdf>. Accessed on March 9, 2011.

ATSDR (Agency for Toxic Substances and Disease Registry). (2011) Toxicological profile information sheet. U.S. Department of Health and Human Services, Public Health Service, Atlanta, GA. Available online at <http://www.atsdr.cdc.gov/toxprofiles/index.asp>. Accessed on March 8, 2011.

CalEPA (California Environmental Protection Agency). (2008) All OEHHA acute, 8-hour and chronic reference exposure levels (chRELs) as on December 18, 2008. Office of Environmental Health Hazard Assessment, Sacramento, CA. Available online at <http://www.oehha.ca.gov/air/allrels.html>. Accessed on March 8, 2011.

CalEPA (California Environmental Protection Agency). (2009) OEHHA toxicity criteria database. Office of Environmental Health Hazard Assessment, Sacramento, CA. Available online at <http://www.oehha.ca.gov/risk/ChemicalDB/index.asp>. Accessed on March 8, 2011.

IARC (International Agency for Research on Cancer). (2011) Monographs on the evaluation of carcinogenic risks to humans. Lyon, France: IARC. Available online at <http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php>. Accessed on March 8, 2011.

Nakamura A; Tateno N; Kojima S; Kaniwa Ma; Kawamura T. (1979) Mutagenicity of halogenated alkanols and their phosphoric acid esters for *Salmonella typhimurium*. *Mutat Res* 66:373–380.

NAS (National Academy of Sciences). (2000) Toxicological risks of selected flame-retardant chemicals. Washington, DC: The National Academies Press. Available online at http://download.nap.edu/cart/deliver.cgi?record_id=9841&type=pdf_chapter&free=1. Accessed on March 9, 2011.

NICNAS (National Industrial Chemicals Notification and Assessment Scheme). (2001) Trisphosphates. Priority existing chemical report no. 17. Commonwealth of Australia, Sydney, Australia. Available online at http://www.nicnas.gov.au/publications/car/pec/PEC17/PEC_17_Full_Report_PDF.pdf. Accessed March 9, 2011.

NIOSH (National Institute for Occupational Safety and Health). (2010) NIOSH pocket guide to chemical hazards. Index of chemical abstracts service registry numbers (CAS No.). Center for Disease Control and Prevention, U.S. Department of Health, Education and Welfare, Atlanta, GA. Available online at <http://www.cdc.gov/niosh/npg/npgdcas.html>. Accessed on March 8, 2011.

NRC (National Research Council) 2000 Toxicological risks of selected flame-retardant Chemicals. Subcommittee on Flame-Retardant Chemicals, Committee on Toxicology, Board on Environmental Studies and Toxicology, Commission on Life Sciences. Available online at <http://www.nap.edu/catalog/9841.html>. Accessed on March 9, 2011.

NTP (National Toxicology Program). (2005) 11th Report on carcinogens. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Research Triangle Park, NC. Available online at <http://ntp-server.niehs.nih.gov/index.cfm?objectid=32BA9724-F1F6-975E-7FCE50709CB4C932>. Accessed on March 8, 2011.

OSHA (Occupational Safety and Health Administration). (2011) Air contaminants: occupational safety and health standards for shipyard employment, subpart Z, toxic and hazardous substances. U.S. Department of Labor, Washington, DC; OSHA Standard 1915.1000. Available online at http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10286. Accessed on March 10, 2011.

U.S. EPA (Environmental Protection Agency). (1994) Chemical assessments and related activities (CARA). Office of Health and Environmental Assessment, Washington, DC; EPA/600/R-94/904. Available online at nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=60001G8L.txt.

U.S. EPA (Environmental Protection Agency). (2009) 2009 Edition of the drinking water standards and health advisories. Office of Water, Washington, DC; EPA/822/R-09/011. Available online at <http://deq.state.wy.us/wqd/groundwater/downloads/dwstandards2009%5B1%5D.pdf>. Accessed March 8, 2011.

U.S. EPA (Environmental Protection Agency). (2011a) Integrated risk information system (IRIS). Office of Research and Development, National Center for Environmental Assessment, Washington, DC. Available online at <http://www.epa.gov/iris/>. Accessed March 8, 2011.

U.S. EPA (Environmental Protection Agency). (2011b) Health effects assessment summary tables (HEAST). 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. Available online at <http://epa-heat.ornl.gov/>. Accessed March 8, 2011.

WHO (World Health Organization). (2011) Online catalogs for the Environmental Health Criteria series. Available online at http://www.who.int/topics/environmental_health/en/. Accessed March 8, 2011.