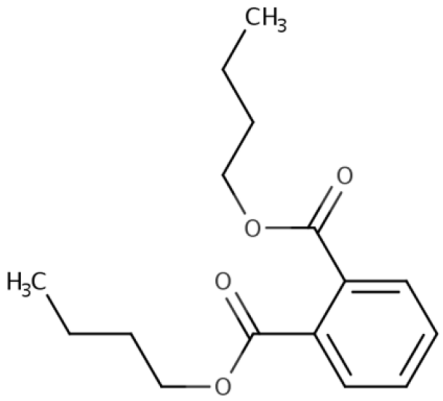
EPA Document# EPA-740-D-24-023
December 2024
Office of Chemical Safety and
Pollution Prevention

United States
Environmental Protection Agency

Draft Environmental Hazard Assessment for Dibutyl Phthalate (DBP)

Technical Support Document for the Draft Risk Evaluation

CASRN 84-74-2



December 2024

TABLE OF CONTENTS

LIST OF TABLES

LIST OF APPENDIX TABLES

LIST OF APPENDIX FIGURES

ABBREVIATIONS AND ACRONYMS

AF	Assessment factor
ChV	Chronic value
CI	Confidence interval
COC	Concentration(s) of concern
EC50	Effect concentration at which 50% of test organisms exhibit an effect
EPA	Environmental Protection Agency
HC05	Hazard concentration that is protective of 95% of the species in the SSD
HV	Hazard value
LC50	Lethal concentration at which 50 percent of test organisms die
LD50	Lethal dose at which 50 percent of test organisms die
LOAEC	Lowest-observed-adverse-effect-concentration
LOAEL	Lowest-observed-adverse-effect-level
LOEC	Lowest-observed-effect-concentration
LOEL	Lowest-observed-effect-level
MATC	Maximum acceptable toxicant concentration
NOAEC	No-observed-adverse-effect-concentration
NOAEL	No-observed-adverse-effect-level
NOEC	No-observed-effect-concentration
NOEL	No-observed-effect-level
OCSPP	Office of Chemical Safety and Pollution Prevention
OPPT	Office of Pollution Prevention and Toxics
POD	Point of departure
QSAR	Quantitative structure-activity relationship
SSD	Species sensitivity distribution
TOC	Total organic carbon
TRV	Toxicity reference value
TSCA	Toxic Substances Control Act
U.S.	United States
Web-ICE	Web-based Interspecies Correlation Estimation

ACKNOWLEGEMENTS

This report was developed by the United States Environmental Protection Agency (U.S. EPA or the Agency), Office of Chemical Safety and Pollution Prevention (OCSPP), Office of Pollution Prevention and Toxics (OPPT).

Acknowledgements

The Assessment Team gratefully acknowledges the participation, review, and input from EPA OPPT and OSCPP senior managers and science advisors. The Agency is also grateful for assistance from the following EPA contractors for the preparation of this draft technical support document: General Dynamics Information Technology, Inc. (Contract No. HHSN316201200013W); ICF, Inc. (Contract No. 68HERC23D0007); SpecPro Professional Services, LLC (Contract No. 68HERC20D0021); and SRC, Inc. (Contract No. 68HERH19D0022 and 68HERC23D0007).

As part of an intra-agency review, this technical support document was provided to multiple EPA Program Offices for review. Comments were submitted by EPA's Office of Research and Development (ORD).

Docket

Supporting information can be found in the public docket, Docket ID EPA-HQ-OPPT-2018-0503.

Disclaimer

Reference herein to any specific commercial products, process, or service by trade name, trademark, manufacturer, or otherwise does not constitute or imply its endorsement, recommendation, or favoring by the United States Government.

Authors: Collin Beachum (Management Lead), Mark Myer (Assessment Lead, Environmental Hazard Assessment Lead), Jennifer Brennan (Assessment Lead, Environmental Hazard Discipline Lead), Christopher Green (Environmental Hazard Discipline Lead), Emily Griffin (Environmental Hazard Assessor)

Contributors: Azah Abdallah Mohamed, Rony Arauz Melendez, Sarah Au, Maggie Clark, Jone Corrales, Daniel DePasquale, Lauren Gates, Ryan Klein, Sydney Nguyen, Brianne Raccor, Maxwell Sall, Andrew Sayer, Joe Valdez, Leora Vegosen.

Technical Support: Mark Gibson, Hillary Hollinger, S. Xiah Kragie

This draft technical support document was reviewed and cleared for release by OPPT and OCSPP leadership.

SUMMARY

This technical document is in support of the *Draft Risk Evaluation for Dibutyl Phthalate (DBP)* (U.S. EPA, 2024). DBP is a common name for the chemical substance 1,2-benzenedicarboxylic acid, 1,2-dibutyl ester (CASRN 84-74-2). See the draft risk evaluation for a complete list of all the technical support documents for DBP.

EPA considered all reasonably available information identified through the systematic review process under the Toxic Substances Control Act (TSCA) to characterize environmental hazard endpoints for DBP. After evaluating the reasonably available information, environmental hazard thresholds were derived for aquatic vertebrates, aquatic invertebrates, benthic invertebrates, aquatic plants and algae, terrestrial vertebrates, soil invertebrates, and terrestrial plants. These hazard thresholds are summarized in Table ES-1. EPA's rationale for selecting these hazard thresholds, as well as the level of confidence in each is based on the weight of scientific evidence, is described in Section 2.42.3 and 0.

Table ES-1. Environmental Hazard Thresholds for DBP

Receptor Group	Exposure Duration	Hazard Threshold (COC or HV)	Citation
Aquatic Vertebrates (Including Amphibians)	Acute (96 hours)	347.6 µg/L	SSD (see Section 2.3.1)
	Chronic (112 days)	1.56 µg/L	(EAG Laboratories, 2018)
Aquatic Invertebrates	Acute (96 hours)	347.6 µg/L	SSD (see Section 2.3.1)
	Chronic (14 days)	12.23 µg/L	(Tagatz et al., 1983)
Benthic Invertebrates	Acute (96 hours)	347.6 µg/L	SSD (see Section 2.3.1)
	Chronic (10 days)	114.3 mg DBP/kg dry sediment	(Call et al., 2001a)
Aquatic Plants and Algae	96 hours	31.6 µg/L	(Adachi et al., 2006)
Terrestrial Vertebrates	17 weeks	80 mg/kg-bw/day	(NTP, 1995)
Soil Invertebrates	21 days	14 mg DBP/kg dry soil	(Jensen et al., 2001)
Terrestrial Plants	40 days	10 mg DBP/kg dry soil	(Gao et al., 2019)
COC = concentration of concern; HV = hazard value			

1 INTRODUCTION

Dibutyl phthalate is an organic substance primarily used as a plasticizer in a wide variety of consumer, commercial and industrial products. DBP may be released during industrial activities and through consumer use, with most releases occurring to air and water. EPA reviewed studies of the toxicity of DBP to aquatic and terrestrial organisms and its potential environmental hazards.

1.1 Approach and Methodology

EPA utilized studies with overall quality determinations of high and medium to characterize the environmental hazards of DBP to surrogate species representing various receptor groups, including aquatic vertebrates, aquatic invertebrates, benthic invertebrates, aquatic plants and algae, terrestrial mammals, soil invertebrates, and terrestrial plants. Mechanistic (transcriptomic and metabolomic) and behavioral points of departure (PODs) from an acute exposure of DBP to fathead minnows were compared to the acute aquatic vertebrate hazard threshold. Hazard studies with mammalian wildlife exposed to DBP were not available; therefore, EPA used ecologically relevant endpoints from the laboratory rat and mouse—model organisms that are commonly used to evaluate human health hazards—to establish a hazard threshold for terrestrial mammals. Although two studies with overall quality determinations of high and medium containing avian hazard data were available for exposures to DBP, no apical hazards were observed in those studies. Because no apical hazards were observed in any avian studies, EPA was not able to establish a definitive hazard threshold for avian species.

TSCA requires that EPA use data and/or information in a manner consistent with the best available science and that the Agency base decisions on the weight of scientific evidence. To meet the TSCA science standards, EPA applies a systematic review process to identify data and information across taxonomic groups for both aquatic and terrestrial organisms with a focus on apical endpoints (*e.g.*, those affecting survival, growth, or reproduction). The data collection, data evaluation, and data integration stages of the systematic review process are used to develop the hazard assessment to support the integrative risk characterization. EPA completed the review of environmental hazard data/information sources during risk evaluation using the data quality review evaluation metrics and the rating criteria described in the 2021 *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* (U.S. EPA, 2021) and the *Draft Systematic Review Protocol for Dibutyl Phthalate (DBP)* (U.S. EPA, 2024c). Studies identified and evaluated by the Agency were assigned an overall quality determination of high, medium, low, or uninformative. Study quality was evaluated based on a rubric that included consideration of the following seven overarching domains: test substance, test design, exposure characterization, test organism, outcome assessment, confounding/variable control, and data presentation/analysis. Several metrics within each of these domains were evaluated for each study, and an overall study quality determination was assigned based on the overall evaluation. Because data on toxicity of DBP are numerous, EPA systematically evaluated all data for this hazard characterization, but relied only on high-quality and medium-quality studies for purposes of risk characterization.

2 ENVIRONMENTAL HAZARD

2.1 Aquatic Species

EPA reviewed 68 studies for DBP toxicity to aquatic organisms. Some studies may have included multiple endpoints, species, and test durations. Of these 68 studies, those that received an overall quality determination of low or uninformative were not considered for quantitative risk evaluation. For the 55 studies that received an overall quality determination of high and medium, those that demonstrated no acute or chronic adverse effects at the highest concentration tested (unbounded no-observed-effect-concentration [NOECs]), or where hazard values exceeded the limit of solubility for DBP in water as determined by EPA at 11.2 mg/L (U.S. EPA, 2024a), are listed in Appendix C. Those studies were excluded from consideration for development of hazard thresholds (see Section 2.3). Of the 68 studies, 55 were considered for the development of hazard thresholds as outlined below.

2.1.1 Acute Toxicity of DBP in Aquatic Vertebrates

EPA reviewed 17 studies that received overall quality determination of high or medium for acute toxicity in aquatic vertebrates (Table 2-1). Two studies received overall quality determinations of low or unacceptable and were not considered. Of the 17 high and medium quality studies, 13 contained acceptable acute endpoints that identified definitive hazard values below the DBP limit of water solubility. Additionally, predicted hazard data for 53 species were generated using EPA's Web-Based Interspecies Correlation Estimation (Web-ICE) tool, including predictions for 31 aquatic vertebrates, 5 aquatic invertebrates, 16 benthic invertebrates, and 1 amphibian species. For the fathead minnow (*Pimephales promelas*), bluegill (*Lepomis macrochirus*), and rainbow trout (*Oncorhynchus mykiss*), the 96-hour mortality LC50s ranged from 0.48 to 2.02 mg/L DBP (Smithers Viscient, 2018; Adams et al., 1995; EnviroSystem, 1991; Defoe et al., 1990; McCarthy and Whitmore, 1985; EG&G Bionomics, 1983a, b; Buccafusco et al., 1981). Additional endpoints were established in two fish species, including a 144-hour mortality LC50 of 0.92 mg/L and 96-hour mortality NOEC/LOEC of 0.53/8.3 mg/Lin the fathead minnow (Smithers Viscient, 2018; EG&G Bionomics, 1984a) and a 72-hour mortality LC50 of 0.63 mg/L in the zebrafish (*Danio rerio*) (Chen et al., 2014). Hazard values for development and growth were also identified in the African clawed frog (*Xenopus laevis*).

For these endpoints, the 96-hour EC50s ranged from 0.9 to 8.40 mg/L. DBP was found to have significant effects on developmental malformations in tadpoles at 0.5 mg/L (0.1 mg/L NOEC) with a 96-hour EC50 of 0.9 mg/L (Lee et al., 2005) at 6.3 mg/L (lowest concentration tested) with a 96-hour EC50 of 7.5 mg/L (Xu and Gye, 2018), and in tadpole embryos at 8.3 mg/L (5.8 mg/L NOEC) with a 96-hour EC5 of 8.4 mg/L (Gardner et al., 2016). The bolded values in Table 2-1 describe data which were used as inputs for generating Web-ICE predictions and within a species-sensitivity distribution analysis (SSD) (Appendix B).

TSCA section 4(h)(1)(B) requires EPA to encourage and facilitate the use of scientifically valid test methods and strategies that reduce or replace the use of vertebrate animals while providing information of equivalent or better scientific quality and relevance that will support regulatory decisions. One avenue of research for reducing the time needed for toxicity testing *in vivo* is the use of transcriptomic and metabolomic points of departure, which allow for studies with much shorter durations that still provide the necessary robust experimental data to characterize hazard and provide important evidence for mechanisms of action and affected cellular and metabolic pathways. A multiomics study was conducted by EPA in which fathead minnows (*Pimephales promelas*) were exposed for 24 hours to several phthalates, including DBP (Bencic et al., 2024). PODs were derived for transcriptomic change (tPOD), metabolomic change (mPOD), and behavioral change (bPOD). Additionally, a 24-hour mortality

NOEC/LOEC of 0.8/2.1 mg/L was identified. At 2.1 mg/L DBP, 100 percent mortality was observed. The tPOD identifies the DBP concentration at which gene expression is significantly affected. RNA was isolated from exposed minnows at each treatment level and analyzed for significant deviation from the control fish, and the tPOD was defined as the median benchmark dose limit (BMDL) for the lowest affected gene ontology. For DBP, the tPOD was 0.12 mg/L. The mPOD identifies the DBP concentration at which the metabolome is significantly affected. The mPOD was defined as the 10th percentile benchmark dose (BMD) for change in metabolomics vs. the control. For DBP, the mPOD was 0.11 mg/L. The bPOD identifies the DBP concentration at which startle behavior is significantly affected. The bPOD was defined as the SD50, or the concentration which causes a 50% reduction in startle response in the fish larvae. For DBP, the bPOD was 0.24 mg/L.

Table 2-1. Acute Toxicity of DBP in Aquatic Vertebrates

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
African clawed frog (*Xenopus laevis*)	0.1/0.5 mg/L	96-hour NOEC/LOEC	Development/ Growth	(Lee et al., 2005) (High)
	0.9 mg/L	96-hour EC50		
	7.5 mg/L	96-hour EC50	Growth	(Xu and Gye, 2018) (High)
	6.3 mg/L	96-hour LOEC		
	8.40 mg/L	96-hour EC50	Growth	(Gardner et al., 2016) (Medium)
	5.8/8.3 mg/L	96-hour NOEC/LOEC		
Fathead minnow (*Pimephales promelas*)	**1.54 mg/L**	96-hour LC50	Mortality	(Adams et al., 1995) (High)
	0.8/2.1 mg/L	24-hour NOEC/ LOEC	Mortality	(Bencic et al., 2024)
	0.92 mg/L	144-hour LC50	Mortality	(EG&G Bionomics, 1984a) (High)
	2.02 mg/L	96-hour LC50	Mortality	(McCarthy and Whitmore, 1985) (Medium)
	0.85 mg/L	96-hour LC50	Mortality	(Defoe et al., 1990) (High)
	1.1 mg/L			
	1.0 mg/L	96-hour LC50	Mortality	(Smithers Viscient, 2018) (Medium)
	0.53/1.4 mg/L	96-hour NOEC/LOEC		

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
	0.8/2.1 mg/L	24-hour NOEC/LOEC	Mortality	(Bencic et al., 2024)
	0.12 mg/L	24-hour tPOD	Transcriptomic change	
	0.11 mg/L	24-hour mPOD	Metabolomic change	
	0.24 mg/L	24-hour bPOD	Behavior	
Bluegill (*Lepomis macrochirus*)	**1.2 mg/L**	96-hour LC50	Mortality	(Buccafusco et al., 1981) (Medium)
	0.85 mg/L	96-hour LC50	Mortality	(EG&G Bionomics, 1983b) (High)
	0.48 mg/L	96-hour LC50	Mortality	(Adams et al., 1995) (High)
Rainbow trout (*Oncorhynchus mykiss*)	**1.60 mg/L**	96-hour LC50	Mortality	(Adams et al., 1995) (High)
	1.60 mg/L	96-hour LC50	Mortality	(EG&G Bionomics, 1983a) (High)
	1.4 mg/L	96-hour LC50	Mortality	(EnviroSystem, 1991) (High)
Zebrafish (*Danio rerio*)	**0.63 mg/L**	72-hour LC50	Mortality	(Chen et al., 2014) (Medium)
Bolded values indicate data used to derive acute aquatic COC using SSD				

2.1.2 Chronic Toxicity of DBP in Aquatic Vertebrates

EPA reviewed 16 studies with overall quality determinations of high or medium for chronic toxicity in aquatic vertebrates (Table 2-2). One study received an overall quality determination of unacceptable and was not considered. Of the 16 high and medium quality studies, 11 contained acceptable chronic endpoints that identified definitive hazard values below the DBP limit of water solubility for five fish species and two amphibians.

In zebrafish, there was a significant effect on offspring mortality resulting from females exposed to 0.1 and 0.5 mg/L DBP for 15 days. In the same study, zebrafish embryos exposed to 0.025 and 0.1 mg/L DBP experienced developmental malformations. Further, exposure to DBP incited liver peroxisome proliferation and up-regulation of aromatases in zebrafish embryos and adult females (Ortiz-Zarragoitia et al., 2006). In rainbow trout, the 99-day growth NOEC/LOEC was 0.10/0.19 mg/L (0.14 mg/L maximum acceptable toxicant concentration [MATC]), representing significant effects on fish length

and weight (Rhodes et al., 1995; EnviroSystem, 1991). Additionally, a 13-day NOEC/LOEC of 0.52/1.0 mg/L (1.3 mg/L LC50) and a 99-day NOEC/LOEC of 0.19/0.40 mg/L (0.28 mg/L MATC) for mortality was identified in the rainbow trout (EnviroSystem, 1991).

In a Bagrid catfish (*Pseudobagrus fulvidraco*) feeding study, which used DBP concentrations of 100, 500, and 1000 mg DBP/kg diet, there was an observed significant reduction in body weight in fish that were fed 1000 mg/kg over 8-weeks resulting in an 8-week NOEC/LOEC of 500/1000 mg DBP/kg diet. Additionally, significant effects of acetylcholinesterase activity were observed in the brain at concentrations of 100 mg DBP/kg diet, in the liver, muscle, and kidney at 500 mg DBP/kg diet, in the heart at 1000 mg DBP/kg diet, and in gill tissue at 1000 mg DBP/kg diet. The authors stated that feeding was conducted at a rate of 3% body weight per day based on group biomass at Week 0 and Week 4. Based on this rate, the three given doses in dietary concentration (100/500/1000 mg DBP/kg diet) can be converted to a dose in terms of fish body weight as 3/15/30 mg DBP/kg-bw/day. No significant effects were observed in fish mortality during the 8-week period (Jee et al., 2009). In the fathead minnow, a 20-day NOEC/LOEC of 0.53/0.97 mg/L and 0.97/1.74 mg/L were identified for hatching rate and larval survival, respectively (McCarthy and Whitmore, 1985).

In a multi-generational Japanese medaka (*Oryzias latipes*) study, an LC50 of 0.82 mg/L was identified in embryos exposed (in an aqueous solution) to 0, 0.67, 0.74, 0.80, 1.0, and 1.3 mg/L DBP. In the F0 generation exposed to DBP concentrations of 0, 12, 65, and 776 mg/kg-bw/day via diet, egg production per female fish was significantly reduced at all test concentrations, however there were no significant effects on survival, growth, or sexual development. In the F1 and F2 generations, there were no effects on survival and growth, but there was an observed increase in hepatic vitellogenin levels in the F2 65 mg/kg-bw/day DBP group (12/65 mg/kg-bw/day NOEL/LOEL). Further, in the F1 and F2 generations, there was no egg production at the highest DBP dose (776 mg/kg-bw/day). (Patyna, 1999). In another multigenerational Japanese medaka study in which parental fish were aqueously exposed to DBP at concentrations of 0.015, 0.038, 0.066, 0.103, and 0.305 mg/L for 218 days, significant effects were observed in growth of both male and female F1 and F2 generations. In the male and female F1 generation (subadults), weight was significantly less when compared to controls at 70-days, resulting in NOEC/LOECs of 0.103/0.305 and 0.0387/0.066 mg/L in males and females, respectively. Additionally, in the female F2 generation (subadults), length was significantly less compared to controls at day 70, resulting in a NOEC/LOEC of 0.0156/0.0387 mg/L. Similarly, in the male and female F2 generation (adults), weight was significantly less compared to controls at 98-days, resulting in NOEC/LOECs of 0.103/0.305 and 0.0156/0.0387 mg/L in males and females, respectively. In this study, unbounded effects (unbounded LOEC) were also observed for growth at the lowest concentration tested. Specifically, male F1 adult weight at 112-days, male F2 adult weight and length at 70-days, and male F2 adult length at 98-days were significantly inhibited at 0.015 mg/L DBP (EAG Laboratories, 2018).

345 **Table 2-2. Chronic Toxicity of DBP in Aquatic Vertebrates**

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
African clawed frog (*Xenopus laevis*)	0.1 mg/L	30-week LOEC	Growth	(Lee and Veeramachaneni, 2005) (High)
	2/10 mg/L	22-day NOEC/LOEC	Growth	(Shen et al., 2011) (High)
	0.00476/0.0134 mg/L	21-day NOEC/LOEC	Growth	(Battelle, 2018) (High)
Japanese wrinkled frog (*Glandirana rugosa*)	0.28/2.8 mg/L	21-day NOEC/LOEC	Growth	(Ohtani et al., 2000) Medium)
Zebrafish (*Danio rerio*)	0.1 mg/L	5-week LOEC	Mortality	(Ortiz-Zarragoitia et al., 2006) (Medium)
Rainbow trout (*Oncorhynchus mykiss*)	0.1/0.19 mg/L	99-day NOEC/LOEC	Growth	(Rhodes et al., 1995) (High)
	1.3 mg/L	13-day LC50	Mortality	(EnviroSystem, 1991) (High)
	0.52/1.0 mg/L	13-day NOEC/LOEC		
	0.28 mg/L	99-day MATC		
	0.19/0.40 mg/L	99-day NOEC/LOEC		
	0.14 mg/L	99-day MATC	Growth	
	0.10/0.19 mg/L	99-day NOEC/LOEC		
Bagrid catfish (*Pseudobagrus fulvidraco*)	15/30 mg/kg-bw/day (feeding study)	8-week NOEC/ LOEC	Growth	(Jee et al., 2009) (High)
Fathead minnow (*Pimephales promelas*)	0.53/0.97 mg/L	20-day NOEC/ LOEC	Mortality – hatch rate	(McCarthy and Whitmore, 1985) (Medium)
	0.97/1.74 mg/L		Mortality – larval survival	
Japanese medaka (*Oryzias latipes*)	<12/12 mg/kg-bw/day (Feeding study)	180-day LOEC	Reproduction – F0 egg production per female	(Patyna, 1999) (High)
	65/776 mg/kg-bw/day (Feeding study)	180-day NOEC/ LOEC	Reproduction – F1 egg production per female	
	65/776 mg/kg-bw/day (Feeding study)	180-day NOEC/ LOEC	Growth – weight, female F1	
	0.82 mg/L	17-day LC50	Mortality	
	0.103/0.305 mg/L	70-day NOEC/ LOEC	Growth – weight, male F1 subadults	(EAG Laboratories, 2018) (High)
	0.0156/0.0387		Growth – length,	

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
Japanese medaka (*Oryzias latipes*)	mg/L		male F1 subadults	
	0.0387/0.066 mg/L		Growth – weight, female F1 subadults	
	0.0156/0.0387 mg/L		Growth – length, female F1 subadults	
	<0.0156 mg/L/ 0.0156 mg/L	112-day LOEC	Growth – weight, male F1 adults	
	0.0156/0.0387 mg/L	112-day NOEC/LOEC	Growth – length, male F1 adults	
	0.066/0.103 mg/L		Growth – weight and length, female F1 adults	
	<0.0156 mg/L/ 0.0156 mg/L	70-day LOEC	Growth – weight and length, male F2 subadults	
	0.0156/0.0387 mg/L	70-day NOEC /LOEC	Growth – length and weight, female F2 subadults	
	<0.0156 mg/L/ 0.0156 mg/L	98-day LOEC	Growth – length, male F2 adults	
	0.103/0.305 mg/L	98-day NOEC /LOEC	Growth – weight, male F2 adults	
	0.0156/0.0387 mg/L		Growth – length and weight, female F2 adults	

Bolded values indicate hazard value used in determining concentration of concern (COC).

2.1.3 Acute Toxicity of DBP in Aquatic Invertebrates

EPA reviewed 11 studies that received overall quality determinations of high or medium for acute toxicity in aquatic invertebrates (Table 2-3). Three studies received overall quality determinations of low or unacceptable and were not considered. All 11 of the high and medium quality studies contained acceptable chronic endpoints that identified definitive hazard values below the DBP limit of water solubility for 9 aquatic invertebrate species. Additionally, predicted hazard data for 53 species were generated using EPA's Web-ICE tool, including predictions for 31 aquatic vertebrates, 5 aquatic invertebrates, 16 benthic invertebrates, and 1 amphibian species.

In the opposum shrimp, the mortality 96-hour LC50s ranged from 0.50 to 0.75 mg/L. Mortality was assessed at 48- and 72-hours, resulting in a 0.87 and 0.77 mg/L LC50, respectively (EG&G Bionomics, 1984b). In the water flea (*Daphnia magna*), the 48-hour mortality LC50s ranged from 2.55 to 5.2 mg/L (Wei et al., 2018; McCarthy and Whitmore, 1985). In the water flea, additional endpoints of immobilization were also identified, resulting in 24-hour LC 50 of 8.0 mg/L and 48-hour EC50 of 2.99 mg/L. In Taiwan abalone (*Haliotis diversicolor*), at DBP concentrations of 0, 0.5, 0.2, 2.0, 10, and 15 mg/L, one study identified abnormal growth of embryos exposed to 10 mg/L DBP, resulting in a 96-hour NOEC/LOEC of 2.0/10 mg/L (Yang et al., 2009). Another Taiwan abalone embryo study that

utilized DBP concentrations of 0, 0.0017, 0.0207, 0.196, 1.984, 20.09, 9.22, and 39.47 mg/L demonstrated significant effects on embryonic development resulting in a 9-hour EC50 of 8.37 mg/L. Additionally, metamorphosis was found to be disrupted at 10 mg/L DBP resulting in a 96-hour NOEC/LOEC of 2.0/10 mg/L. Lastly, there was a significant increase in population growth and a negative effect on sexual reproduction in the rotifer (*Brachionus calyciflorus*) with a resulting 0.5/1.0 mg/L 48-hour no-observed-adverse-effect-concentration (NOAEC)/lowest-observed-adverse-effect-concentration (LOAEC) and 1.0/2.0 mg/L 96-hour NOAEC/LOAEC, respectively (Cruciani et al., 2015). The bolded values in Table 2-3 describe data which were used as inputs for generating Web-ICE predictions and within an SSD (Appendix B).

Table 2-3. Acute Toxicity of DBP in Aquatic Invertebrates

Test Organism (Species_	Hazard Values	Endpoint	Effect	Citation (Study Quality)
Opossum shrimp (*Americamysis bahia*)	**0.75 mg/L**	96-hour LC50	Mortality	(EG&G Bionomics, 1984b)
	0.77 mg/L	72-hour LC50	Mortality	
	0.87 mg/L	48-hour LC50	Mortality	
	0.50 mg/L	96-hour LC50	Mortality	(Adams et al., 1995) (High)
Water flea (*Daphnia magna*)	**2.99 mg/L**	48-hour EC50	Immobilization	
Taiwan abalone (*Haliotis diversicolor*)	2/10 mg/L	96-hour NOEC/ LOEC	Development/Growth	(Yang et al., 2009) (Medium)
Taiwan abalone (*Haliotis diversicolor*)	8.37 mg/L	9-hour EC50	Development/Growth	(Liu et al., 2009) (Medium)
	0.0207/0.196 mg/L	96-hour NOEC/ LOEC	Development/Growth – metamorphosis	
Water flea (*Daphnia magna*)	**5.2 mg/L**	48-hour LC50	Mortality	(McCarthy and Whitmore, 1985) (Medium)
	2.55 mg/L	48-hour LC50	Mortality	(Wei et al., 2018) (High)
	4.31 mg/L		Mortality	
	2.83 mg/L		Mortality	
	8.0 mg/L	24-hour LC50	Immobilization	(Huang et al., 2016) (High)
Rotifer (*Brachionus calyciflorus*)	1.0/2.0 mg/L	96-hour NOAEC/ LOAEC	Reproduction	(Cruciani et al., 2015) (Medium)
	0.5/1.0 mg/L	48-hour NOAEC/ LOAEC	Population	
Bolded values indicate data used to derive acute aquatic COC using SSD.				

2.1.4 Chronic Toxicity of DBP in Aquatic Invertebrates

EPA reviewed 13 studies which received an overall quality determination of high or medium for chronic toxicity in aquatic invertebrates (Table 2-4). One study received an overall quality determination of low and was not considered. Of the 13 high and medium quality studies, 8 contained chronic endpoints that

identified definitive hazard values below the DBP limit of water solubility for 10 aquatic invertebrate species.

A 21-day mortality NOEC/LOEC of 0.96/2.5 mg/L and a 21-day mortality LC50 of 1.92 mg/L were identified in the water flea (*Daphnia magna*). Reproduction, population, development, and growth endpoints were also identified. For reproduction, there was an observed decrease of fecundity in three studies resulting in a range of NOEC/LOECs of 0.07/0.23 (number of days between eggs laid) to 1.05/1.92 mg/L (1.64 mg/L, 21-day EC50). In the water flea, there was also an observed reduction in population growth rate (total neonates) with a NOEC/LOEC of 0.42/0.48 mg/L and a reduction in development/growth (length) with a NOAEC/LOAEC of 0.278/2.78 mg/L (Wei et al., 2018; Defoe et al., 1990; Springborn Bionomics, 1984b). In the rotifer (*Brachionus calyciflorus*) at aqueous concentrations of 0, 0.000005, 0.00005, 0.0005, 0.005, 0.05, 0.5, and 5.0 mg/L, significant effects on mortality and reproductive rates were observed after 6 days, resulting in a NOEC/LOEC of 0.05/0.5 mg/L for both endpoints (Zhao et al., 2009).

Table 2-4. Chronic Toxicity of DBP in Aquatic Invertebrates

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
Water flea (*Daphnia magna*)	0.07/0.23 mg/L	21-day NOAEC/ LOAEC	Reproduction – # days between egg laid	(Wei et al., 2018) (High)
	<0.07/0.07 mg/L		Reproduction – Fecundity	
	0.42/0.48 mg/L	21-day NOAEC/ LOAEC	Population	
	0.278/2.78 mg/L	14-day NOAEC/ LOAEC	Development/ Growth	(Seyoum and Pradhan, 2019) (Medium)
	0.96/2.5 mg/L	21-day NOAEC/ LOAEC	Mortality	(Springborn Bionomics, 1984b) (Medium)
	0.96/2.5 mg/L	21-day NOAEC/ LOAEC	Reproduction	
	1.92 mg/L	21-day LC50	Mortality	(Defoe et al., 1990) (High)
	1.64 mg/L	21-day EC50	Reproduction	
	1.05/1.91 mg/L	21-day NOAEC/ LOAEC		
Scud (*Gammarus pulex*)	0.1/0.5 mg/L	20-day NOAEC/ LOAEC	Behavior	(Thurén and Woin, 1991) (Medium)
Amphipod crustacean (Corophium *acherusicum*)	**0.044/0.34 mg/L**	14-day NOAEC/ LOAEC	Population – Abundance	(Tagatz et al., 1983) (Medium)
Rotifer (*Brachionus calyciflorus*)	0.05/0.5 mg/L	6-day NOAEC/LOAEC	Mortality	(Zhao et al., 2009) (Medium)
Rotifer (*Brachionus calyciflorus*)	0.05/0.5 mg/L	6-day NOAEC/LOAEC	Reproduction	
Bolded values indicate hazard value used in determining COC.				

2.1.5 Acute Toxicity of DBP in Benthic Invertebrates

EPA reviewed four studies that received an overall quality determination of high or medium for acute toxicity in aquatic benthic invertebrates (Table 2-5). All four studies contained acute endpoints that identified definitive hazard values below the DBP limit of water solubility for three aquatic invertebrate species. In the harpacticoid copepod (*Nitocra spinipes*) and the midge (*Paratanytarsus parthenogeneticus*), the 96-hour mortality LC50s ranged from 1.7 to 6.29 mg/L (Adams et al., 1995; Linden et al., 1979). In the midges (*Paratanytarsus parthenogeneticus* and *Chironomus plumosus*), the 48-hour mortality LC50s ranged from 4.0 to 5.8 mg/L (EG&G Bionomics, 1984c; Streufort, 1978).

Table 2-5. Acute Toxicity of DBP in Aquatic Benthic Invertebrates

Test Organism	Hazard Values	Endpoint	Effect	Citation (Study Quality)
Harpacticoid copepod (*Nitocra spinipes*)	**1.7 mg/L**	96-hour LC50	Mortality	(Linden et al., 1979) (Medium)
Midge (*Paratanytarsus parthenogeneticus*)	**5.8 mg/L**	48-hour LC50	Mortality	(EG&G Bionomics, 1984c) (High)
Midge (*Paratanytarsus parthenogeneticus*)	6.29 mg/L	96-hour LC50	Mortality	(Adams et al., 1995) (High)
Midge (*Chironomus plumosus*)	**4.0 mg/L**	48-hour LC50	Mortality	(Streufort, 1978) (Medium)
Bolded values indicate data used to derive acute aquatic COC using SSD.				

2.1.6 Chronic Toxicity of DBP in Benthic Invertebrates

EPA reviewed five studies which received an overall quality determination of high or medium for chronic toxicity in benthic invertebrates (Table 2-6). All five studies contained acceptable chronic endpoints that identified definitive hazard values below the DBP limit of water solubility for six benthic invertebrate species. A study (Call et al., 2001a) examining the effects of DBP in sediment pore water and sediment for high, medium, and low TOC (total organic carbon) in *Hyalella azteca* resulted in 10-day development/growth (decrease in weight compared to controls) NOEC/LOECs of 4.76/10.7 mg/L and 3,410/26,200 mg/kg, 4.20/12.9 mg/L and 748/3,340 mg/kg, and 0.70/4.59 mg/L and 41.6/360 mg/kg, respectively. In that study, there were no significant effects on *H. azteca* mortality. In the midge (*Chironomus tentans*), effects on mortality and growth were observed in the high, medium, and low TOC sediment groups. For high TOC, a 10-day NOEC/LOEC of 0.448/5.85 mg/L in sediment pore water and 508/3550 mg/kg in sediment was observed for an increase in weight. For medium TOC, a 10-day NOEC/LOEC of 3.85/16 mg/L in sediment pore water and 423/3090 mg/kg in sediment was observed for an increase in weight relative to controls. For mortality, the 10-day NOEC/LOEC for sediment pore water and sediment in high, medium, and low TOC was 0.448/5.85 mg/L and 508/3550 mg/kg, 3.85/16 mg/L and 423/3090 mg/kg, and 0.672/4.59 mg/L and 50.1/315 mg/kg, respectively (Call et al., 2001a). Another benthic invertebrate study examined the effects of DBP aqueous exposures and observed significant effects in the midge and *H. azteca*. Specifically, in the midge, a 10-day growth and development (weight) NOEC/LOEC of 1.78/4.52 mg/L (2.81 mg/L EC50) and a 10-day mortality LC50 of 2.64 mg/L was observed. In *H. azteca*, a 10-day mortality LC50 of 0.63 mg/L was identified (Call et al., 2001b).

Lake Superior Research Institute (1997) also examined the effects of aqueous and sediment (high, medium, and low TOC) DBP exposures in the midge and the scud. Ten-day LC50s were calculated via multiple methods including Trimmed Spearman-Karber, probit analysis, and/or linear interpolation. In the midge, the high, medium, and low TOC pore water 10-day mortality LC50s ranged from 4.22 to 6.21 mg/L, 10.3 mg/L (one value), and 6.86 to 6.95 mg/L, respectively. The high, medium, and low TOC sediment 10-day mortality LC50s ranged from 4,730 to 5,213 mg/kg, 2,261 to 4,730 mg/kg, and 706 to 827 mg/kg, respectively. Most LC50s were unable to be calculated for the scud due to low mortality, however there was a calculated 10-day mortality LC50 of 52,363 mg/kg in the medium sediment TOC group. That study also conducted water only tests in which 10-day mortality LC50s for the midge ranged from 2.64 to 3.08 mg/L and 0.59 to 0.63 mg/L for the scud (Lake Superior Research Institute, 1997).

In the mollusk (several species), segmented worm (*several species*), *Actiniaria* (unidentified species), and sea squirt (*Molgula manhattensis*), the 14-day population (abundance and diversity) NOEC/LOECs were 0.34/3.7 mg/L. In the amphipod crustacean (*Corophium acherusicum*), the abundance NOEC/LOEC was slightly more sensitive at 0.044/0.34 mg/L (Tagatz et al., 1983). Two additional endpoints were available in two studies for the worm (*Lumbriculus variegatus*) and the scud (*Gammarus pulex*). In the worm, a 2.48 mg/L (in water) 10-day LC50 was identified for mortality (Call et al., 2001b). In the scud (*Gammarus pulex*), there was a significant effect on distance moved and changes in direction resulting in a 20-day NOAEC/ LOAEC of 0.1/0.5 mg/L (in water) (Thurén and Woin, 1991).

Table 2-6. Chronic Toxicity of DBP in Benthic Invertebrates

Test Organism (Species) and TOC	Hazard Values	Endpoint	Effect	Citation (Study Quality)
Hyalella azteca high TOC	4.76/10.7 mg/L	10-day NOAEC/ LOAEC	Development/ Growth	(Call et al., 2001a) (High)
	3,410/26,200 mg/kg dry sediment			
Hyalella azteca Medium TOC	4.20/12.9 [a] mg/L	10-day NOAEC/ LOAEC	Development/ Growth	(Call et al., 2001a) (High)
	748/ 3340 mg/kg dry sediment			
	52,363 mg/kg bulk sediment (Probit)	10-day LC50	Mortality	(Lake Superior Research Institute, 1997) (High)
Hyalella azteca low TOC	0.70/4.59 mg/L	10-day NOAEC/ LOAEC	Development/ Growth	(Call et al., 2001a) (High)
	41.6/360 mg/kg dry sediment			
Midge (*Chironomus tentans*) high TOC	6.12 mg/L (Probit)	10-day LC50	Mortality	(Lake Superior Research Institute, 1997) (High)
	6.21 mg/L (Linear Interpolation)			
	5,213 mg/kg (Linear Interpolation)			
	4.22 mg/L (Trimmed Spearman-Karber)			
	4,730 mg/kg (Trimmed Spearman-Karber)			
	0.448/5.85 mg/L	10-day NOAEC/ LOAEC	Development/ Growth	(Call et al., 2001a)

Test Organism (Species) and TOC	Hazard Values	Endpoint	Effect	Citation (Study Quality)
Midge (*Chironomus tentans*) high TOC	508/3,550 mg/kg dry sediment	10-day NOAEC/ LOAEC		(High)
	0.448/5.85 mg/L	10-day NOAEC/ LOAEC	Mortality	
	4.22 mg/L	10-day LC50		
	508/3,550 mg/kg dry sediment	10-day NOAEC/ LOAEC		
	4,730 mg/kg dry sediment	10-day LC50		
Midge (*Chironomus tentans*) medium TOC	2,261 mg/kg dry sediment (Linear Interpolation)	10-day LC50	Mortality	(Lake Superior Research Institute, 1997) (High)
	10.3 mg/L (Trimmed Spearman-Karber)			
	4,730 mg/kg (Trimmed Spearman-Karber)			
	423/3,090 mg/kg dry sediment	10-day NOAEC/ LOAEC	Development/ Growth	(Call et al., 2001a) (High)
	3.85/16 mg/L	10-day NOAEC/ LOAEC		
	423/3,090 mg/kg dry sediment	10-day NOAEC/ LOAEC	Mortality	
	1,664 mg/kg dw	10-day LC50		
	3.85/16 mg/L	10-day NOAEC/ LOAEC		
	10.3 mg/L	10-day LC50		
Midge (*Chironomus tentans*) low TOC	6.95 mg/L (Trimmed Spearman-Karber)	10-day LC50	Mortality	(Lake Superior Research Institute, 1997) (High)
	827 mg/kg (Trimmed Spearman-Karber)			
	6.88 mg/L (Probit)			
	820 mg/kg (Probit)			
	6.86 mg/L (Linear Interpolation)			
	706 mg/kg dry sediment (Linear Interpolation)			
	0.672/4.59 mg/L	10-day NOAEC/ LOAEC		(Call et al., 2001a) (High)
	50.1/315 mg/kg dry sediment	10-day NOAEC/ LOAEC		
Midge (*Chironomus tentans*)	1.78/4.52 mg/L	10-day NOAEC/ LOAEC	Development/ Growth	(Call et al., 2001b) (High)
	2.81 mg/L	10-day EC50		
	2.64 mg/L	10-day LC50	Mortality	

Test Organism (Species) and TOC	Hazard Values	Endpoint	Effect	Citation (Study Quality)
Hyalella azteca	0.63 mg/L	10-day LC50	Mortality	(Call et al., 2001b) (High)
Midge (*Chironomus tentans*) water only test	2.64 mg/L (Trimmed Spearman-Karber) 3.08 mg/L (Linear Interpolation)	10-day LC50	Mortality	(Lake Superior Research Institute, 1997) (High)
Hyalella Azteca water only test	0.63 mg/L (Trimmed Spearman-Karber) 0.62 mg/L (Probit) 0.59 mg/L (Linear Interpolation)	10-day LC50	Mortality	(Lake Superior Research Institute, 1997) (High)
Mollusk (*several species*)	0.34/3.7 mg/L	14-day NOAEC/ LOAEC	Population – Abundance and Diversity	(Tagatz et al., 1983) (Medium)
Segmented worm (*several species*)	0.34/3.7 mg/L	14-day NOAEC/ LOAEC	Population – Abundance and Diversity	
Amphipod crustacean (Corophium *acherusicum*)	**0.044/0.34 mg/L**	14-day NOAEC/ LOAEC	Population – Abundance	
Actiniaria (unidentified species)	0.34/3.7 mg/L	14-day NOAEC/ LOAEC	Population – Diversity	
Sea squirt (*Molgula manhattensis*)	0.34/3.7 mg/L	14-day NOAEC/ LOAEC	Population – Abundance and Diversity	
Worm (*Lumbriculus variegatus*)	2.48 mg/L	10-day LC50	Mortality	(Call et al., 2001b) (High)
Scud (*Gammarus pulex*)	0.1/0.5 mg/L	20-day NOAEC/ LOAEC	Behavior	(Thurén and Woin, 1991) (Medium)

TOC = total organic carbon
[a] Value slightly greater than DBP water solubility. Species included for mollusk are *Diastoma varium*, *Laevicardium mortoni*, *Tellina* sp., *Anomalocardia auberiana*, *Marginella apicina*, *Morula didyma*, *Anadara transversa*, *Mitrella lunata*, *Crassostrea virginica*, *Eupleura sulcidentata*, *Mangelia quadrata*, *Thais haemastoma*, *Bursatella leachii pleii*, *Atrina rigida*, and *Polinices duplicatus*. Species included for the segmented worm include *Haploscoloplos robustus*, *Tharyx marioni*, *Loimia viridis*, *Scoloplos rubra*, *Mediomastus californiensis*, *Malacoceros vanderhorsti*, *Aricidea fragilis*, *Armandia agilis*, *Axiothella mucosa*, *Nephtys picta*, *Prionospio heterobranchia*, Unidentified Sabellidae, *Amphictene* sp., *Galathowenia* sp., *Glycera americana*, *Lumbrineris* sp., *Magelona rosea*, *Minuspio* sp., *Neanthes succinea*, and *Pectinaria gouldii*.
Bolded values indicate hazard value used in determining COC.

2.1.7 Toxicity of DBP in Aquatic Plants and Algae

EPA reviewed seven studies which received overall quality determinations of high or medium for toxicity in aquatic plants and algae (Table 2-7). Three studies received overall quality determinations of low or unacceptable and were not considered. Of the 7 high and medium quality studies, 3 contained acceptable endpoints that identified definitive hazard values below the DBP limit of water solubility for one species of green algae (*Selenastrum capricornutum*). A 10-day static toxicity test examined the percent increase or decrease of chlorophyll α at DBP concentrations of 0.05, 0.08, 0.13, 0.39, 0.77, and 1.45 mg/L. Chlorophyll *a* was found to increase slightly at lower concentrations, then decreased at higher concentrations with an observed 100 percent decrease in chlorophyll α at 1.45 mg/L DBP

resulting in a 10-day EC50 of 0.75 mg/L. The study authors noted that there was considerable loss of phthalate esters from the test solutions and thus the EC50 values were calculated based on concentrations measured at the beginning of the study (Springborn Bionomics, 1984c). Two other studies examined the effects of DBP on *S. capricornutum* abundance. Adams et al. (1995) identified a 96-hour EC50 of 0.40 in *S. capricornutum* with DBP concentrations ranging from 0.21 to 377 mg/L and Adachi et al. (2006) identified a 96-hour NOEC/LOEC of 0.1/1.0 mg/L in *S. capricornutum* at concentrations ranging from 0.1 to 10 mg/L.

Table 2-7. Toxicity of DBP in Aquatic Plants and Algae

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
Green algae (*Selenastrum capricornutum*)	0.75 mg/L	10-day EC50	Population (Chlorophyll α concentration)	(Springborn Bionomics, 1984c) (High)
	0.40 mg/L	96-hour EC50	Population (Abundance)	(Adams et al., 1995) (High)
	0.1/1 mg/L	96-hour NOEC/ LOEC	Population (Abundance)	(Adachi et al., 2006) (Medium)
Bolded values indicate hazard value used in determining COC.				

2.2 Terrestrial Species

EPA reviewed 35 studies for DBP toxicity to terrestrial organisms. Some studies may have included multiple endpoints, species, and test durations. Of these 35 studies, those that received an overall quality determination of low or uninformative were not considered for quantitative risk evaluation. For the 30 studies that received an overall quality determination of high and medium, those that demonstrated no acute or chronic adverse effects at the highest dose tested (unbounded NOAELs) are listed in Appendix C and were excluded from consideration for development of hazard thresholds. In addition to the 30 high or medium quality terrestrial wildlife studies, EPA considered 13 terrestrial vertebrate studies for toxicity to DBP in human health animal model rodent species that contained ecologically relevant reproductive endpoints (Table_Apx C-7).

2.2.1 Toxicity of DBP in Terrestrial Vertebrates

No reasonably available information was identified for exposures of DBP to mammalian wildlife. EPA reviewed 13 studies for toxicity to DBP in human health animal model rodent studies that contained ecologically relevant reproductive endpoints (Table_Apx C-7). EPA's decision to focus on ecologically relevant (population level) reproductive endpoints in the rat and mouse data set for DBP for consideration of a hazard threshold in terrestrial mammals is due to the known sensitivity of these taxa to DBP in eliciting phthalate syndrome (U.S. EPA, 2024b). Of the 13 rat and mouse studies containing ecologically relevant reproductive endpoints, EPA selected the study with the most sensitive LOAEL for deriving the hazard threshold for terrestrial mammals (Table 2-8). The most sensitive endpoint resulted from a Sprague-Dawley rat (*Rattus norvegicus*) study in which a 17-week LOAEL for significant reduction in number of live pups per litter was observed at 80 mg/kg-bw/day DBP intake in dams (NTP, 1995).

Table 2-8. Toxicity of DBP to Terrestrial Vertebrates

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
Rat (*Rattus norvegicus*)	**80 mg/kg-bw/day**	17-week LOAEL	Reproduction	(NTP, 1995) (High)

2.2.2 Toxicity of DBP in Soil Invertebrates

EPA reviewed 14 studies that received an overall quality determination of high or medium for acute toxicity in soil invertebrates (Table 2-9). One study received an overall quality determination of low and was not considered. Of the 14 high and medium quality studies, 12 contained acute endpoints that identified definitive hazard values below the DBP limit of water solubility for five soil invertebrate species.

In the European house dust mite (*Dermatophagoides pteronyssinus*), American house dust mite (*Dermatophagoides farina*), and copra mite (*Tyrophagus putrescentiae*), the 24-hour mortality LC50s with fabric contact to DBP were found to range from 0.017 to 0.03 mg/cm^2 and 0.077 to 0.079 mg/cm^2 (LD50s) via direct application of DBP (Wang et al., 2011; Kim et al., 2008, 2007; Kang et al., 2006; Tak et al., 2006; Kim et al., 2004). In the earthworm (*Eisenia fetida*), the 48-hour mortality LC50 via DBP on filter paper ranged from 1.3 to 6.8 mg/cm^2 (Du et al., 2015; Neuhauser et al., 1985). Because filter paper contact is not considered a relevant exposure pathway for soil invertebrates due to the absorbed amount of chemical via dermal contact being uncertain, EPA did not establish a hazard threshold from the filter paper data set. In the nematode (*Caenorhabditis elegans*), the 24-hour reproduction NOEC/LOEC were 2.783/27.83 mg/L and 27.83/139.17 mg/L for hatching rate and brood size, respectively. Specifically, nematodes exposed to DBP at concentrations of 0.0278, 2.78, 27.8, and 139 mg/L experienced an increase in embryonic lethality (reduced hatch rate) at 27.8 mg/L and a decrease in mean number of eggs laid at 139 mg/L (Shin et al., 2019).

In the springtail (*Folsomia fimetaria*), the 21-day mortality LC10 and LC50 for juveniles was 11.3 and 19.4 mg/kg, respectively, and 33 and 305 mg/kg, respectively, for adults. Adult springtail reproduction was also significantly affected with an observed 21-day EC10 and EC50 of 14 and 68 mg/kg (Jensen et al., 2001). A 14-day earthworm (*Eisenia fetida*) study identified a mortality LC50 of 2,364.8 mg/kg. In this study, mechanistic endpoints were also observed; superoxide dismutase and catalase were found to be significantly reduced at 100 mg/kg DBP on day 28; glutathione-S-transferase was increased after day 21 in the 10 to 50 mg/kg DBP group; glutathione was found to increase on days 7 to 28 in the 50 mg/kg DBP group; and malondialdehyde was greater in all dosage groups and time frames compared to controls (Du et al., 2015).

Table 2-9. Toxicity of DBP in Soil Invertebrates

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
European house dust mite (*Dermatophagoides pteronyssinus*)	0.07779 mg/cm^2 (Direct application)	24-hour LD50	Mortality	(Kang et al., 2006) (Medium)
	0.02323 mg/cm^2 (Fabric contact)	24-hour LC50		(Wang et al., 2011) (Medium)
	0.02851 mg/cm^2 (Fabric contact)	24-hour LC50		(Kim et al., 2008) (Medium)

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
	0.03159 mg/cm^3 (Fabric contact)	24-hour LC50		(Kim et al., 2004) (Medium)
	0.01881 mg/cm^2 (Fabric contact)	24-hour LC50		(Kim et al., 2007) (Medium)
American house dust mite (*Dermatophagoides farina*)	0.07954 mg/cm^2 (Direct application)	24-hour LD50	Mortality	(Kang et al., 2006) (Medium)
	0.02189 mg/cm^2 (Fabric contact)	24-hour LC50		(Wang et al., 2011) (Medium)
	0.0281 mg/cm^2 (Fabric contact)	24-hour LC50		(Kim et al., 2008) (Medium)
	0.03392 mg/cm^3 (Fabric contact)	24-hour LC50		(Kim et al., 2004) (Medium)
	0.01739 mg/cm^2 (Fabric contact)	24-hour LC50		(Kim et al., 2007) (Medium)
Copra mite (*Tyrophagus putrescentiae*)	0.02523 mg/cm^2 (Fabric contact)	24-hour LC50	Mortality	(Tak et al., 2006) (Medium)
Earthworm (Eisenia fetida)	6.8 mg/cm^2 (Filter paper)	48-hour LC50	Mortality	(Du et al., 2015) (Medium)
	1.360 mg/cm^2 (Filter paper)	48-hour LC50	Mortality	(Neuhauser et al., 1985) (Medium)
Nematode (*Caenorhabditis elegans*)	2.783/27.83 mg/L in solution	24-hour NOEC/LOEC	Reproduction (Hatch rate)	(Shin et al., 2019) (High)
	27.83/139.17 mg/L in solution	24-hour NOEC/LOEC	Reproduction (Brood size)	
Springtail (*Folsomia fimetaria*) – Juvenile	11.3 mg/kg dry soil	21-day LC10	Mortality	(Jensen et al., 2001) (High)
	19.4 mg/kg dry soil	21-day LC50		
Springtail (*Folsomia fimetaria*) – Adult	33 mg/kg dry soil	21-day LC10		
	305 mg/kg dry soil	21-day LC50		
	14 mg/kg dry soil	21-day EC10	Reproduction	
	68 mg/kg dry soil	21-day EC50		
Earthworm (*Eisenia fetida*)	2364.8 mg/kg dry soil	14-day LC50	Mortality	(Du et al., 2015) (Medium)
Bolded values indicate hazard value used in determining a hazard value.				

2.2.3 Toxicity of DBP in Terrestrial Plants

EPA reviewed 12 studies that received an overall quality determination of high or medium for hazard in terrestrial plants (Table 2-10). Three studies received overall quality determinations of low or

unacceptable and were not considered. Of the 12 high and medium quality studies, 6 contained acceptable endpoints that identified definitive hazard values for 10 terrestrial plant species.

The main endpoint observed to be affected by exposure to DBP was growth. In the dutch clover (*Trifolium repens*), turnip (*Brassica rapa* ssp. rapa), rippleseed plantain (*Plantago major*), and velvetgrass (*Holcus lanatus*), there was an observed reduction in total biomass after DBP administration via fumigation, resulting in a 62-day growth EC10s of 0.00033, 0.00077, 0.00239, 0.00879 mg/m^3, respectively. Similarly, in the common bean (*Phaseolus vulgaris*) that was harvested after 42 days, there was an observed reduction in total biomass resulting in an EC10 of 0.00232 mg/m^3 (Dueck et al., 2003). Because fumigation is not considered a relevant exposure pathway for soil invertebrates due to the exposure of the amount of chemical being uncertain, EPA did not establish a hazard threshold from the fumigation data set. For plants exposed to DBP via soil, there was an observed reduction in biomass resulting in a 72-hour EC50, 72-hour NOEC/LOEC, and 45-day NOEC/LOEC of 1,559 mg/kg, 5/20 mg/kg, and 10/100 mg/kg in mung bean (*Vigna radiata*), bread wheat (*Triticum aestivum*), and false bok choy (*Brassica parachinensis*), respectively (Zhao et al., 2016; Ma et al., 2015; Ma et al., 2014). Unbound LOAECs were also observed in which significant effects on growth were observed at the lowest concentration tested. Specifically, in the common onion (*Allium cepa*), alfalfa (*Medicago sativa*), radish (*Raphanus sativus*), cucumber (*Cucumis sativus*), and common oat (*Avena sativa*), growth was significantly less compared to controls at 5 mg/kg soil (Ma et al., 2015). In false bok choy there were also observed mechanistic effects including a reduction in chlorophyll content, intercellular CO_2 concentration, and catalase, as well as an increase in malondialdehyde—all of which resulted in a NOEC/LOEC of 10/100 mg/kg (Zhao et al., 2016).

In bread wheat exposed to DBP at concentrations of 0, 5, 10, 20, 30, and 50 mg/L, significant decreases in the growth of roots and shoots up until germination were identified resulting in growth EC10s and EC50s of 5.08 and 37.70 mg/L and 8.02 and 42.73 mg/L, respectively. Additionally, seed germination was inhibited by DBP and was found to be 76.51 percent at 40 mg/L (Gao et al., 2017). Similarly, a 40-day LOEL of 10 mg/kg DBP (lowest concentration used in the study) for reduced weight in bread wheat was observed (Gao et al., 2019). In rapeseed (*Brassica napus*), a reduction in weight was also observed at the lowest concentration used in the study resulting in an unbound LOEC of 50 mg/kg (Kong et al., 2018). Lastly, in the Chinese sprangletop (*Leptochloa chinensis*) and rice (*Oryza sativa*) exposed to DBP concentrations of 1.2, 2.4, and 4.8 kg/ha via soil surface, there was an observed reduced seedling growth (emergence) and weight in sprangletop resulting in a 14-day NOEC/LOEC of 1.2/2.4 kg/ha and reduced root length, shoot height, and weight in rice resulting in a 14-day NOEC/LOEC 2.4/4.8 kg/ha (Chuah et al., 2014).

Table 2-10. Toxicity of DBP in Terrestrial Plants

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
Dutch clover (*Trifolium repens*)	0.00033 mg/m^3 (Fumigation)	62-day EC10	Growth	(Dueck et al., 2003) (High)
Turnip (*Brassica rapa ssp. rapa*)	0.00077 mg/m^3 (Fumigation)	62-day EC10	Growth	
Rippleseed plantain (*Plantago major*)	0.00239 mg/m^3 (Fumigation)	62-day EC10	Growth	
Velvetgrass (*Holcus lanatus*)	0.00879 mg/m^3 (Fumigation)	62-day EC10	Growth	
Common bean	0.00232 mg/m^3	42-day EC10	Growth	

Test Organism (Species)	Hazard Values	Endpoint	Effect	Citation (Study Quality)
(*Phaseolus vulgaris*)	(Fumigation)			
Mung bean (*Vigna radiata*)	1559 mg/kg dry soil	72-hour EC50	Growth	(Ma et al., 2014) (Medium)
Common onion (*Allium cepa*)	<5 mg/kg soil/5 mg/kg soil	168-hour LOEC	Growth	(Ma et al., 2015) (High)
Alfalfa (*Medicago sativa*)	<5 mg/kg soil/5 mg/kg soil	72-hour LOEC		
Radish (*Raphanus sativus*)	<5 mg/kg soil/5 mg/kg soil			
Cucumber (*Cucumis sativus*)	<5 mg/kg soil/5 mg/kg soil			
Common oat (*Avena sativa*)	<5 mg/kg soil/5 mg/kg soil			
Bread wheat (*Triticum aestivum*)	5/20 mg/kg soil	72-hour NOEC/ LOEC		
	5.08 mg/L	Until germination EC10	Growth (Roots)	(Gao et al., 2017) (High)
	37.70 mg/L	Until germination, EC50		
	8.02 mg/L	Until germination EC10	Growth (Shoots)	
	42.73 mg/L	Until germination EC50		
	30/40 mg/L	Until germination NOEC/LOEC	Reproduction (Germination)	
	<10 mg/kg dry soil/10 mg/kg dry soil	40-day LOEL	Growth	(Gao et al., 2019) (High)
False bok choy (*Brassica parachinensis*)	10/100 mg/kg dry soil	45-day NOAEC/ LOAEC	Growth	(Zhao et al., 2016) (Medium)
Chinese sprangletop (*Leptochloa chinensis*)	1.2/2.4 kg/ha	14-day NOEC/ LOEC	Growth	(Chuah et al., 2014) (Medium)
	<500 mg/L	7-day LOEC	Reproduction (Germination)	
Rice (*Oryza sativa*)	2.4/4.8 kg/ha	14-day NOEC/ LOEC	Growth	
Rapeseed (Brassica napus)	<50 mg/kg dry soil/50 mg/kg dry soil	30-day LOEC	Growth	(Kong et al., 2018) (Medium)
Bolded values indicate hazard value used in determining a hazard value.				

2.3 Hazard Thresholds

EPA calculates hazard thresholds to identify potential concerns to aquatic and terrestrial species. After weighing the scientific evidence, EPA selects the appropriate toxicity value from the integrated data to use for hazard thresholds. See 0 for more details about how EPA weighed the scientific evidence and

Section 2.4 for the weight of scientific evidence conclusions.

2.3.1 Acute Aquatic Concentration of Concern

For aquatic species EPA uses probabilistic approaches (*e.g.*, an SSD) when enough data are available, and deterministic approaches (*e.g.*, deriving a geometric mean of several comparable values) when more limited data are available. An SSD is a type of probability distribution of toxicity values from multiple species. It can be used to visualize which species are most sensitive to a toxic chemical exposure, and to predict a concentration of a toxic chemical that is hazardous to a percentage of test species. This hazardous concentration is represented as an HC_p, where p is the percent of species below the threshold. EPA used an HC_{05} (a Hazardous Concentration threshold for 5% of species) to estimate a concentration that would protect 95 percent of species. This HC_{05} can then be used to derive a COC, which is the estimated hazardous concentration of DBP in water for aquatic organisms. For the deterministic approaches, COCs are calculated by dividing a hazard value by an assessment factor (AF) according to EPA methods (U.S. EPA, 2016, 2014, 2012). However, for the probabilistic approach used for acute aquatic hazard in this TSD, the lower bound of the 95 percent confidence interval (CI) of the HC_{05} can be used to account for uncertainty instead of dividing by an AF. EPA has more confidence in the probabilistic approach when enough data are available because an HC_{05} is representative of a larger portion of species in the environment. Generally, EPA considers the probabilistic approach for aquatic hazard (*i.e.*, an SSD) appropriate when hazard values for at least eight species are represented in the data set.

The aquatic acute COC for DBP was derived from an SSD that contained 96-hour LC50s for 9 species identified in systematic review, bolstered by an additional 53 predicted LC50 values from the Web-ICE v4.0 toxicity value estimation tool. Web-ICE (Web-based Interspecies Correlation Estimation) is a tool developed by U.S. EPA's Office of Research and Development that estimates the acute toxicity of a chemical to a species, genus, or family from the known toxicity of the chemical to a surrogate species. It was used to obtain estimated acute toxicity values for DBP in species that were not represented in the empirical data set. All empirical studies included in the SSD were rated high or medium quality. After reviewing the possible statistical distributions for the SSD, the maximum likelihood method was chosen with a Gumbel distribution. This choice was based on an examination of p-values for goodness of fit, visual examination of Q-Q plots, and evaluation of the line of best fit near the low-end of the SSD. The HC05 for this distribution is 414.9 µg/L DBP. After taking the lower 5th percentile of this HC05 as an alternative to the use of assessment factors, the acute aquatic COC for vertebrates and invertebrates is 347.6 µg/L DBP.

See Appendix B for details of the SSD that was used to derive the acute aquatic COC for DBP.

The multiomics-based PODs derived by EPA in Bencic et al. (2024) suggest that *Pimephales promelas* (fathead minnow) larvae exhibited changes in gene expression, metabolite levels, and swimming behavior at concentrations of DBP near the SSD-derived COC. EPA did not use the multiomics-based PODs for hazard thresholds because it is uncertain if these sub-organismal and individual-level effects (e.g., behavior) at short exposure durations scale up to ecologically relevant outcomes, such as survival and reproduction, in wild fish populations. Notably, the PODs derived from the multiomics study are similar to the SSD-derived acute aquatic COC (Table 2-11). This provides additional confidence in the acute aquatic COC for DBP, as the multiomics approach resulted in a similar hazard value to that derived from empirical and modeled data in the SSD.

Table 2-11. Acute Aquatic COC and Multiomics PODs

Acute Aquatic COC (SSD-Derived)	Transcriptomic POD	Metabolomic POD	Behavioral POD
347.6 µg/L	120 µg/L	110 µg/L	240 µg/L

2.3.2 Chronic Aquatic Vertebrate Concentration of Concern

EPA reviewed 17 studies on chronic toxicity in aquatic vertebrates. The most sensitive organism for which a clear population-level fitness endpoint could be obtained was for Japanese medaka (*O. latipes*) (EAG Laboratories, 2018). This study was rated high quality. In this multi-generational study, the growth of the F1 and F2 generations of fish was significantly affected by exposure to DBP. In male F1 generation Japanese medaka, there was a significant inhibition of bodyweight at the lowest concentration studied, with an unbounded LOEC value of 15.6 µg/L DBP. The ChV (Chronic value, the geometric mean of the NOEC and LOEC) for bodyweight inhibition in female F1 generation Japanese medaka was 82.4 µg/L DBP. In the F2 generation, the ChV for bodyweight inhibition in male fish was 177.2 µg/L DBP, while the ChV for bodyweight inhibition in F2 female fish was 24.6 µg/L DBP. The most sensitive of these endpoints is the unbounded LOEC for inhibition of bodyweight in F1 males at 15.6 µg/L DBP. At the lowest dose (15.6 µg/L), bodyweight was inhibited by 13.4 percent relative to the vehicle control, and there was a statistically significant trend toward greater bodyweight inhibition with increasing dose, culminating at 34.0 percent inhibition at the highest dose (305 µg/L). Based on the presence of a statistically significant dose-response relationship and a population-level fitness endpoint, the 112-day ChV for bodyweight inhibition in F1 male Japanese medaka was selected to derive the chronic COC for aquatic vertebrates.

Because the most sensitive endpoint in this study was an unbounded LOEC, an AF of 10 was applied. This is to account for the uncertainty in the actual threshold dose, which may have been lower than the lowest dose studied. After applying an AF of 10, the chronic COC for aquatic vertebrates is 1.56 µg/L DBP.

2.3.3 Chronic Aquatic Invertebrate Concentration of Concern

EPA reviewed 13 studies on chronic toxicity from DBP in aquatic invertebrates. The most sensitive organism for which a clear population-level fitness endpoint could be obtained was for the marine amphipod crustacean *Monocorophium acherusicum* (Tagatz et al., 1983), with a 14-day ChV of 122.3 µg/L DBP for reduction in population abundance. Populations were reduced by 91 percent at the LOEC, which was 340 µg/L DBP. Higher doses resulted in a complete loss of amphipods in the aquaria. This study was rated medium quality. Based on the presence of a clear dose-response relationship and a population-level fitness endpoint, the 14-day ChV for reduction in population abundance in the marine amphipod crustacean was selected to derive the chronic COC for aquatic invertebrates. After applying an AF of 10, the chronic COC for aquatic invertebrates is 12.23 µg/L DBP.

2.3.4 Acute Benthic Concentration of Concern

Acute toxicity data from three empirical studies, representing LC50 estimates for three species of benthic invertebrates, were included in the SSD for acute aquatic organisms. The acute aquatic COC (see Section 2.3.1), because it was derived from an SSD that contained empirical LC50 data for benthic invertebrates as well as WebICE-derived predicted LC50s for additional benthic species including worms (*Lumbriculus variegatus*), snails (*Physella gyrina*, *Lymnaea stagnalis*), and copepods (*Tigriopus japonicus*), is expected to encompass the level of concern for benthic invertebrates as well. The acute benthic invertebrate COC is therefore 347.6 µg/L DBP in water. There were no studies available to

characterize the acute toxicity of DBP in sediment to benthic invertebrates; therefore, no COC was derived for the sediment exposure pathway.

2.3.5 Chronic Benthic Concentration of Concern

EPA reviewed five studies on chronic toxicity from DBP in benthic invertebrates. Of these, the most sensitive was the midge (*Chironomus tentans*) (Lake Superior Research Institute, 1997), with a 10-day ChV for population loss of 1,143.3 mg DBP/kg dry sediment in medium-TOC sediments (4.80% TOC). This study was rated high quality. This ChV was the middle of three for the midge; the experiment was repeated with low, medium, and high TOC sediments and toxicity decreased with the increase in TOC, as expected for a relatively hydrophobic compound like DBP based on equilibrium partitioning theory. The chosen endpoint for deriving the COC, medium-TOC, was selected because it is the closest to the assumed TOC level (4%) used in Point Source Calculator to estimate DBP exposure in benthic organisms. Population was reduced by 76.7 percent at the LOEC, which was 3,090 mg DBP/kg dry sediment. Higher doses resulted in a similar degree of population loss in the medium-TOC treatment; however, all population losses were significantly different from controls. This endpoint was considered acceptable to derive a COC because of population-level relevance and a demonstrated dose-response relationship. After applying an AF of 10 to the ChV at 1,143.3 mg/kg, the chronic COC for benthic invertebrates is 114.3 mg DBP/kg dry sediment.

2.3.6 Aquatic Plant and Algae Concentration of Concern

EPA reviewed six studies on toxicity from DBP in aquatic plants and algae. Of these, the most sensitive was green algae (*Selenastrum capricornutum*) (Adachi et al., 2006) with a 96-hour ChV of 316 µg/L DBP for reduced population abundance. This study was rated medium quality. There was significant reduction in the algal population at the LOEC, which was 1,000 µg/L DBP, relative to an increase in the algal population at the NOEC of 100 µg/L DBP and in controls. The population reduction was increased with a higher dose of DBP. Therefore, this endpoint was considered acceptable to derive a COC because of population-level relevance and a demonstrated dose-response relationship. After applying an AF of 10, the COC for aquatic plants and algae is 31.6 µg/L DBP.

2.3.7 Terrestrial Vertebrate Hazard Value

EPA reviewed 15 studies on toxicity from DBP in terrestrial vertebrates. Of these, the most sensitive among acceptable-quality studies was the Sprague-Dawley rat (*Rattus norvegicus*) (NTP, 1995), with a 17-week LOAEL for significant reduction in number of live pups per litter at 80 mg/kg-bw/day DBP intake in dams. This study was assigned an overall quality determination of high.

The above referenced study also found a LOAEL for reduced bodyweight in F2 pups at the same dose (80 mg/kg-bw/day). The lowest bounded NOAEL/LOAEL pair for which a ChV could be calculated was significantly reduced bodyweight in F1 pups at a ChV of 115.4 mg/kg-bw/day, but this effect was not as sensitive as reduced number of live pups per litter. Other effects of DBP exposure included significantly decreased female body weight in dams, significantly reduced male sex ratio (percentage of male pups), significantly decreased mating index and pregnancy index in the F1 generation, and significantly reduced male pup weight gain.

Because the most sensitive endpoint in this study was an unbounded LOAEL, the actual threshold dose may have been lower than the lowest dose studied. However, no information was available in the study to adjust the value to account for this uncertainty. Other reproductive endpoints for which bounded NOAEL/LOAEL pairs were observed in rats and mice (see Table_Apx C-7) indicated ChV that were higher than this unbounded LOAEL; therefore, it is not clear whether an adjustment for uncertainty is necessary to adequately characterize the toxicity of DBP to terrestrial mammals. Based on reduction in

live pups per litter, the results found in NTP (1995) indicated that toxicity in terrestrial vertebrates occurs at 80 mg/kg-bw/day.

2.3.8 Soil Invertebrate Hazard Value

EPA reviewed 10 studies on acute toxicity from DBP in terrestrial invertebrates; however, the majority (8 of the 10 studies identified) focused on the use of DBP as a pesticide fumigant and the DBP dose that was experienced by the invertebrates studied could not be determined from the available data. There were two studies identified for which doses could be determined—for the fruit fly (*Drosophila melanogaster*) (Misra et al., 2014) and the nematode (*Caenorhabditis elegans*) (Shin et al., 2019). Both studies were rated medium quality. For the fruit fly, the 72-hour LC50 value in feed (an agar-grape juice solution) was 505,100 mg/L. This exposure was not considered ecologically relevant, as the dose would need to be present in fruit at a concentration that is not possible based on the physicochemical properties of DBP. Such a fruit would be nearly 33 percent DBP by mass. For the nematode, after 24-hours there was no significant mortality observed at any dose examined up to the NOEL of 139.17 mg/L DBP in a buffered water solution. However, this study did not observe any effect of DBP at any dose examined; therefore, this exposure is not appropriate for use in calculating a hazard value.

The same study also examined hatch rate in the nematode (*Caenorhabditis elegans*) on agar plates and had a 24-hour ChV of 8.8 mg/L DBP in agar. However, the magnitude of this effect was small even at the highest DBP dose (an increase in embryonic mortality from approximately 3 to 8%), and it was unclear whether a change of this magnitude has a population-level relevance. Therefore, this study was not considered acceptable to derive a hazard threshold.

EPA reviewed two studies on chronic toxicity from DBP in soil invertebrates. Of these, the most sensitive was the springtail (*Folsomia fimetaria*) (Jensen et al., 2001) with a 21-day EC10 of 14 mg DBP/kg dry soil for reduced reproduction. This study was rated high quality. Reproduction was reduced by approximately 60 percent at the lowest concentration tested, which was 100 mg DBP/kg dry soil, with reproduction completely eliminated at higher doses. Therefore, this endpoint was considered acceptable to derive a hazard value because of population-level relevance and a clear dose-response relationship.

The hazard value for soil invertebrates is calculated as the geometric mean of ChV, EC20, and EC10 values for mortality, reproduction, or growth endpoints from acceptable studies. Because the data set contained one EC10 for reproduction of 14 mg DBP/kg dry soil, this value will be used as the hazard value for soil invertebrates**.**

2.3.9 Terrestrial Plant Hazard Value

EPA reviewed 12 studies on toxicity from DBP in vascular plants. An unbounded LOEL for growth at 10 mg DBP/kg dry soil was obtained in a study rated high quality for a 40-day exposure in bread wheat (*Triticum aestivum*) (Gao et al., 2019), and at 50 mg DBP/kg dry soil for rapeseed (*Brassica napus*) in a medium quality study (Kong et al., 2018). The most sensitive endpoint was the LOEL for reduction in leaf and root biomass in bread wheat seedlings observed in Gao et al. (2019), which was 10 mg/kg dry soil. There was a clear dose-response observed, with biomass reduction increasing as the dose of DBP increased. At the highest dose (40 mg/kg), root and leaf biomass were reduced by 29.93 and 32.10 percent, respectively. Because the most sensitive endpoint in this study was an unbounded LOAEL, the actual threshold dose may have been lower than the lowest dose studied. However, no information was available in the study to adjust the value to account for this uncertainty. The HV for terrestrial plants for DBP derived from this study is 10 mg/kg dry soil.

The most sensitive ChV expressed in water concentration (mg/L) was calculated for growth inhibition

for a 42-day exposure in bok choy (*Brassica rapa ssp. Chinensis*) (Liao et al., 2009) at 3.16 mg/L DBP in hydroponic solution. This study was rated medium quality. Biomass was reduced by 27 percent at the LOAEL (10 mg/L), with a clear dose-response at increasing doses up to 76 percent reduced biomass at the highest dose (100 mg/L). However, this study was conducted in hydroponic solution rather than in soil; therefore, it was not considered ecologically relevant for the purpose of deriving a hazard value. Other ChVs included a 72-hour exposure in bread wheat (*Triticum aestivum*) (Ma et al., 2015) at 100 mg DBP/kg wet soil. This study was rated high quality. Unbounded LOELs for growth inhibition were also obtained from (Ma et al., 2015) for a 72-hour exposure in the common oat (*Avena sativa*), a 168-hour exposure in the common onion (*Allium cepa*), a 72-hour exposure in alfalfa (*Medicago sativa*), and a 72-hour exposure in the radish (*Raphanus sativus*). All of the aforementioned unbounded LOELs were at 5 mg/kg wet soil. However, because the study did not provide information on the water content of the soil, this study was not considered acceptable to derive a hazard value. Furthermore, in this study a comparator non-food crop plant (perennial ryegrass, *Lolium perenne*) had no observable effects on growth even at the highest dose of 500 mg/kg wet soil.

Other studies investigated soil fumigation, application to fields (in kg/hectare), or direct application to leaves (in µg/cm2), and the dose to each plant could not be calculated from the information given. Another study, rated medium quality, examined a 45-day exposure in false bok choy (*Brassica parachinensis*) with a ChV of 31.62 mg DBP/kg dry soil (Zhao et al., 2016); however, the lowest dose (10 mg DBP/kg dry soil) resulted in statistically increased growth relative to controls.

2.4 Weight of Scientific Evidence and Conclusions

After calculating the hazard thresholds that were carried forward to characterize risk, a table describing the weight of the scientific evidence and uncertainties was completed to support EPA's decisions (Table 2-12). See 0 for more detail on how EPA weighed the scientific evidence.

Table 2-12. DBP Evidence Table Summarizing the Overall Confidence Derived from Hazard Thresholds

Types of Evidence	Quality of the Database	Consistency	Strength and Precision	Biological Gradient/Dose-Response	Relevance	Hazard Confidence
Aquatic						
Acute Aquatic (SSD)	+++	+++	+++	+++	+++	Robust
Chronic Aquatic Vertebrates	+++	++	+++	+++	+++	Robust
Chronic Aquatic Invertebrates	+++	+++	+++	+++	+++	Robust
Chronic Benthic Invertebrates	++	+++	+++	++	+++	Robust
Aquatic Plants & Algae	++	+++	++	++	++	Moderate
Terrestrial						
Terrestrial Vertebrates	+++	++	++	+++	++	Moderate
Soil Invertebrates	++	++	+++	+++	+++	Robust
Terrestrial Plants	++	++	++	++	++	Moderate

Types of Evidence	Quality of the Database	Consistency	Strength and Precision	Biological Gradient/Dose-Response	Relevance	Hazard Confidence

[a] Relevance includes biological, physical/chemical, and environmental relevance.
+++ Robust confidence suggests thorough understanding of the scientific evidence and uncertainties. The supporting weight of the scientific evidence outweighs the uncertainties to the point where it is unlikely that the uncertainties could have a significant effect on the hazard estimate.
++ Moderate confidence suggests some understanding of the scientific evidence and uncertainties. The supporting scientific evidence weighed against the uncertainties is reasonably adequate to characterize hazard estimates.
+ Slight confidence is assigned when the weight of the scientific evidence may not be adequate to characterize the scenario, and when the assessor is making the best scientific assessment possible in the absence of complete information. There are additional uncertainties that may need to be considered.

2.4.1 Quality of the Database; Consistency; Strength (Effect Magnitude) and Precision; and Biological Gradient (Dose-Response)

For the acute aquatic assessment, the database consisted of 28 studies with overall quality determinations of high/medium with both aquatic invertebrates and vertebrates represented. Data from nine of these studies were supplemented by using Web-ICE version 4.0 to obtain additional estimated acute toxicity values and generate a subsequent SSD output; therefore, a robust confidence was assigned to quality of the database. DBP had similar effects on the same species across multiple studies, well within one order of magnitude. For example, 96-hour LC50 values in the fathead minnow (*Pimephales promelas*) ranged from 0.85 mg/L to 2.02 mg/L across three independent studies, from 0.48 mg/L to 1.2 mg/L in the bluegill (*Lepomis macrochirus*) across three independent studies, and from 1.4 to 1.60 mg/L in the rainbow trout (*Oncorhynchus mykiss*) across two independent studies. For the water flea (*Daphnia magna*), 48-hour LC50s ranged from 2.55 mg/L to 5.2 mg/L across two independent studies. Because LC50 values were comparable among independent studies conducted in well-characterized test organisms, a robust confidence was assigned to consistency of the acute aquatic assessment. The effects observed in the DBP empirical data set for acute aquatic assessment were mortality, with 48-, 72-, or 96-hour LC50s represented empirically (depending on species) with additional predicted LC50 values reported from Web-ICE. Because more than 50 species were represented in the acute data set with LC50 values, robust confidence was assigned to the strength and precision consideration. Dose-response is a prerequisite of obtaining reliable LC50 values and was observed in the empirical studies that were used in the SSD. Because dose-response was observed in the empirical studies, a robust confidence was assigned to the dose-response consideration.

For the chronic aquatic vertebrate assessment, the database consisted of 16 studies with overall quality determinations of high/medium. Of these studies, 11 contained acceptable chronic endpoints that identified definitive hazard values below the DPB limit of water solubility for 5 fish species and 2 amphibians, resulting in robust confidence for quality of the database. DBP had chronic effects on growth which spanned several orders of magnitude among aquatic vertebrate taxa, with effects on growth in the African clawed frog (*Xenopus laevis*) ranging from NOEC/LOEC pairs of 0.00476/0.0134 mg/L to 2/10 mg/L in 21- and 22-day independent studies, respectively. Among fish, effects on growth ranged from an unbounded LOEC at 0.0156 mg/L in Japanese medaka (*Oryzias latipes*) to 0.19/0.40 mg/L in rainbow trout (*Oncorhynchus mykiss*) in 112-day and 99-day studies, respectively. Among the same species, in a three-generation reproductive study that received a high quality study evaluation, (EAG Laboratories, 2018), effects on growth in Japanese medaka (*Oryzias latipes*) ranged from an unbounded LOEC at 0.0156 mg/L in F1 male fish to a NOEC/LOEC pair at 0.103/0.305 mg/L in F2 male fish. Because chronic effects were seen at concentrations that spanned several orders of magnitude among aquatic vertebrates, a moderate confidence was assigned to the consistency consideration. In the study chosen to derive the COC, EAG Laboratories (2018), bodyweight was inhibited by 13.4 percent

relative to the vehicle control, and there was a statistically significant trend toward greater bodyweight inhibition with increasing dose, culminating at 34.0 percent inhibition at the highest dose (305 µg/L). Similarly strong dose-response effects were observed in other studies in the database. Because there was a strong biologically relevant effect and dose-response effects were observed in the study chosen to derive the COC and among other studies in the database, a robust confidence was assigned to the strength and precision consideration and the dose-response consideration for the chronic aquatic invertebrate assessment.

For the chronic aquatic invertebrate assessment, the database consisted of 13 studies with overall quality determinations of high/medium. Of these studies, 8 contained acceptable chronic endpoints that identified definitive hazard values below the DPB limit of water solubility for 10 aquatic invertebrate species, resulting in robust confidence for quality of the database. DBP had similar effects on the same species across multiple studies, within one order of magnitude. For example, in the water flea (*Daphnia magna*), 21-day mortality studies resulted in paired NOEC/LOECs of 0.96/2.5 mg/L, and an LC50 of 1.92 mg/L, in independent studies. Paired 21-day NOEC/LOECs for reproductive effects on the number of juveniles produced ranged from 0.42/0.48 mg/L to 0.96/2.5 mg/L across three independent studies. In other species, effects on population, reproduction, and mortality were observed. Because effects were similar across multiple studies and were seen at concentrations that were within an order of magnitude within the same species, a robust confidence was assigned to the consistency consideration. In the study chosen to derive the COC, (Tagatz et al., 1983), populations of the marine amphipod *Monocorophium acherusicum* were reduced by 91 percent at the LOEC. Higher doses resulted in a complete loss of amphipods in the aquaria. Similarly strong dose-response effects were observed in other studies in the database. Because there was a strong biologically relevant effect and dose-response effects were observed in the study chosen to derive the COC and among other studies in the database, a robust confidence was assigned to the strength and precision consideration and dose-response consideration for the chronic aquatic invertebrate assessment.

For the chronic benthic invertebrate assessment, the database consisted of three studies with overall quality determinations of high. Reporting of these studies was extremely detailed and included multiple species, endpoints, durations, and organic carbon contents, but only two species were represented. Additionally, some of the results were repeated among the three studies and the author lists overlapped, and it was unclear in some cases whether certain experiments were conducted independently among the three studies. This lack of clarity about whether the studies were conducted independently resulted in a moderate confidence assigned for the quality of the database consideration. In the studies examined, the experiment was repeated with low, medium, and high TOC sediments and toxicity decreased with the increase in TOC, as expected for a relatively hydrophobic compound like DBP based on equilibrium partitioning theory. Among the same species, effects were generally within one order of magnitude for repeated experiments in the same TOC. Because effects were seen at comparable concentrations within species, a robust confidence was assigned to the consistency consideration. In the study chosen to derive the COC, Lake Superior Research Institute (1997), population in the midge (*Chironomus tentans*) was reduced by 76.7 percent at the LOEC, which was 3,090 mg DBP/kg dry sediment. Population reduction in other treatments and TOC levels was generally as expected given equilibrium partitioning theory. Because the effect size of DBP exposure was large, and other treatments resulted in effects that were as expected based on equilibrium partitioning theory, a robust confidence was assigned to the strength and precision consideration for the chronic benthic invertebrate assessment. Higher doses resulted in a similar degree of population loss in the medium-TOC treatment; however, all population losses were significantly different from controls. There was a clear dose-response effect observed in other studies in the database, and among sub-studies using different TOC levels. Because dose-response was non-monotonic in the medium-TOC treatment—but was as expected, with higher doses increasing the

observed population loss, in other sub-studies involving different TOC levels within the same study—a moderate confidence was assigned to the dose-response consideration for the chronic benthic invertebrate assessment.

For the aquatic plants and algae assessment, the database consisted of seven high/medium quality studies for toxicity in aquatic plants and algae. Of these studies, three contained acceptable endpoints that identified definitive hazard values below the DBP limit of water solubility for one species of green algae (*Selenastrum capricornutum*). Because only one species was identified, and several of the studies in the database were not acceptable because exposure concentrations were above the limit of solubility for DBP, confidence was decreased in the quality of the database. However, because three independent studies were available in the species examined, a moderate confidence level was assigned for the quality of the database. DBP had similar effects on population, measured as either chlorophyll α concentration or cell abundance, in three independent studies. Effects were within an order of magnitude, ranging from a 96-hour NOEC/LOEC pair at 0.1/1 mg/L to a 10-day EC50 at 0.75 mg/L. Because effects on the same species were observed at DBP concentrations within one order of magnitude, a robust confidence was assigned to the consistency consideration. In the study chosen to derive the COC, (Adachi et al., 2006), a significant reduction in the algal population at the LOEC, which was 1,000 µg/L DBP, relative to an increase in the algal population at the NOEC of 100 µg/L DBP and in controls. The population reduction was increased with a higher dose of DBP. Due to the increase in algal population at the NOEC relative to controls, a moderate confidence was assigned to the strength and precision and dose-response considerations for the aquatic plants and algae assessment.

For the terrestrial vertebrate assessment, the database consisted of 2 high/medium quality studies for toxicity in environmentally relevant terrestrial vertebrates (chicken, *Gallus gallus*, and Japanese quail, *Coturnix japonica*), supplemented by 13 high/medium quality studies for toxicity in human-relevant terrestrial vertebrates (rat, *Rattus norvegicus*, and mouse, *Mus musculus*). Because 15 studies representing four species were identified, a robust confidence was assigned to the quality of the database. Among the two avian species, no effects were observed on growth at any DBP dose. Among studies in rats, effects on reproduction were observed at NOEC/LOEC pairs ranging from 100/200 mg/kg-bw/day from gestational day 1 to 14 (Giribabu et al., 2014), to 10,000/20,000 mg/kg-bw/day from gestational day 0 to 20 (NTP, 1995). In mice, effects on reproduction were observed at NOEC/LOEC pairs ranging from 50/300 mg/kg-bw/day from gestational day 7 to 9 (Xia et al., 2011) to 10,000/20,000 mg/kg-bw/day from gestational day 0 to postnatal day 28 (NTP, 1995). Because effective doses spanned two orders of magnitude among independent studies in the same species, but effective doses for similar reproductive endpoints were much closer within each study, a moderate confidence was assigned to the consistency consideration for terrestrial vertebrates. In the study chosen to derive the HV, (NTP, 1995), 17-week LOAEL for significant reduction in number of live pups per litter was identified at 80 mg/kg-bw/day DBP intake in dams. That study also found a LOAEL for reduced bodyweight in F2 pups at the same dose (80 mg/kg-bw/day). The lowest bounded NOAEL/LOAEL pair for which a ChV could be calculated was significantly reduced bodyweight in F1 pups at a ChV of 115.4 mg/kg-bw/day, but this effect was not as sensitive as reduced number of live pups per litter.

Other effects of DBP exposure included significantly decreased female body weight in dams, significantly reduced male sex ratio (percentage of male pups), significantly decreased mating index and pregnancy index in the F1 generation, and significantly reduced male pup weight gain. Because clear dose-response relationships were found for many endpoints, robust confidence was assigned for the dose-response consideration. However, the effect size for reduction in live pups per litter was relatively small (a 7.8% reduction in litter size at the LOAEL, with a 17% reduction at the highest dose

administered), leading to a moderate confidence for the strength and precision consideration for the terrestrial vertebrate assessment.

For the soil invertebrate assessment, the database consisted of three high/medium quality studies, of which two contained acceptable chronic endpoints that identified definitive hazard values below the DPB limit of water solubility for two soil invertebrate species. Because only two high/medium quality studies were identified that contained usable hazard values, and two species were represented, a moderate confidence was assigned to the quality of the database. Among multiple endpoints and lifestages, 21-day LC50 values in the springtail (*Folsomia fimetaria*) ranged from 19.4 mg/kg dry soil in juveniles to 305 mg/kg dry soil in adults. No comparison to other studies was available for the EC10 and EC50 values for reproduction in springtails, or for the 14-day LC50 value from a second study in the earthworm (*Eisenia fetida*). Because comparisons among organisms within the same study or for the same organisms among independent studies were not possible given the available data, but no inconsistencies were observed among the studies examined (*i.e.*, widely different toxicities among the same organism), a moderate confidence evaluation was assigned to the consistency criterion.

In the study chosen to derive the HV, (Jensen et al., 2001), reproduction was reduced by approximately 60 percent at the lowest concentration tested, which was 100 mg DBP/kg dry soil, with reproduction completely eliminated at higher doses. Clear dose-response relationships were observed in other studies in the data set for soil invertebrates. Because there was a strong biologically relevant effect and dose-response effects were observed in the study chosen to derive the HV and among other studies in the database, robust confidence was assigned to the strength and precision and dose-response criteria for the soil invertebrate assessment.

For the terrestrial plant assessment, the database comprised 12 high/medium quality studies, of which 6 contained acceptable endpoints that identified definitive hazard values below the DBP limit of water solubility for 10 terrestrial plant species. However, the majority of acceptable studies characterized doses in a way that was unsuitable for a hazard determination (in mg/m^3 soil fumigation, kg DBP/ha agricultural application, or mg/kg wet soil). These dosing regimes made it impossible to characterize dose in the unit EPA uses for exposure estimates to terrestrial plants, mg/kg dry soil. After filtering the database to only those endpoints that characterized dose in mg/kg dry soil, four studies remained. Because most of the studies characterized doses in a way that was not useful for developing a hazard value, moderate confidence was assigned to the quality of the database. Effects on growth were observed at a wide range of concentrations among terrestrial plants, ranging from unbounded 72- or 168-hour LOECs at 5 mg/kg soil in agricultural crops including common oat (*Avena sativa*), alfalfa (*Medicago sativa*), radish (*Raphanus sativus*), cucumber (*Cucumis sativus*), and common onion (*Allium cepa*), to an unbounded 72-hour NOEC at 500 mg/kg soil in perennial ryegrass (*Lolium perenne*) and a 72-hour EC50 at 1559 mg/kg dry soil in the mung bean (*Vigna radiata*).

Since consistent growth effects were seen in a variety of species, but the observed effects were distributed over a wide range of concentrations, a moderate confidence was assigned to the consistency consideration. In the study selected to derive the HV, (Gao et al., 2019), the most sensitive endpoint was the LOEL for reduction in leaf and root biomass in bread wheat seedlings at 10 mg/kg dry soil. There was a clear dose-response observed, with biomass reduction increasing as the dose of DBP increased. At the highest dose (40 mg/kg), root and leaf biomass were reduced by 29.93 and 32.10 percent, respectively. However, for other studies in the data set, strong and precise effects of DBP on plant growth were not observed, and dose-response was not observed in all studies. For example, in Zhao et al. (2016), a 45-day exposure in false bok choy (*Brassica parachinensis*) had a ChV of 31.62 mg DBP/kg dry soil; however, the lowest dose (10 mg DBP/kg dry soil) resulted in statistically increased

growth relative to controls. A strong biologically relevant effect was not observed among all studies in the database, and dose-response effects were not observed among some studies in the database. Because of the added uncertainty from some studies in similar plants showing a lack of strong biologically relevant effects or clear dose-response, moderate confidence was assigned to the strength and precision and dose-response considerations for the terrestrial plants assessment.

2.4.2 Relevance (Biological; Physical/Chemical; Environmental)

For the acute aquatic assessment, mortality was observed in the empirical data for 9 invertebrates and fish, several of which are considered representative test species for aquatic assessments; mortality was predicted in 53 additional species using Web-ICE. Although modeled approaches such as Web-ICE can have more uncertainty than empirical data when determining the hazard or risk, the use of the probabilistic approach within this risk evaluation increases confidence compared to a deterministic approach. The use of the lower 95 percent CI of the HC05 in the SSD instead of a fixed AF also increases confidence, as it is a more data-driven way of accounting for uncertainty. Because empirical data was available for mortality for nine species, and predicted mortality data was available for 53 more through Web-ICE, robust confidence was assigned to the relevance consideration for the acute aquatic assessment.

For the chronic aquatic vertebrate assessment, ecologically relevant population level effects (growth and mortality) were observed in seven different species, five of which are considered representative test species for aquatic toxicity tests (African clawed frog, *Xenopus laevis*; zebrafish, *Danio rerio*; rainbow trout, *Oncorhynchus mykiss*; fathead minnow, *Pimephales promelas*; and Japanese medaka, *Oryzias latipes*). Because relevant population level effects were observed in several species, including representative test species, robust confidence was assigned to the relevance consideration for the chronic aquatic vertebrate assessment.

For the chronic aquatic invertebrate assessment, ecologically relevant population level effects (mortality and reproduction) were observed in 10 species, 2 of which (water flea, *Daphnia magna*, and the worm *Lumbriculus variegatus*) are considered representative test species for aquatic toxicity tests. Although the COC was derived from a less-common species (the amphipod crustacean *Monocorophium acherusicum*), effects on reproduction were seen at similar DBP doses in *Daphnia magna*, which increases confidence in the biological relevance of effects that are expected to occur at the COC. Because ecologically relevant effects were observed in 10 species, including 2 representative test species, robust confidence was assigned to the relevance consideration for the chronic aquatic invertebrate assessment.

For the chronic benthic invertebrate assessment, ecologically relevant population level effects (growth and mortality) were observed in two different species (scud, *Hyalella azteca*, and midge, *Chironomus plumosus*), both of which are considered representative test species for benthic toxicity tests. Because ecologically relevant effects were observed in two representative test species, robust confidence was assigned to the relevance consideration for the chronic benthic invertebrate assessment.

For the aquatic plant and algae assessment, an ecologically relevant population level effect (population abundance, measured as either chlorophyll α concentration or cell count) was observed in one species of green algae (*Selenastrum capricornutum*). This species is ubiquitous in the environment and is considered a representative test species for algal toxicity tests. However, because only one species was represented in the database, moderate confidence was assigned to the relevance consideration for the aquatic plant and algae assessment.

For the terrestrial vertebrate assessment, ecologically relevant population level effects were not observed in ecologically relevant species. Data from human-relevant terrestrial vertebrates (rat, *Rattus norvegicus*, and mouse, *Mus musculus*) were used to supplement the data set. A relevant population-level effect (reproduction) was observed in both species. Because the study used to develop the COC was conducted in rats, which are less ecologically relevant than other potential vertebrate species, moderate confidence was assigned to the relevance consideration for the terrestrial vertebrate assessment.

For the soil invertebrate assessment, ecologically relevant endpoints (mortality and reproduction) were observed for two ecologically relevant species (springtail, *Folsomia fimetaria*, and earthworm, *Eisenia fetida*). Both species are considered representative test species for soil invertebrate toxicity testing. Because ecologically relevant effects were observed in two representative test species, robust confidence was assigned to the relevance consideration for the chronic benthic invertebrate assessment. Robust confidence was also assigned to the relevance consideration for the soil invertebrate assessment.

For the terrestrial plant assessment, an ecologically relevant endpoint (growth) was observed for 10 plant species. However, of those species for which doses were measured in a way that was usable for determining an HV (in mg/kg dry soil), only agricultural crops were represented. Additionally, for non-food crop plants represented in the data set (Norway spruce, *Picea abies*, and perennial ryegrass, *Lolium perenne*), no effects were observed at any tested DBP dose. This raises doubts whether ecologically relevant effects of DBP exposure can be expected to occur in a non-agricultural context, so moderate confidence was assigned to the relevance consideration for the terrestrial plant assessment.

3 CONCLUSIONS

EPA considered all reasonably available information identified through the systematic review process under TSCA to characterize environmental hazard endpoints for DBP. The following bullets summarize the hazard values and overall hazard confidence:

- Aquatic species:
  - LC50 values from nine exposures to DBP in fish and aquatic invertebrates were used alongside quantitative structure-activity relationship (QSAR)-derived hazard estimates to develop an SSD. The lower confidence interval of the HC_{05} was used as the COC and indicated that acute toxicity occurs at 347.6 µg/L. EPA has robust confidence that this hazard value represents the level of acute DBP exposure at which ecologically relevant effects will occur in fish and aquatic invertebrates.
  - A three-generation reproductive study in Japanese medaka (*Oryzias latipes*) found significantly reduced bodyweight in F1 male fish after a 112-day exposure to DBP. The COC based on this study indicated that chronic toxicity in aquatic vertebrates occurs at 1.56 µg/L. EPA has robust confidence that this hazard value represents the level of chronic DBP exposure at which ecologically relevant effects will occur in aquatic vertebrates.
  - A 14-day exposure to DBP in the marine amphipod crustacean *Monocorophium acherusicum* found a significant reduction in population abundance. The COC based on this study indicated that chronic toxicity in aquatic invertebrates occurs at 12.23 µg/L. EPA has robust confidence that this hazard value represents the level of chronic DBP exposure at which ecologically relevant effects will occur in aquatic invertebrates.
  - A 96-hour exposure to DBP in the green algae *Selenastrum capricornutum* found a significant reduction in population growth. The COC based on this study indicated that toxicity in aquatic plants and algae occurs at 31.6 µg/L. EPA has moderate confidence that this hazard value represents the level of DBP exposure at which ecologically relevant effects will occur in algae, because hazard information for only one species was identified in the database, and several of the studies in the database were not acceptable since exposure concentrations were above the limit of solubility for DBP.
- Benthic species:
  - A 10-day exposure to DBP in the midge (*Chironomus tentans*) in sediment found a significant reduction in population abundance. The COC based on this study indicated that chronic toxicity in benthic invertebrates occurs at 114.3 mg/kg dry sediment. EPA has robust confidence that this hazard value represents the level of chronic DBP exposure at which ecologically relevant effects will occur in benthic invertebrates.
- Terrestrial species:
  - A 17-week perinatal exposure to DBP in Sprague-Dawley rats (*Rattus norvegicus*) found a significant reduction in number of live pups born per litter. The HV derived from this study indicated that chronic toxicity in terrestrial vertebrates occurs at 80 mg/kg-bw/day. EPA has moderate confidence that this hazard value represents the level of DBP exposure at which ecologically relevant effects will occur in terrestrial vertebrates, because effective doses for reproductive effects spanned two orders of magnitude among independent studies in the same species, effect sizes were relatively small, and human-toxicology model organisms were used instead of ecologically relevant species.
  - A 21-day exposure to DBP in the springtail (*Folsomia fimetaria*) found a significant reduction in reproduction. The HV derived from this study indicated that chronic toxicity in soil invertebrates occurs at 14 mg/kg dry soil. EPA has robust confidence that this hazard value represents the level of DBP exposure at which ecologically relevant effects

will occur in soil invertebrates.

- A 40-day exposure to DBP in bread wheat (*Triticum aestivum*) found a significant reduction in leaf and root biomass in seedlings. The HV derived from this study indicated that toxicity in terrestrial plants occurs at 10 mg/kg dry soil. EPA has moderate confidence that this hazard value represents the level of DBP exposure at which ecologically relevant effects will occur in terrestrial plants, because most of the studies characterized doses in a way that was not useful for developing a hazard value, and because only agricultural crops were represented in the studies for which an adverse effect of DBP exposure was observed.

REFERENCES

Abdul-Ghani, S; Yanai, J; Abdul-Ghani, R; Pinkas, A; Abdeen, Z. (2012). The teratogenicity and behavioral teratogenicity of di(2-ethylhexyl) phthalate (DEHP) and di-butyl Phthalate (DBP) in a chick model. Neurotoxicol Teratol 34: 56-62. http://dx.doi.org/10.1016/j.ntt.2011.10.001

Adachi, A; Asa, K; Okano, T. (2006). Efficiency of rice bran for removal of di-n-butyl phthalate and its effect on the growth inhibition of Selenastrum capricornutum by di-n-butyl phthalate. Bull Environ Contam Toxicol 76: 877-882. http://dx.doi.org/10.1007/s00128-006-1000-4

Adams, WJ; Biddinger, GR; Robillard, KA; Gorsuch, JW. (1995). A summary of the acute toxicity of 14 phthalate esters to representative aquatic organisms. Environ Toxicol Chem 14: 1569-1574. http://dx.doi.org/10.1002/etc.5620140916

Aoki, KA; Harris, CA; Katsiadaki, I; Sumpter, JP. (2011). Evidence suggesting that di-n-butyl phthalate has antiandrogenic effects in fish. Environ Toxicol Chem 30: 1338-1345. http://dx.doi.org/10.1002/etc.502

BASF Aktiengesellschaft. (1989). Report on the study of the acute toxicity of dibutylphthalat on the Golden Orfe (Leuciscus idus L., golden variety). (10F0449/895178). Ludwigshafen, Germany.

Battelle. (2018). 21-d amphibian metamorphosis assay (AMA) of dibutyl phthalate with African clawed frog, xenopus laevis. (BATT01-00397). Washington, DC: U.S. Environmental Protection Agency.

Bello, UM; Madekurozwa, M, -C; Groenewald, HB; Aire, TA; Arukwe, A. (2014). The effects on steroidogenesis and histopathology of adult male Japanese quails (Coturnix coturnix japonica) testis following pre-pubertal exposure to di(n-butyl) phthalate (DBP). Comp Biochem Physiol C Toxicol Pharmacol 166: 24-33. http://dx.doi.org/10.1016/j.cbpc.2014.06.005

Bencic, DC; Flick, RW; Bell, ME; Henderson, WM; Huang, W; Purucker, ST; Glinski, DA; Blackwell, BR; Christen, CH; Stacy, EH; Biales, AD. (2024). A multiomics study following acute exposures to phthalates in larval fathead minnows (Pimephales promelas) – The potential application of omics data in risk evaluations under TSCA (internal use only). (EPA/600/X-24/098). Cincinnati, OH: U.S. Environmental Protection Agency.

Bhatia, H; Kumar, A; Chapman, JC; McLaughlin, MJ. (2015). Long-term exposures to di-n-butyl phthalate inhibit body growth and impair gonad development in juvenile Murray rainbowfish (Melanotaenia fluviatilis). J Appl Toxicol 35: 806-816. http://dx.doi.org/10.1002/jat.3076

Bhatia, H; Kumar, A; Du, J; Chapman, J; McLaughlin, MJ. (2013). Di-n-butyl phthalate causes antiestrogenic effects in female murray rainbowfish (Melanotaenia fluviatilis). Environ Toxicol Chem 32: 2335-2344. http://dx.doi.org/10.1002/etc.2304

Bhatia, H; Kumar, A; Ogino, Y; Gregg, A; Chapman, J; McLaughlin, MJ; Iguchi, T. (2014). Di-n-butyl phthalate causes estrogenic effects in adult male Murray rainbowfish (Melanotaenia fluviatilis). Aquat Toxicol 149: 103-115. http://dx.doi.org/10.1016/j.aquatox.2014.01.025

Buccafusco, RJ; Ells, SJ; Leblanc, GA. (1981). Acute toxicity of priority pollutants to bluegill (Lepomis macrochirus). Bull Environ Contam Toxicol 26: 446-452. http://dx.doi.org/10.1007/BF01622118

Burnham, KP; Anderson, DR. (2002). Model selection and multimodel inference: a practical information-theoretic approach (2nd ed.). New York: Springer. http://www.springer.com/statistics/statistical+theory+and+methods/book/978-0-387-95364-9

Call, DJ; Cox, DA; Geiger, DL; Genisot, KI; Markee, TP; Brooke, LT; Polkinghorne, CN; Vandeventer, FA; Gorsuch, JW; Robillard, KA; Parkerton, TF; Reiley, MC; Ankley, GT; Mount, DR. (2001a). An assessment of the toxicity of phthalate esters to freshwater benthos. 2. Sediment exposures. Environ Toxicol Chem 20: 1805-1815. http://dx.doi.org/10.1002/etc.5620200826

Call, DJ; Markee, TP; Geiger, DL; Brooke, LT; Vandeventer, FA; Cox, DA; Genisot, KI; Robillard, KA; Gorsuch, JW; Parkerton, TF; Reiley, MC; Ankley, GT; Mount, DR. (2001b). An assessment of the toxicity of phthalate esters to freshwater benthos. 1. Aqueous exposures. Environ Toxicol Chem 20: 1798-1804. http://dx.doi.org/10.1002/etc.5620200825

Chen, P; Li, S; Liu, L; Xu, N. (2015). Long-term effects of binary mixtures of 17α-ethinyl estradiol and dibutyl phthalate in a partial life-cycle test with zebrafish (Danio rerio). Environ Toxicol Chem 34: 518-526. http://dx.doi.org/10.1002/etc.2803

Chen, X; Xu, S; Tan, T; Lee, ST; Cheng, SH; Lee, FWF; Xu, SJL; Ho, KC. (2014). Toxicity and estrogenic endocrine disrupting activity of phthalates and their mixtures. Int J Environ Res Public Health 11: 3156-3168. http://dx.doi.org/10.3390/ijerph110303156

Chuah, TS; Oh, HY; Habsah, M; Norhafizah, MZ; Ismail, BS. (2014). Potential of crude extract and isolated compounds from golden beard grass (Chrysopogon serrulatus) for control of sprangletop (Leptochloa chinensis) in aerobic rice systems. Crop and Pasture Science 65: 461-469. http://dx.doi.org/10.1071/CP13339

Cruciani, V; Iovine, C; Thomé, JP; Joaquim-Justo, C. (2015). Impact of three phthalate esters on the sexual reproduction of the Monogonont rotifer, Brachionus calyciflorus. Ecotoxicology 25: 192-200. http://dx.doi.org/10.1007/s10646-015-1579-5

Defoe, DL; Holcombe, GW; Hammermeister, DE; Biesinger, KE. (1990). Solubility and toxicity of eight phthalate esters to four aquatic organisms. Environ Toxicol Chem 9: 623-636.

Deng, J; Zhang, Y; Hu, J; Jiao, J; Hu, F; Li, H; Zhang, S. (2017). Autotoxicity of phthalate esters in tobacco root exudates: Effects on seed germination and seedling growth. Pedosphere 27: 1073-1082. http://dx.doi.org/10.1016/S1002-0160(17)60374-6

Du, L; Li, G; Liu, M; Li, Y; Yin, S; Zhao, J. (2015). Biomarker responses in earthworms (Eisenia fetida) to soils contaminated with di-n-butyl phthalates. Environ Sci Pollut Res Int 22: 4660-4669. http://dx.doi.org/10.1007/s11356-014-3716-8

Dueck, TA; Van Dijk, CJ; David, F; Scholz, N; Vanwalleghem, F. (2003). Chronic effects of vapour phase di-n-butyl phthalate (DBP) on six plant species. Chemosphere 53: 911-920. http://dx.doi.org/10.1016/S0045-6535(03)00580-0

EAG Laboratories. (2018). Dibutyl phthalate: Medaka extended one generation reproduction test (final report). (83260). Washington, DC: U.S. Environmental Protection Agency.

EG&G Bionomics. (1983a). Acute toxicity of fourteen phthalate esters to rainbow trout (Salmo gairdneri) under flow-through conditions (final report) report no BW-83-3-1373 [TSCA Submission]. (Bionomics Report No. BW-83-3-1373. OTS0508403. 42005 B4-5. 40-8326144. TSCATS/206776). Washington, DC: Chemical Manufacturers Association. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0508403.xhtml

EG&G Bionomics. (1983b). Exhibit III: Acute toxicity of thirteen phthalate esters to bluegill (Lepomis macrochirus) [TSCA Submission]. In Exhibit III: Acute toxicity of thirteen phthalate esters to fathead minnow (Pimephales promelas) under flow-through conditions. (Bionomics report No. BW-83-3-1368. OTS0508481. 42005 G5-2. 40-8326129. TSCATS/038115). Washington, DC: Chemical Manufacturers Association. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0508481.xhtml

EG&G Bionomics. (1984a). Acute toxicity of thirteen phthalate esters to fathead minnows (Pimephales promelas) under flow-through conditions [TSCA Submission]. (BW-83-3-1374; EPA/OTS Doc #FYI-AX-0184-0286). Washington, DC: Chemical Manufacturers Association. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS00002860.xhtml

EG&G Bionomics. (1984b). Acute toxicity of twelve phthalate esters to mysid shrimp (Mysidopsis bahia) [TSCA Submission]. (EPA/OTS Doc #40-8426078). Washington, DC: Chemical Manufacturers Association. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0508405.xhtml

EG&G Bionomics. (1984c). Acute toxicity of twelve phthalate esters to Paratanytarsus parthenogenica (final report) report no BW-83-6-1424 [TSCA Submission]. (EPA/OTS Doc #40-8426146). Chemical Manufacturers Association. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0508404.xhtml

Ema, M; Amano, H; Itami, T; Kawasaki, H. (1993). Teratogenic evaluation of di-n-butyl phthalate in rats. Toxicol Lett 69: 197-203. http://dx.doi.org/10.1016/0378-4274(93)90104-6

EnviroSystem. (1991). Early life-stage toxicity of di-n-butyl phthalate (DnBP) to the rainbow trout (Oncorhynchus mykiss) under flow-through conditions [TSCA Submission]. (9102-CMA. OTS0533141. 42005 L5-5. 40-9126399). Washington, DC: Chemical Manufacturers Association. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0533141.xhtml

Erkmen, B; Benli, ACK; Agus, HH; Yildirim, Z; Mert, R; Erkoc, F. (2017). Impact of sublethal di-n-butyl phthalate on the aquaculture fish species Nile tilapia (Oreochromis niloticus): Histopathology and oxidative stress assessment. Aquaculture Research 48: 675-685. http://dx.doi.org/10.1111/are.12914

Etterson, M. (2020). Species Sensitivity Distribution (SSD) Toolbox. Duluth, MN: U.S. Environmental Protection Agency. Retrieved from https://www.epa.gov/sciencematters/species-sensitivity-distribution-toolbox-new-tool-identify-and-protect-vulnerable

Gao, M; Dong, Y; Zhang, Z; Song, W; Qi, Y. (2017). Growth and antioxidant defense responses of wheat seedlings to di-n-butyl phthalate and di (2-ethylhexyl) phthalate stress. Chemosphere 172: 418-428. http://dx.doi.org/10.1016/j.chemosphere.2017.01.034

Gao, M; Guo, Z; Dong, Y; Song, Z. (2019). Effects of di-n-butyl phthalate on photosynthetic performance and oxidative damage in different growth stages of wheat in cinnamon soils. Environ Pollut 250: 357-365. http://dx.doi.org/10.1016/j.envpol.2019.04.022

Gardner, ST; Wood, AT; Lester, R; Onkst, PE; Burnham, N; Perygin, DH; Rayburn, J. (2016). Assessing differences in toxicity and teratogenicity of three phthalates, Diethyl phthalate, Di-n-propyl phthalate, and Di-n-butyl phthalate, using Xenopus laevis embryos. J Toxicol Environ Health A 79: 71-82. http://dx.doi.org/10.1080/15287394.2015.1106994

Giribabu, N; Sainath, SB; Reddy, PS. (2014). Prenatal di-n-butyl phthalate exposure alters reproductive functions at adulthood in male rats. Environ Toxicol 29: 534-544. http://dx.doi.org/10.1002/tox.21779

Gray, LE; Ostby, J; Sigmon, R; Ferrell, J; Rehnberg, G; Linder, R; Cooper, R; Goldman, J; Laskey, J. (1988). The development of a protocol to assess reproductive effects of toxicants in the rat [Review]. Reprod Toxicol 2: 281-287. http://dx.doi.org/10.1016/0890-6238(88)90032-9

Gu, S; Zheng, H; Xu, Q; Sun, C; Shi, M; Wang, Z; Li, F. (2017). Comparative toxicity of the plasticizer dibutyl phthalate to two freshwater algae. Aquat Toxicol 191: 122-130. http://dx.doi.org/10.1016/j.aquatox.2017.08.007

Huang, B; Li, D; Yang, Y. (2016). Joint toxicity of two phthalates with waterborne copper to Daphnia magna and Photobacterium phosphoreum. Bull Environ Contam Toxicol 97: 380-386. http://dx.doi.org/10.1007/s00128-016-1879-3

Isogai, Y; Komoda, Y; Okamoto, T. (1972). Biological activities of n-butyl phthalate and its analogous compounds on various bioassays of plant growth regulators. Scientific papers of the College of General Education, University of Tokyo 22: 129-135.

Jee, JH; Koo, JG; Keum, YH; Park, KH; Choi, SH; Kang, JC. (2009). Effects of dibutyl phthalate and di-ethylhexyl phthalate on acetylcholinesterase activity in bagrid catfish, Pseudobagrus fulvidraco (Richardson). J Appl Ichthyol 25: 771-775. http://dx.doi.org/10.1111/j.1439-0426.2009.01331.x

Jensen, J; van Langevelde, J; Pritzl, G; Krogh, PH. (2001). Effects of di(2-ethylhexyl) phthalate and dibutyl phthalate on the collembolan Folsomia fimetaria. Environ Toxicol Chem 20: 1085-1091. http://dx.doi.org/10.1002/etc.5620200520

Kang, SW; Kim, HK; Lee, WJ; Ahn, YJ. (2006). Toxicity of bisabolangelone from Ostericum koreanum roots to Dermatophagoides farinae and Dermatophagoides pteronyssinus (Acari : Pyroglyphidae). J Agric Food Chem 54: 3547-3550. http://dx.doi.org/10.1021/jf060140d

Khalil, S. R.; Abd Elhakim, Y; El-Murr, AE. (2016). Sublethal concentrations of di-n-butyl phthalate

promote biochemical changes and DNA damage in juvenile Nile tilapia (Oreochromis niloticus). Jpn J Vet Res 64: 67-80.

Kim, HK; Tak, JH; Ahn, YJ. (2004). Acaricidal activity of Paeonia suffruticosa root bark-derived compounds against Dermatophagoides farinae and Dermatophagoides pteronyssinus (Acari: Pyroglyphidae). J Agric Food Chem 52: 7857-7861. http://dx.doi.org/10.1021/jf048708a

Kim, HK; Yun, YK; Ahn, YJ. (2007). Toxicity of atractylon and atractylenolide III identified in Atractylodes ovata rhizome to Dermatophagoides farinae and Dermatophagoides pteronyssinus. J Agric Food Chem 55: 6027-6031. http://dx.doi.org/10.1021/jf0708802

Kim, HK; Yun, YK; Ahn, YJ. (2008). Fumigant toxicity of cassia bark and cassia and cinnamon oil compounds to Dermatophagoides farinae and Dermatophagoides pteronyssinus (Acari: Pyroglyphidae). Exp Appl Acarol 44: 1-9. http://dx.doi.org/10.1007/s10493-008-9129-y

Kong, X; Jin, D; Jin, S; Wang, Z; Yin, H; Xu, M; Deng, Y. (2018). Responses of bacterial community to dibutyl phthalate pollution in a soil-vegetable ecosystem. J Hazard Mater 353: 142-150. http://dx.doi.org/10.1016/j.jhazmat.2018.04.015

Kuang, QJ; Zhao, WY; Cheng, SP. (2003). Toxicity of dibutyl phthalate to algae. Bull Environ Contam Toxicol 71: 602-608. http://dx.doi.org/10.1007/s00128-003-8559-9

Lake Superior Research Institute. (1997). Sediment toxicity testing program for phthalate esters. (Unpublished Report PE-88.0-SED-WIS). Arlington, VA: Chemical Manufacturers Association.

Lamb, J; Chapin, R; Teague, J; Lawton, A; Reel, J. (1987). Reproductive effects of four phthalic acid esters in the mouse. Toxicol Appl Pharmacol 88: 255-269. http://dx.doi.org/10.1016/0041-008X(87)90011-1

Laughlin Rb, JR; Neff, JM; Hrung, YC; Goodwin, TC; Giam, CS. (1978). The effects of three phthalate esters on the larval development of the grass shrimp Palaemonetes pugio (Holthuis). Water Air Soil Pollut 9: 323-336.

Lee, SK; Owens, GA; Veeramachaneni, DN. (2005). Exposure to low concentrations of di-n-butyl phthalate during embryogenesis reduces survivability and impairs development of Xenopus laevis frogs. J Toxicol Environ Health A 68: 763-772. http://dx.doi.org/10.1080/15287390590930243

Lee, SK; Veeramachaneni, DNR. (2005). Subchronic exposure to low concentrations of di-n-butyl phthalate disrupts spermatogenesis in Xenopus laevis frogs. Toxicol Sci 84: 394-407. http://dx.doi.org/10.1093/toxsci/kfi087

Liao, CS; Yen, JH; Wang, YS. (2009). Growth inhibition in Chinese cabbage (Brassica rapa var. chinensis) growth exposed to di-n-butyl phthalate. J Hazard Mater 163: 625-631. http://dx.doi.org/10.1016/j.jhazmat.2008.07.025

Linden, E; Bengtsson, BE; Svanberg, O; Sundstrom, G. (1979). The acute toxicity of 78 chemicals and pesticide formulations against two brackish water organisms, the bleak (Alburnus alburnus) and the harpacticoid Nitocra spinipes. Chemosphere 8: 843-851. http://dx.doi.org/10.1016/0045-6535(79)90015-8

Liu, Y; Guan, Y; Yang, Z; Cai, Z; Mizuno, T; Tsuno, H; Zhu, W; Zhang, X. (2009). Toxicity of seven phthalate esters to embryonic development of the abalone Haliotis diversicolor supertexta. Ecotoxicology 18: 293-303. http://dx.doi.org/10.1007/s10646-008-0283-0

Løkke, H; Rasmussen, L. (1983). Phytotoxicological effects of Di-(2-ethyl hexyl)-phthalate and Di-n-butyl-phthalate on higher plants in laboratory and field experiments. Environ Pollut Ser A 32: 179-199. http://dx.doi.org/10.1016/0143-1471(83)90035-1

Ma, T; Teng, Y; Christie, P; Luo, Y. (2015). Phytotoxicity in seven higher plant species exposed to di-n-butyl phthalate or bis (2-ethylhexyl) phthalate. Front Env Sci Eng 9: 259-268. http://dx.doi.org/10.1007/s11783-014-0652-2

Ma, TT; Christie, P; Luo, YM; Teng, Y. (2014). Physiological and antioxidant responses of germinating mung bean seedlings to phthalate esters in soil. Pedosphere 24: 107-115.

http://dx.doi.org/10.1016/S1002-0160(13)60085-5
McCarthy, JF; Whitmore, DK. (1985). Chronic toxicity of di-n-butyl and di-n-octyl phthalate to daphnia-magna and the fathead minnow. Environ Toxicol Chem 4: 167-179. http://dx.doi.org/10.1002/etc.5620040206
Medlin, LK. (1980). Effects of di-n-butyl phthalate and salinity on the growth of the diatom Skeletonema costatum. Bull Environ Contam Toxicol 25: 75-78. http://dx.doi.org/10.1007/BF01985490
Melin, C; Egneus, H. (1983). Effects of di-n-butyl phthalate on growth and photosynthesis in algae and on isolated organelles from higher plants. Physiol Plant 59: 461-466. http://dx.doi.org/10.1111/j.1399-3054.1983.tb04230.x
Misra, S; Singh, A; Ch, R; Sharma, V; Mudiam, MKR; Ram, KR. (2014). Identification of Drosophila-based endpoints for the assessment and understanding of xenobiotic-mediated male reproductive adversities. Toxicol Sci 141: 278-291. http://dx.doi.org/10.1093/toxsci/kfu125
Mylchreest, E; Cattley, RC; Foster, PMD. (1998). Male reproductive tract malformations in rats following gestational and lactational exposure to di(n-butyl) phthalate: An antiandrogenic mechanism? Toxicol Sci 43: 47-60. http://dx.doi.org/10.1006/toxs.1998.2436
Neuhauser, EF; Loehr, RC; Malecki, MR; Milligan, DL; Durkin, PR. (1985). The toxicity of selected organic chemicals to the earthworm Eisenia fetida. J Environ Qual 14: 383-388. http://dx.doi.org/10.2134/jeq1985.00472425001400030015x
Nikonorow, M; Mazur, H; Piekacz, H. (1973). Effect of orally administered plasticizers and polyvinyl chloride stabilizers in the rat. Toxicol Appl Pharmacol 26: 253-259. http://dx.doi.org/10.1016/0041-008X(73)90259-7
Ntp. (1984). Di(n-butyl) phthalate: Reproduction and fertility assessment in CD-1 mice when administered in the feed (pp. 1-197). (NTP-84-411). Research Triangle Park, NC: National Toxicology Program, National Institute of Environmental Health Sciences. http://ntp.niehs.nih.gov/testing/types/repro/abstracts/racb/index-14.html
NTP. (1995). NTP technical report on the toxicity studies of dibutyl phthalate (CAS No. 84-74-2) administered in feed to F344/N rats and B6C3F1 mice (pp. 1-G5). (ISSN 1521-4621 Toxicity Report Series Number 30; NIH Publication 95-3353). Research Triangle Park, NC: National Toxicology Program. https://ntp.niehs.nih.gov/publications/reports/tox/000s/tox030
Ohtani, H; Miura, I; Ichikawa, Y. (2000). Effects of dibutyl phthalate as an environmental endocrine disruptor on gonadal sex differentiation of genetic males of the frog Rana rugosa. Environ Health Perspect 108: 1189-1193. http://dx.doi.org/10.2307/3434832
Ortiz-Zarragoitia, M; Trant, JM; Cajaravillet, MP. (2006). Effects of dibutylphthalate and ethynylestradiol on liver peroxisomes, reproduction, and development of zebrafish (Danio rerio). Environ Toxicol Chem 25: 2394-2404. http://dx.doi.org/10.1897/05-456R.1
Patyna, PJ. (1999) Reproductive effects of phthalate esters in Japanese medaka (Oryzias latipes). (Doctoral Dissertation). Rutgers The State University of New Jersey - New Brunswick, New Brunswick, NJ. Retrieved from https://primo.lib.umn.edu/primo-explore/openurl?url_ver=Z39.88-2004&rft_val_fmt=info:ofi%2Ffmt:kev:mtx:dissertation&genre=dissertations%20%26%20theses&sid=ProQ:Dissertations%20%26%20Theses%20@%20CIC%20Institutions&atitle=&title=Reproductive%20effects%20of%20phthalate%20esters%20in%20Japanese%20medaka%20(Oryzias%20latipes)&issn=&date=1999-01-01&volume=&issue=&spage=&au=Patyna,%20Przemyslaw%20J.&isbn=0599385669&jtitle=&btitle=&rft_id=info:eric%2F&rft_id=info:doi%2F&vid=DULUTH&institution=DULUTH&url_ctx_val=&url_ctx_fmt=null&isSerivcesPage=true
Rhodes, JE; Adams, WJ; Biddinger, GR; Robillard, KA; Gorsuch, JW. (1995). Chronic toxicity of 14 phthalate esters to Daphnia magna and rainbow trout (Oncorhynchus mykiss). Environ Toxicol

Chem 14: 1967-1976. http://dx.doi.org/10.1002/etc.5620141119

Seyoum, A; Pradhan, A. (2019). Effect of phthalates on development, reproduction, fat metabolism and lifespan in Daphnia magna. Sci Total Environ 654: 969-977. http://dx.doi.org/10.1016/j.scitotenv.2018.11.158

Shen, O; Wu, W; Du, G; Liu, R; Yu, L; Sun, H; Han, X; Jiang, Y; Shi, W; Hu, W; Song, L; Xia, Y; Wang, S; Wang, X. (2011). Thyroid disruption by Di-n-butyl phthalate (DBP) and mono-n-butyl phthalate (MBP) in Xenopus laevis. PLoS ONE 6: e19159. http://dx.doi.org/10.1371/journal.pone.0019159

Shin, N; Cuenca, L; Karthikraj, R; Kannan, K; Colaiácovo, MP. (2019). Assessing effects of germline exposure to environmental toxicants by high-throughput screening in C. elegans. PLoS Genet 15: e1007975. http://dx.doi.org/10.1371/journal.pgen.1007975

Shiota, K; Chou, MJ; Nishimura, H. (1980). Embryotoxic effects of di-2-ethylhexyl phthalate (DEHP) and di-n-butyl phthalate (DBP) in mice. Environ Res 22: 245-253. http://dx.doi.org/10.1016/0013-9351(80)90136-X

Shiota, K; Nishimura, H. (1982). Teratogenicity of di(2-ethylhexyl) phthalate (DEHP) and di-n-butyl phthalate (DBP) in mice. Environ Health Perspect 45: 65-70. http://dx.doi.org/10.2307/3429385

Smithers Viscient. (2018). Di-n-butyl phthalate - short-term reproduction assay with fathead minnow (Pimephales promelas) following OPPTS 890.1350 and OECD 229 guidelines. (Smithers Viscient Study No. 13784.6123). Washington, DC: U.S. Environmental Protection Agency.

Springborn Bionomics. (1984a). Acute toxicity of thirteen phthalate esters to the sheepshead minnow (Cyprinodon variegatus) (final report) [TSCA Submission]. (BP-84-2-14/10823.8000. OTS0508409. 40-8426151. 42005 B4-11. TSCATS/206782). Washington, DC: Chemical Manufacturers Association. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0508409.xhtml

Springborn Bionomics. (1984b). Chronic toxicity of fourteen phthalate esters to Daphnia magna with cover letter dated 032585 [TSCA Submission] (pp. 95). (Report No. BW-84-5-1567. OTS0000392-0. FYI-AX-0485-0392. TSCATS/032642). Wareham, MA: Chemical Manufacturers Association. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS00003920.xhtml

Springborn Bionomics. (1984c). FYI Submission: Toxicity of fourteen phthalate esters to the freshwater green alga Selenastrum capricornutum [TSCA Submission]. (EPA/OTS Doc #FYI-OTS-0485-0392). Washington, DC: Chemical Manufacturers Association. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS00003920.xhtml

Streufort, JM. (1978). Some effects of two phthalic acid esters on the life cycle of the midge (Chironomus plumosus) [TSCA Submission]. (OTS0000013-0. FYI-AX-1178-0013. TSCATS/029296). Washington, DC: Manufacturing Chemists Association. https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS00000130.xhtml

Tagatz, ME; Deans, CH; Moore, JC; Plaia, GR. (1983). Alterations in composition of field-developed and laboratory-developed estuarine benthic communities exposed to di-normal-butyl phthalate. Aquat Toxicol 3: 239-248. http://dx.doi.org/10.1016/0166-445X(83)90044-9

Tak, JH; Kim, HK; Lee, SH; Ahn, YJ. (2006). Acaricidal activities of paeonol and benzoic acid from Paeonia suffruticosa root bark and monoterpenoids against Tyrophagus putrescentiae (Acari: Acaridae). Pest Manag Sci 62: 551-557. http://dx.doi.org/10.1002/ps.1212

Thurén, A; Woin, P. (1991). Effects of phthalate esters on the locomotor activity of the freshwater amphipod Gammarus pulex. Bull Environ Contam Toxicol 46: 159-166. http://dx.doi.org/10.1007/BF01688270

U.S. EPA. (1998). Guidelines for ecological risk assessment [EPA Report]. (EPA/630/R-95/002F). Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum. https://www.epa.gov/risk/guidelines-ecological-risk-assessment

U.S. EPA. (2005). Guidelines for carcinogen risk assessment [EPA Report]. (EPA630P03001F). Washington, DC. https://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf

U.S. EPA. (2012). Benchmark dose technical guidance [EPA Report]. (EPA100R12001). Washington, DC: U.S. Environmental Protection Agency, Risk Assessment Forum. https://www.epa.gov/risk/benchmark-dose-technical-guidance

U.S. EPA. (2014). Framework for human health risk assessment to inform decision making. Final [EPA Report]. (EPA/100/R-14/001). Washington, DC: U.S. Environmental Protection, Risk Assessment Forum. https://www.epa.gov/risk/framework-human-health-risk-assessment-inform-decision-making

U.S. EPA. (2016). Weight of evidence in ecological assessment [EPA Report]. (EPA/100/R-16/001). Washington, DC: Office of the Science Advisor. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100SFXR.txt

U.S. EPA. (2021). Draft systematic review protocol supporting TSCA risk evaluations for chemical substances, Version 1.0: A generic TSCA systematic review protocol with chemical-specific methodologies. (EPA Document #EPA-D-20-031). Washington, DC: Office of Chemical Safety and Pollution Prevention. https://www.regulations.gov/document/EPA-HQ-OPPT-2021-0414-0005

U.S. EPA. (2024a). Draft Environmental Exposure Assessment for Diisodecyl Phthalate (DIDP). Washington, DC: Office of Pollution Prevention and Toxics. https://www.regulations.gov/document/EPA-HQ-OPPT-2024-0073-0024

U.S. EPA. (2024b). Draft Non-cancer Human Health Hazard Assessment for Dibutyl Phthalate (DBP). Washington, DC: Office of Pollution Prevention and Toxics.

U.S. EPA. (2024c). Draft Systematic Review Protocol for Dibutyl Phthalate (DBP). Washington, DC: Office of Pollution Prevention and Toxics.

Wang, Z; Kim, HK; Tao, W; Wang, M; Ahn, YJ. (2011). Contact and fumigant toxicity of cinnamaldehyde and cinnamic acid and related compounds to Dermatophagoides farinae and Dermatophagoides pteronyssinus (Acari: Pyroglyphidae). J Med Entomol 48: 366-371. http://dx.doi.org/10.1603/ME10127

Wei, J; Shen, Q; Ban, Y; Wang, Y; Shen, C; Wang, T; Zhao, W; Xie, X. (2018). Characterization of Acute and Chronic Toxicity of DBP to Daphnia magna. Bull Environ Contam Toxicol 101: 214-221. http://dx.doi.org/10.1007/s00128-018-2391-8

Williams, MJ; Wiemerslage, L; Gohel, P; Kheder, S; Kothegala, LV; Schioth, HB. (2016). Dibutyl Phthalate Exposure Disrupts Evolutionarily Conserved Insulin and Glucagon-Like Signaling in Drosophila Males. Endocrinology 157: 2309-2321. http://dx.doi.org/10.1210/en.2015-2006

Wine, RN; Li, LH; Barnes, LH; Gulati, DK; Chapin, RE. (1997). Reproductive toxicity of di-n-butylphthalate in a continuous breeding protocol in Sprague-Dawley rats. Environ Health Perspect 105: 102-107. http://dx.doi.org/10.1289/ehp.97105102

Wolf, C; Lambright, C; Mann, P; Price, M; Cooper, RL; Ostby, J; Gray, LE, Jr. (1999). Administration of potentially antiandrogenic pesticides (procymidone, linuron, iprodione, chlozolinate, p,p'-DDE, and ketoconazole) and toxic substances (dibutyl- and diethylhexyl phthalate, PCB 169, and ethane dimethane sulphonate) during sexual differentiation produces diverse profiles of reproductive malformations in the male rat. Toxicol Ind Health 15: 94-118. http://dx.doi.org/10.1177/074823379901500109

Xia, H; Chi, Y, i; Qi, X; Su, M; Cao, Y; Song, P; Li, X; Chen, T; Zhao, A; Zhang, Y; Cao, Y; Ma, X; Jia, W. (2011). Metabolomic evaluation of di-n-butyl phthalate-induced teratogenesis in mice. Metabolomics 7: 559-571. http://dx.doi.org/10.1007/s11306-011-0276-5

Xu, Y; Gye, MC. (2018). Developmental toxicity of dibutyl phthalate and citrate ester plasticizers in Xenopus laevis embryos. Chemosphere 204: 523-534.

http://dx.doi.org/10.1016/j.chemosphere.2018.04.077

Yang, ZH; Zhang, XJ; Cai, ZH. (2009). Toxic effects of several phthalate esters on the embryos and larvae of abalone Haliotis diversicolor supertexta. Chin J Oceanol Limnol 27: 395-399. http://dx.doi.org/10.1007/s00343-009-9103-5

Zhao, HM; Du, H; Xiang, L; Li, YW; Li, H; Cai, QY; Mo, CH; Cao, G; Wong, MH. (2016). Physiological differences in response to di-n-butyl phthalate (DBP) exposure between low- and high-DBP accumulating cultivars of Chinese flowering cabbage (Brassica parachinensis L.). Environ Pollut 208: 840-849. http://dx.doi.org/10.1016/j.envpol.2015.11.009

Zhao, LL; Xi, YL; Huang, L; Zha, CW. (2009). Effects of three phthalate esters on the life-table demography of freshwater rotifer Brachionus calyciflorus Pallas. Aquatic Ecology 43: 395-402. http://dx.doi.org/10.1007/s10452-008-9179-6

APPENDICES

Appendix A RUBRIC FOR WEIGHT OF THE SCIENTIFIC EVIDENCE

The weight of the scientific evidence fundamentally means that the evidence is weighed (*i.e.*, ranked) and weighted (*i.e.*, a piece or set of evidence or uncertainty may have more importance or influence in the result than another). Based on the weight of the scientific evidence and uncertainties, a confidence statement was developed that qualitatively ranks (*i.e.*, robust, moderate, slight, or indeterminate) the confidence in the hazard threshold. The qualitative confidence levels are described below.

The evidence considerations and criteria detailed within U.S. EPA (2021) guides the application of strength-of-evidence judgments for environmental hazard effect within a given evidence stream and were adapted from Table 7-10 of the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021).

EPA used the strength-of-evidence and uncertainties from U.S. EPA (2021) for the hazard assessment to qualitatively rank the overall confidence rating for environmental hazard (Table_Apx A-1). Confidence levels of robust (+ + +), moderate (+ +), slight (+), or indeterminant are assigned for each evidence property that corresponds to the evidence considerations (U.S. EPA, 2021). The rank of the *Quality of the Database* consideration is based on the systematic review overall quality determination (High, Medium, or Low) for studies used to calculate the hazard threshold, and whether there are data gaps in the toxicity data set. Another consideration in the *Quality of the Database* is the risk of bias (*i.e.*, how representative is the study to ecologically relevant endpoints). Additionally, because of the importance of the studies used for deriving hazard thresholds, the *Quality of the Database* consideration may have greater weight than the other individual considerations. The high, medium, and low systematic review overall quality determination ranks correspond to the evidence table ranks of robust (+ + +), moderate (+ +), or slight (+), respectively. The evidence considerations are weighted based on professional judgment to obtain the overall confidence for each hazard threshold. In other words, the weights of each evidence property relative to the other properties are dependent on the specifics of the weight of the scientific evidence and uncertainties that are described in the narrative and may or may not be equal. Therefore, the overall score is not necessarily a mean or defaulted to the lowest score. The confidence levels and uncertainty type examples are described below.

A.1 Confidence Levels

- Robust (+ + +) confidence suggests thorough understanding of the scientific evidence and uncertainties. The supporting weight of the scientific evidence outweighs the uncertainties to the point where it is unlikely that the uncertainties could have a significant effect on the exposure or hazard estimate.
- Moderate **(**+ +) confidence suggests some understanding of the scientific evidence and uncertainties. The supporting scientific evidence weighed against the uncertainties is reasonably adequate to characterize exposure or hazard estimates.
- Slight (+) confidence is assigned when the weight of the scientific evidence may not be adequate to characterize the scenario, and when the assessor is making the best scientific assessment possible in the absence of complete information. There are additional uncertainties that may need to be considered.

A.2 Types of Uncertainties

The following uncertainties may be relevant to one or more of the weight of scientific evidence

considerations listed above and will be integrated into that property's rank in the evidence table:

- *Scenario Uncertainty:* Uncertainty regarding missing or incomplete information needed to fully define the exposure and dose.
    - The sources of scenario uncertainty include descriptive errors, aggregation errors, errors in professional judgment, and incomplete analysis.
- *Parameter Uncertainty:* Uncertainty regarding some parameter.
    - Sources of parameter uncertainty include measurement errors, sampling errors, variability, and use of generic or surrogate data.
- *Model Uncertainty:* Uncertainty regarding gaps in scientific theory required to make predictions on the basis of causal inferences.
    - Modeling assumptions may be simplified representations of reality.

Table 2-12 summarizes the weight of the scientific evidence and uncertainties, while increasing transparency on how EPA arrived at the overall confidence level for each exposure hazard threshold. Symbols are used to provide a visual overview of the confidence in the body of evidence, while de-emphasizing an individual ranking that may give the impression that ranks are cumulative (*e.g.*, ranks of different categories may have different weights).

Table_Apx A-1. Considerations that Inform Evaluations of the Strength of the Evidence within an Evidence Stream (*i.e.*, Apical Endpoints, Mechanistic, or Field Studies)

Consideration	Increased Evidence Strength (of the Apical Endpoints, Mechanistic, or Field Studies Evidence)	Decreased Evidence Strength (of the Apical Endpoints, Mechanistic, or Field Studies Evidence)
The evidence considerations and criteria laid out here guide the application of strength-of-evidence judgments for an outcome or environmental hazard effect within a given evidence stream. Evidence integration or synthesis results that do not warrant an increase or decrease in evidence strength for a given consideration are considered "neutral" and are not described in this table (and, in general, are captured in the assessment-specific evidence profile tables).		
Quality of the database[a] (risk of bias)	• A large evidence base of *high*- or *medium*-quality studies increases strength. • Strength increases if relevant species are represented in a database.	• An evidence base of mostly *low*-quality studies decreases strength. • Strength also decreases if the database has data gaps for relevant species, *i.e.*, a trophic level that is not represented. • Decisions to increase strength for other considerations in this table should generally not be made if there are serious concerns for risk of bias; in other words, all the other considerations in this table are dependent upon the quality of the database.
Consistency	Similarity of findings for a given outcome (*e.g.*, of a similar magnitude, direction) across independent studies or experiments increases strength, particularly when consistency is observed across species, life stage, sex, wildlife populations, and across or within aquatic and terrestrial exposure pathways.	• Unexplained inconsistency (*i.e.*, conflicting evidence; see U.S. EPA (2005) decreases strength.) • Strength should not be decreased if discrepant findings can be reasonably explained by study confidence conclusions; variation in population or species, sex, or life stage; frequency of exposure (*e.g.*, intermittent or continuous); exposure levels (low or high); or exposure duration.
Strength (effect magnitude) and precision	• Evidence of a large magnitude effect (considered either within or across studies) can increase strength. • Effects of a concerning rarity or severity can also increase strength, even if they are of a small magnitude. • Precise results from individual studies or across the set of studies increases strength, noting that biological significance is prioritized over statistical significance. • Use of probabilistic model (*e.g.*, Web-ICE, SSD) may increase strength.	Strength may be decreased if effect sizes that are small in magnitude are concluded not to be biologically significant, or if there are only a few studies with imprecise results.
Biological gradient/dose-response	• Evidence of dose-response increases strength. • Dose-response may be demonstrated across studies or within studies and it can be dose- or duration-dependent.	• A lack of dose-response when expected based on biological understanding and having a wide range of doses/exposures evaluated in the evidence base can decrease strength.

Consideration	Increased Evidence Strength (of the Apical Endpoints, Mechanistic, or Field Studies Evidence)	Decreased Evidence Strength (of the Apical Endpoints, Mechanistic, or Field Studies Evidence)
	• Dose response may not be a monotonic dose-response (monotonicity should not necessarily be expected, *e.g.*, different outcomes may be expected at low vs. high doses due to activation of different mechanistic pathways or induction of systemic toxicity at very high doses). • Decreases in a response after cessation of exposure (*e.g.*, return to baseline fecundity) also may increase strength by increasing certainty in a relationship between exposure and outcome (this particularly applicable to field studies).	• In experimental studies, strength may be decreased when effects resolve under certain experimental conditions (*e.g.*, rapid reversibility after removal of exposure). • However, many reversible effects are of high concern. Deciding between these situations is informed by factors such as the toxicokinetics of the chemical and the conditions of exposure, see (U.S. EPA, 1998), endpoint severity, judgments regarding the potential for delayed or secondary effects, as well as the exposure context focus of the assessment (*e.g.*, addressing intermittent or short-term exposures). • In rare cases, and typically only in toxicology studies, the magnitude of effects at a given exposure level might decrease with longer exposures (*e.g.*, due to tolerance or acclimation). • Like the discussion of reversibility above, a decision about whether this decreases evidence strength depends on the exposure context focus of the assessment and other factors. • If the data are not adequate to evaluate a dose-response pattern, then strength is neither increased nor decreased.
Biological relevance	Effects observed in different populations or representative species suggesting that the effect is likely relevant to the population or representative species of interest (*e.g.*, correspondence among the taxa, life stages, and processes measured or observed and the assessment endpoint).	An effect observed only in a specific population or species without a clear analogy to the population or representative species of interest decreases strength.
Physical/chemical relevance	Correspondence between the substance tested and the substance constituting the stressor of concern.	The substance tested is an analog of the chemical of interest or a mixture of chemicals which include other chemicals besides the chemical of interest.
Environmental relevance	Correspondence between test conditions and conditions in the region of concern.	The test is conducted using conditions that would not occur in the environment.

[a] Database refers to the entire data set of studies integrated in the environmental hazard assessment and used to inform the strength of the evidence. In this context, database does *not* refer to a computer database that stores aggregations of data records such as the ECOTOX Knowledgebase.

1508

Appendix B SPECIES SENSITIVITY DISTRIBUTION FOR ACUTE AQUATIC HAZARD

The SSD Toolbox is a resource that can fit SSDs to environmental hazard data (Etterson, 2020). It runs on Matlab 2018b (9.5) for Windows 64 bit. For this draft DBP risk evaluation, EPA created one SSD with the SSD Toolbox Version 1.1 to evaluate acute aquatic vertebrate and invertebrate toxicity. The use of this probabilistic approach increases confidence in the hazard threshold identification as it is a more data-driven way of accounting for uncertainty. For the acute SSD, acute exposure hazard data for aquatic vertebrates and invertebrates were curated to prioritize study quality and to assure comparability between toxicity values. For example, the empirical data set included only LC_{50}s for high and medium quality acute duration assays that measured mortality for aquatic vertebrates and invertebrates. Table_Apx B-1 shows the empirical data that were used in the SSD. To further improve the fit and representativeness of the SSD, Web-ICE acute toxicity predictions for 53 additional species were added (Table_Apx B-2).

With this data set, the SSD Toolbox was used to apply a variety of algorithms to fit and visualize SSDs with different distributions. An HC_{05} is calculated for each (Table_Apx B-2)

The SSD Toolbox's output contained several methods for choosing an appropriate distribution and fitting method, including goodness-of-fit, standard error, and sample-size corrected Akaike Information Criterion (AIC_c, (Burnham and Anderson, 2002)). Most P values for goodness-of-fit were above 0.05, showing no evidence for lack of fit. The distribution and model with the lowest AIC_c value, and therefore the best fit for the data was the Gumbel Model (Figure_Apx B-1). Because numerical methods may lack statistical power for small sample sizes, a visual inspection of the data were also used to assess goodness-of-fit. For the Q-Q plot, the horizontal axis gives the empirical quantiles while the vertical axis gives the predicted quantiles (from the fitted distribution). The Q-Q plot demonstrates a good model fit with the data points in close proximity to the line across the data distribution. Q-Q plots were visually used to assess the goodness-of-fit for the distributions (Figure_Apx B-2) with the Gumbel distribution demonstrating the best fit near the low end of the distribution, which is the region from which the HC05 is derived. The results for this model (Figure_Apx B-3) predicted 5 percent of the species (HC05) to have their LC50s exceeded at 415 µg/L (348 to 517 µg/L 95% CI). The HC_{50} was estimated at 1,159 µg/L (951 to 1,444 µg/L 95% CI) and the HC_{95} was estimated at 7,213 µg/L (4,376 to 11,443 µg/L 95% CI).

Table_Apx B-1. Species Sensitivity Distribution (SSD) Model Input for Acute Exposure Toxicity in Aquatic Vertebrates and Invertebrates – Empirical Data

Species	Description	Acute Toxicity Value LC50 (µg/L)	Citation(s)
Americamysis bahia	Aquatic invertebrate	612	(Adams et al., 1995; EG&G Bionomics, 1984b)
Danio rerio	Aquatic invertebrate	630	(Chen et al., 2014)
Lepomis macrochirus	Aquatic vertebrate	788	(Adams et al., 1995; EG&G Bionomics, 1983b; Buccafusco et al., 1981)
Pimephales promelas	Aquatic vertebrate	1,178	(Smithers Viscient, 2018; Adams et al., 1995; Defoe et al., 1990; McCarthy and Whitmore, 1985; EG&G Bionomics, 1984a)

Species	Description	Acute Toxicity Value LC50 (µg/L)	Citation(s)
Oncorhynchus mykiss	Aquatic vertebrate	1,497	(Adams et al., 1995; EnviroSystem, 1991; EG&G Bionomics, 1983a)
Nitocra spinipes	Benthic invertebrate	1,700	(Linden et al., 1979)
Daphnia magna	Aquatic invertebrate	3,443	(Wei et al., 2018; Adams et al., 1995; McCarthy and Whitmore, 1985)
Chironomus plumosus	Benthic invertebrate	4,648	(Streufort, 1978)
Paratanytarsus parthenogeneticus	Benthic invertebrate	5,800	(EG&G Bionomics, 1984c)

Table_Apx B-2. SSD Model Predictions[a] for Acute Exposure Toxicity to Aquatic Vertebrates (Fish)

Distribution[b]	HC05 (µg/L)	P value
Normal	381	0.0839
Logistic	348	0.0100
Triangular	364	0.4386
Gumbel	**415**	**0.0559**
Weibull	239	0.0280
Burr	400	0.0150

[a] The SSD was generated using SSD Toolbox v1.1.
[b] The model with the lowest AICc value, and therefore the best model fit, is bolded in this table.

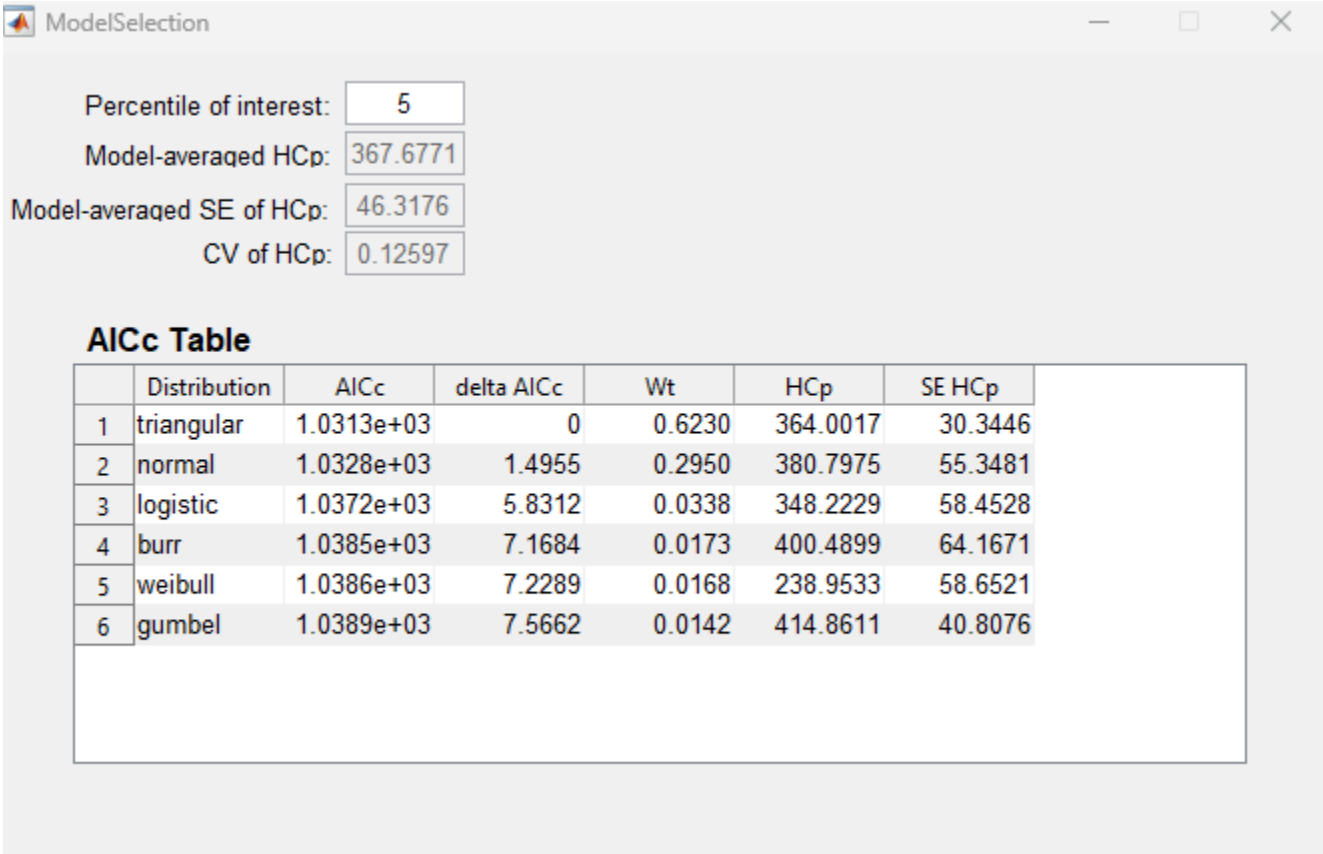
Table_Apx B-3. Species Sensitivity Distribution (SSD) Model Input for Acute Exposure Toxicity in Aquatic Vertebrates and Invertebrates – Web-ICE Data

Species	Description	Acute Toxicity Value LC50 (µg/L)
Gammarus pseudolimnaeus	Benthic invertebrate	228
Menidia peninsulae	Aquatic vertebrate	327
Lagodon rhomboides	Aquatic vertebrate	451
Catostomus commersonii	Aquatic vertebrate	501
Menidia menidia	Aquatic vertebrate	502
Caecidotea brevicauda	Benthic invertebrate	532
Perca flavescens	Aquatic vertebrate	535
Allorchestes compressa	Benthic invertebrate	545
Cyprinodon bovinus	Aquatic vertebrate	546

Species	Description	Acute Toxicity Value LC50 (µg/L)
Jordanella floridae	Aquatic vertebrate	547
Sander vitreus	Aquatic vertebrate	549
Crassostrea virginica	Benthic invertebrate	595
Ptychocheilus lucius	Aquatic vertebrate	647
Oncorhynchus kisutch	Aquatic vertebrate	673
Oncorhynchus clarkii	Aquatic vertebrate	674
Salvelinus namaycush	Aquatic vertebrate	782
Salmo salar	Aquatic vertebrate	796
Lumbriculus variegatus	Benthic invertebrate	818
Salvelinus fontinalis	Aquatic vertebrate	853
Oreochromis mossambicus	Aquatic vertebrate	872
Micropterus salmoides	Aquatic vertebrate	908
Oncorhynchus tshawytscha	Aquatic vertebrate	920
Simocephalus vetulus	Aquatic invertebrate	930
Amblema plicata	Benthic invertebrate	1,039
Cyprinus carpio	Aquatic vertebrate	1,342
Acipenser brevirostrum	Aquatic vertebrate	1,342
Cyprinodon variegatus	Aquatic vertebrate	1,463
Xyrauchen texanus	Aquatic vertebrate	1,505
Oncorhynchus gilae	Aquatic vertebrate	1,506
Lasmigona complanata	Benthic invertebrate	1,521
Salmo trutta	Aquatic vertebrate	1,528
Poecilia reticulata	Aquatic vertebrate	1,541
Menidia beryllina	Aquatic vertebrate	1,573
Ictalurus punctatus	Aquatic vertebrate	1,581
Megalonaias nervosa	Benthic invertebrate	1,751
Lepomis cyanellus	Aquatic vertebrate	1,823
Lithobates catesbeianus	Amphibian	1,938
Oryzias latipes	Aquatic vertebrate	2,097
Oncorhynchus nerka	Aquatic vertebrate	2,141

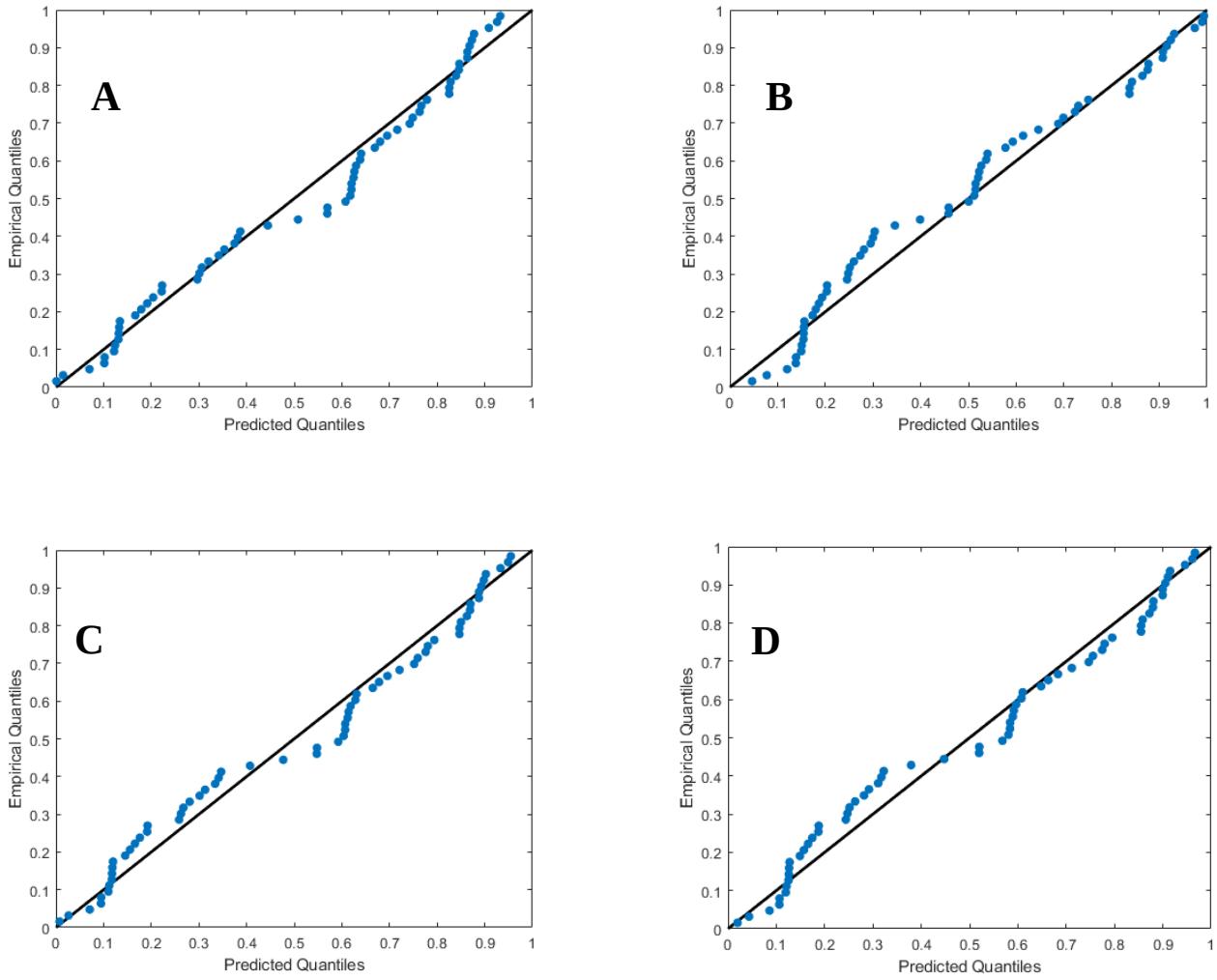
Species	Description	Acute Toxicity Value LC50 (µg/L)
Utterbackia imbecillis	Benthic invertebrate	2,244
Carassius auratus	Aquatic vertebrate	2,275
Ceriodaphnia dubia	Aquatic invertebrate	2,372
Thamnocephalus platyurus	Aquatic invertebrate	2,855
Margaritifera falcata	Benthic invertebrate	2,858
Daphnia pulex	Aquatic invertebrate	2,892
Physa gyrina	Benthic invertebrate	3,052
Branchinecta lynchi	Aquatic invertebrate	3,142
Lampsilis siliquoidea	Benthic invertebrate	3,155
Notropis mekistocholas	Aquatic vertebrate	3,447
Gammarus fasciatus	Benthic invertebrate	3,539
Tigriopus japonicus	Benthic invertebrate	3,642
Lymnaea stagnalis	Benthic invertebrate	3,738
Paratanytarsus dissimilis	Benthic invertebrate	5,419

1552

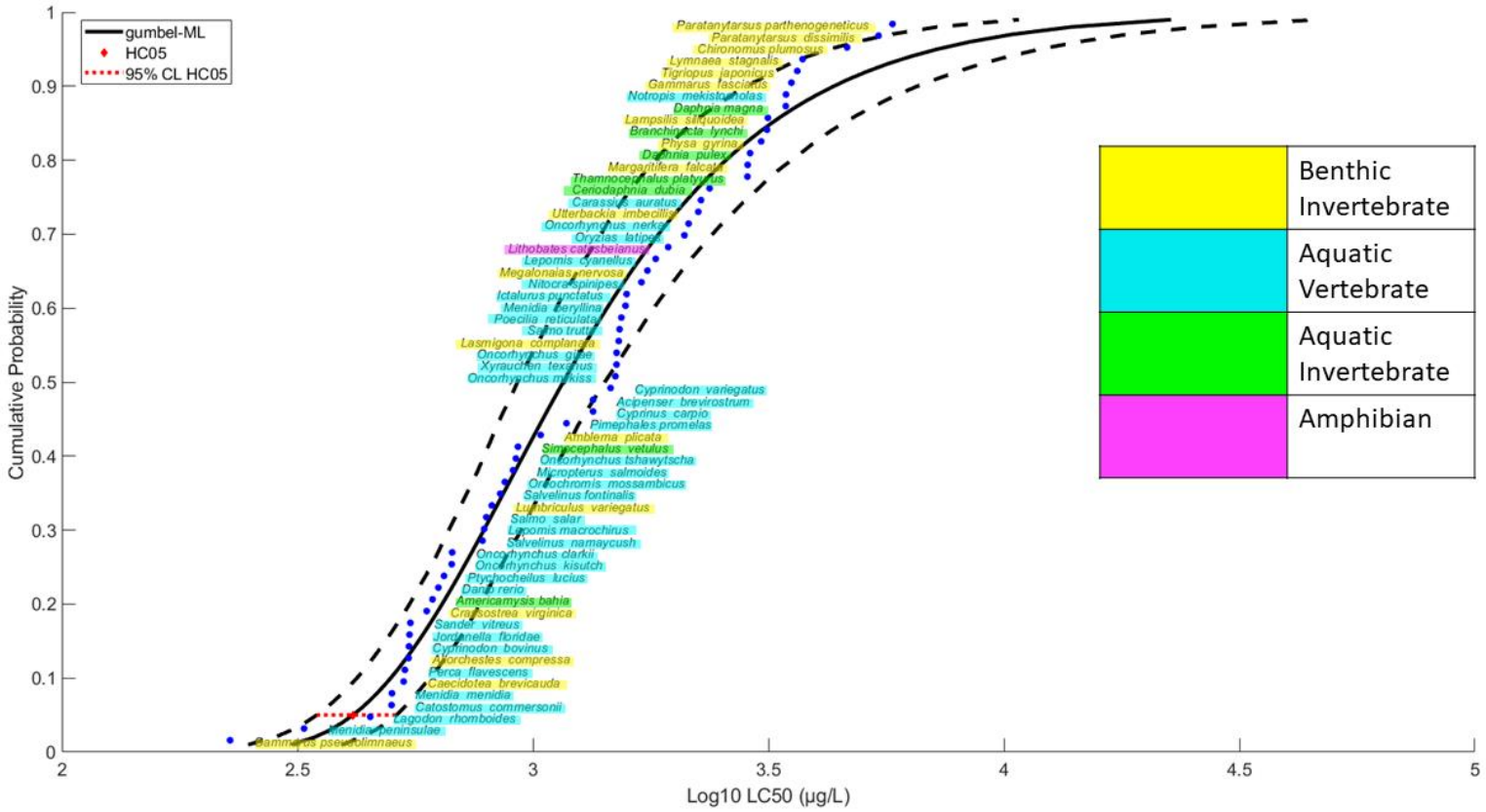


	Distribution	AICc	delta AICc	Wt	HCp	SE HCp
1	triangular	1.0313e+03	0	0.6230	364.0017	30.3446
2	normal	1.0328e+03	1.4955	0.2950	380.7975	55.3481
3	logistic	1.0372e+03	5.8312	0.0338	348.2229	58.4528
4	burr	1.0385e+03	7.1684	0.0173	400.4899	64.1671
5	weibull	1.0386e+03	7.2289	0.0168	238.9533	58.6521
6	gumbel	1.0389e+03	7.5662	0.0142	414.8611	40.8076

Figure_Apx B-1. AICc for the Six Distribution Options in the SSD Toolbox for Acute DBP Toxicity to Aquatic Vertebrates and Invertebrates (Etterson, 2020)



Figure_Apx B-2. Q-Q Plots of Acute DBP Toxicity to Aquatic Vertebrates and Invertebrates with the A) Gumbel, B) Weibull, C) Burr, and D) Logistic Distributions (Etterson, 2020)



Figure_Apx B-3. Species Sensitivity Distribution (SSD) for Acute DBP Toxicity to Aquatic Vertebrates and Invertebrates (Etterson, 2020)

Appendix C ENVIRONMENTAL HAZARD STUDIES

This appendix summarizes the aquatic and terrestrial endpoints and studies not included in the DBP quantitative risk evaluation, due to hazard values above the limit of solubility, lack of observed toxic effects, or inconsistency in the reported dose-response relationship.

Table_Apx C-1. Acute Aquatic Vertebrate Toxicity of DBP

Test Organism (Species)	Hazard Values	Duration	Endpoint	Citation (Study Quality)
African clawed frog (*Xenopus laevis*)	14.1/21.0 mg/L	96-hour NOEC/LOEC	Mortality	(Xu and Gye, 2018) (High)
	12.88 mg/L	96-hour LC50	Mortality	(Gardner et al., 2016) (Medium)
	11.7/14.7 mg/L	96-hour NOEC/LOEC		
Sheepshead Minnow (*Cyprinodon variegatus*)	>0.6 mg/L	96-hour NOEC	Mortality	(Springborn Bionomics, 1984a) (High)
Nile tilapia (*Oreochromis niloticus*)	11.8 mg/L	96-hour LC50	Mortality	(Khalil et al., 2016) (Medium)
	>10 mg/L	96-hour NOEC	Mortality	(Erkmen et al., 2017) (High)
			Growth	
Ide (*Leuciscus idus*)	>10 mg/L	96-hour NOEC	Mortality	(BASF Aktiengesellschaft, 1989) (Medium)

1571 **Table_Apx C-2. Chronic Aquatic Vertebrate Toxicity of DBP**

Test Organism (Species)	Hazard Values	Duration	Endpoint	Citation (Study Quality)
Zebrafish (*Danio rerio*)	>0.1 mg/L	5-week NOEC	Mortality	(Ortiz-Zarragoitia et al., 2006) (Medium)
	>0.5 mg/L	95-day NOEC	Mortality	(Chen et al., 2015) (High)
			Growth	
			Reproduction	
Three-spined stickleback *(Gasterosteus aculeatus)*	>0.0352 mg/L	22-day NOEC	Growth	(Aoki et al., 2011) (Medium)
Fathead minnow (*Pimephales promelas*)	>0.062 mg/L	21-day NOEC	Growth	(Smithers Viscient, 2018) (Medium)
			Mortality	
			Reproduction	
Crimson-spotted rainbowfish *(Melanotaenia fluviatilis)*	>0.457 mg/L	7-day NOEC	Growth	(Bhatia et al., 2013) (High)
			Mortality	
	>113 mg/L	7-day NOEC	Growth	(Bhatia et al., 2014) (High)
			Mortality	
	>0.05 mg/L (Nominal)	90-day NOEC	Mortality	(Bhatia et al., 2015) (High)
	>0.005 mg/L (Nominal)		Growth	
Japanese medaka (*Oryzias latipes*)	>12 mg/kg bw/d	540-day NOEC	Growth	(Patyna, 1999) (High)
			Reproduction	

1572
1573

Table_Apx C-3. Acute Aquatic Invertebrate Toxicity of DBP

Test Organism (Species)	Hazard Values	Duration	Endpoint	Citation (Study Quality)
Opossum shrimp (*Americamysis bahia*)	>1.3 mg/L	24-hour LC50	Mortality	(EG&G Bionomics, 1984c)(High)

Table_Apx C-4. Chronic Aquatic Invertebrate Toxicity of DBP

Test Organism (Species)	Hazard Values	Duration	Endpoint	Citation (Study Quality)
Water flea (*Daphnia magna*)	>2.08 mg/L	16-day NOAEC	Reproduction	(McCarthy and Whitmore, 1985)(Medium)
Midge (*Chironomus plumosus*)	>0.695 mg/L	40-day NOAEC	Growth	(Streufort, 1978)(Medium)
Daggerblade grass shrimp (*Palaemonetes pugio*)	>21.5 mg/L	38-day NOAEC	Development/ Growth	(Laughlin Rb et al., 1978)(Medium)

Table_Apx C-5. Chronic Benthic Invertebrate Toxicity of DBP

Test Organism	Hazard Values	Duration	Endpoint	Citation (Study Quality)
Scud (*Hyalella azteca*) high TOC	>71,900 mg/kg dw	10-day LC50	Mortality	(Call et al., 2001a)(High)
	>13.2 mg/L	10-day NOAEC		
Scud (*Hyalella azteca*) medium TOC	>29,500 mg/kg dw	10-day LC50	Mortality	(Call et al., 2001a)(High)
	82.4 mg/L (Probit)	10-day LC50	Mortality	(Lake Superior Research Institute, 1997) (High)
Scud (*Hyalella azteca*) low TOC	>62.9 mg/L	10-day NOAEC	Mortality	(Call et al., 2001a)(High)
	>17,400 mg/kg dw	10-day LC50		
Midge (*Chironomus tentans*) medium TOC	12.2 mg/L (Linear Interpolation)	10-day LC50	Mortality	(Lake Superior Research Institute, 1997) (High)
	3.85/16 mg/L	10-day NOAEC/ LOAEC		(Call et al., 2001a)(High)
Midge (*Chironomus tentans*) low TOC	>74.2 mg/L	10-day NOAEC/ LOAEC	Development/ Growth	(Call et al., 2001a)(High)
	>17,000 mg/kg dry sediment	10-day NOAEC		

Table_Apx C-6. Aquatic Plants and Algae Toxicity of DBP

Test Organism (Species)	Hazard Values	Duration	Endpoint	Citation (Study Quality)
Green algae (*Selenastrum capricornutum*)	2.78/27.8 mg/L	7-day NOEC/LOEC	Population (Biomass)	(Melin and Egneus, 1983) (Medium)
Green algae (*Scenedesmus acutus var. acutus*)	15.3 mg/L	96-hour EC50	Population (Abundance)	(Gu et al., 2017) (High)
Green algae (*Scenedesmus acutus var. acutus*)	30.2 mg/L	96-hour EC50	Population (Abundance)	(Kuang et al., 2003) (Medium)
	39.8 mg/L		Population (Population growth rate)	
	44.7 mg/L		Population (Chlorophyll α concentration)	
Diatom (*Skeletonema costatum*)	200/500 mg/L	4-day NOEC/LOEC	Population (Population growth rate)	(Medlin, 1980) (Medium)

1586 **Table_Apx C-7. Terrestrial Vertebrate Toxicity of DBP**

Test Organism (Species)	Hazard Values	Duration	Endpoint	Citation
Rat (*Rattus norvegicus*)	1250/2,500 ppm	GD–0 PND 28	Reproduction	(NTP, 1995)
	100/200 mg/kg-bw/day	GD 1–14		(Giribabu et al., 2014)
	120/600 mg/kg-bw/day	GD 0–20		(Nikonorow et al., 1973)
	250/500 mg/kg-bw/day	PND 21–25		(Wolf et al., 1999)
	250/500 mg/kg-bw/day	PND 21–25		(Gray et al., 1988)
	500/1,000 mg/kg-bw/day	PND 21–25		
	256/509 mg/kg-bw/day	17 weeks		(NTP, 1995) (Wine et al., 1997)
	385/794 mg/kg-bw/day	17 weeks		
	5,000/10,000 ppm	63 days		
	500/630 mg/kg-bw/day	GD 7–15		(Ema et al., 1993)
	630/750 mg/kg-bw/day	GD 7–15		
	500/1,000 mg/kg-bw/day	GD 15–17		
	1,000/1,500 mg/kg-bw/day	GD 12–14		
	500/750 mg/kg-bw/day	GD 3–PND 20		(Mylchreest et al., 1998)
	579/879 mg/kg-bw/day	4 weeks post-weaning		(NTP, 1995)
	7,500/10,000 mg/kg-bw/day	GD 0–PND 28		
	10,000/20,000 mg/kg-bw/day	GD 0–20		
	10,000/20,000 mg/kg-bw/day	GD 0–PND 28		
	10,000/30,000 mg/kg-bw/day	PND 1–22		
Mice	50/300 mg/kg-bw/day	GD 7–9		(Xia et al., 2011)
	370/660 mg/kg-bw/day	GD 0–18		(Shiota and Nishimura, 1982) (Shiota et al., 1980)
	660/2,100 mg/kg-bw/day	Gd 0–18		

Test Organism (Species)	Hazard Values	Duration	Endpoint	Citation
	3,000/10,000 mg/kg-bw/day	15 weeks		(NTP, 1995)
	5,000/7,500 mg/kg-bw/day	GD 0–PND 28		
	7,500/10,000 ppm	GD 0–PND 28		
	10,000/20,000 ppm	GD 0–PND 28		
	525/1,750 mg/kg-bw/day	18 weeks		(Ntp, 1984) (Lamb et al., 1987)
	525/1,750 mg/kg-bw/day	18 weeks		(Ntp, 1984)
Chicken (*Gallus gallus*)	>100 mg/kg egg	NR (until hatching) NOEL	Mortality	(Abdul-Ghani et al., 2012) (High)
			Growth	
Japanese quail (*Coturnix japonica*)	>400 mg/kg bw/d	30-day NOEL	Growth	(Bello et al., 2014) (Medium)

Table_Apx C-8. Acute Soil Invertebrate Toxicity of DBP

Test Organism (Species)	Hazard Values	Duration	Endpoint	Citation (Study Quality)
European house dust mite (*Dermatophagoides pteronyssinus*)	>0.152 mg/cm^3 (Fumigation)	24-hour NOEC	Mortality	(Kang et al., 2006) (Medium)
American house dust mite (*Dermatophagoides farina*)	>0.152 mg/cm^3 (Fumigation)	24-hour NOEC	Mortality	(Kang et al., 2006) (Medium)
Fruit fly (*Drosophila melanogaster*)	505,100 mg/L feed	72-hour LC50	Mortality	(Misra et al., 2014) (Medium)
	278.3/2783 mg/L feed	72-hour NOEC/LOEC (Adult exposure)	Reproduction	
	27.83/139.17 mg/L in solution	24-hour NOEC/LOEC		
Nematode (*Caenorhabditis elegans*)	>139.17 mg/L	24-hour NOEC	Mortality	(Shin et al., 2019) (High)
	27.83/139.17 mg/L in solution	24-hour NOEC/LOEC	Reproduction (Brood size)	

Table_Apx C-9. Chronic Soil Invertebrate Toxicity of DBP

Test Organism (Species)	Hazard Values	Duration	Endpoint	Citation (Study Quality)
Fruit fly (*Drosophila melanogaster*)	>0.418 mg/L feed	NR (egg until 5 to 6 days post hatch)	Mortality	(Williams et al., 2016) (Medium)

Table_Apx C-10. Terrestrial Plant Toxicity of DBP

Test Organism	Hazard Values	Duration	Endpoint	Citation (Study Quality)
Tobacco (*Nicotiana tabacum*)	>2783 mg/L	7-day NOEC	Growth	(Deng et al., 2017) (High)
	139.17/278.34 mg/L	3-day NOEC/LOEC	Reproduction (Germination)	
Norway spruce (*Picea abies*)	>0.010 mg/m^3 (Fumigation)	76-day NOEC	Growth	(Dueck et al., 2003) (High)
Perennial ryegrass (*Lolium perenne*)	>500 mg/kg soil	72-hour NOEC	Growth	(Ma et al., 2015) (High)
Rapeseed (*Brassica napus*)	<2.4 µg/cm^2 leaf	15-day LOEL	Physiology (Injury – Chlorosis)	(Løkke and Rasmussen, 1983) (Medium)
Common yarrow (*Achillea millefolium*)	>2.9 µg/cm^2 leaf	15-day NOEL	Physiology (Injury – Chlorosis)	
White mustard (*Sinapis alba*)	<3.5 µg/cm^2 leaf	15-day LOEL	Physiology (Injury – Chlorosis)	
Rice (*Oryza sativa*)	>100 mg/L	5-day NOEC	Growth	(Isogai et al., 1972) (Medium)

Appendix D SUPPLEMENTAL SUBMITTED DATA TO BE CONSIDERED FOR FINAL RISK EVALUATION

On July 10, 2024, EPA received supplemental information from DBP Consortium member companies related to ecotoxicity data supporting the risk evaluation for DBP. The Agency was unable to incorporate this data into the draft DBP ecological hazard assessment due to its late submission in the draft risk evaluation development process. However, EPA has included these data in the DBP risk evaluation docket (Docket ID: EPA-HQ-OPPT-2018-0503) and will be considering the submission in the development of the final risk evaluation for DBP.