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United States
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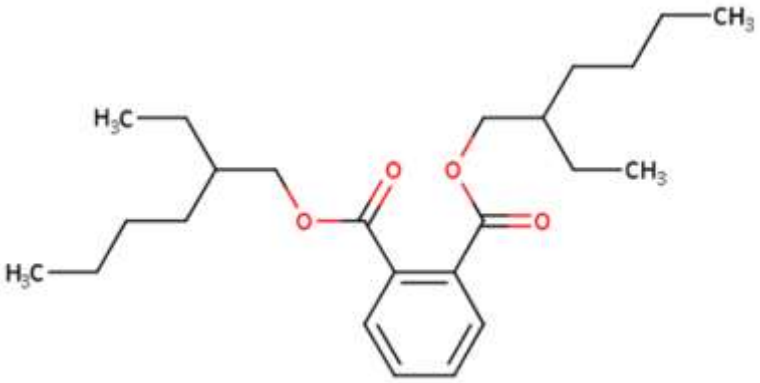
Environmental Hazard Assessment for Diethylhexyl Phthalate (DEHP)

Technical Support Document for the Risk Evaluation

CASRN 117-81-7



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KEY ABBREVIATIONS AND ACRONYMS

AF	Assessment factor
CASRN	Chemical Abstracts Service Registry Number
ChV	Chronic value
COC	Concentration(s) of concern
DEHP	Diethylhexyl phthalate
ECCC	Environment and Climate Change Canada
ECHA	European Chemicals Agency
EC50	Effect concentration at which 50 percent of test organisms exhibit an effect
EPA	Environmental Protection Agency (U.S.)
GSI	Gonadosomatic index
HV	Hazard value
LC50	Lethal concentration at which 50 percent of test organisms die
LOAEC	Lowest-observable-adverse-effect concentration
LOAEL	Lowest-observable-adverse-effect level
NOAEC	No-observable-adverse-effect concentration
NOAEL	No-observable-adverse-effect level
OCSPP	Office of Chemical Safety and Pollution Prevention (EPA)
OPPT	Office of Pollution Prevention and Toxics (EPA)
PNEC	Predicted no effect concentration
SSD	Species sensitivity distribution
TRV	Toxicity reference value
TSD	Technical support document
TSCA	Toxic Substances Control Act
U.S.	United States

SUMMARY

This technical support document (TSD) accompanies the Toxic Substances Control Act (TSCA) *Risk Evaluation for Diethylhexyl Phthalate (DEHP)*. EPA (or the Agency) considered all reasonably available information identified by the Agency through its systematic review process under TSCA to characterize environmental hazard endpoints for DEHP. Hazard data for aquatic exposures in fish indicated no acute toxicity up to and exceeding the limit of water solubility (3.0 µg/L). Similarly, hazard data for aquatic invertebrates indicated no acute or chronic toxicity up to the limit of solubility, as well as no toxicity to aquatic plants and algae.

EPA calculated two concentrations of concern (COCs) for aquatic organisms. For chronic exposures to aquatic vertebrates, the COC was from two studies showing decreased body weight in 21-day old male embryos and in 21-day old female fry Japanese medaka (*O. latipes*). For chronic exposures to sediment-dwelling organisms, a COC was based on significant effects in body volume in *C. riparius* at every concentration tested. For terrestrial species, hazard data for DEHP were available for mammals, avian taxa, and terrestrial plants. Dietary exposure data for mice were used to establish a hazard value (HV) for terrestrial mammals at based on effects on decreased survival in offspring during lactation in a reproduction study of mice. The terrestrial plant hazard threshold resulted in a geometric mean of 10 mg/kg soil for a decrease in growth (Ma et al., 2015). The avian hazard threshold was derived from a study that employed pre-hatch egg injections with DEHP in the chicken (*Gallus gallus domesticus*). In that study, observations of gastroschisis and omphalocele were found in chicks hatched from eggs at doses of 20 mg DEHP/kg of egg and above. Hazard thresholds for DEHP are summarized in Table S-1.

Table S-1. Environmental Hazard Thresholds for DEHP

Receptor Group	Exposure Duration	Hazard Threshold (COC or HV)	Citation(s)
Aquatic vertebrates	Chronic	0.0032 µg/L	(Chikae et al., 2004a; Chikae et al., 2004b)
Sediment-dwelling aquatic vertebrates	Chronic	0.03 µg/L	(Kwak and Lee, 2005)
Terrestrial vertebrates	Chronic	80.79 mg/kg-day	(Tanaka, 2002)
Avian	Chronic	10 mg/kg of egg	(Abdul-Ghani et al., 2012)
Terrestrial plants	72-hours	10 mg/kg soil	(Ma et al., 2015)
COC = concentration of concern; HV = hazard value			

1 INTRODUCTION

Diethylhexyl phthalate (DEHP) is an organic, colorless liquid primarily used as a plasticizer in a wide variety of consumer, commercial, and industrial products. Like most phthalates, EPA expects DEHP to cause adverse effects on aquatic organisms through a non-specific, narcotic mode of toxic action (Parkerton and Konkel, 2000). The European Commission Joint Research Centre ECJRC (2008) was not able to designate a predicted no effect concentration (PNEC) concentration due to a lack of reliable chronic duration studies at the time of publication. Conversely, Health Canada (2020) derived a PNEC of 0.07 µg/l from a 21-day exposure of DEHP to zebrafish embryos (Corradetti et al., 2013). EPA reviewed studies of the toxicity of DEHP to aquatic and terrestrial organisms and its potential environmental hazards.

2 APPROACH AND METHODOLOGY

During scoping and problem formulation, EPA reviewed potential environmental health hazards associated with DEHP. EPA identified sources of environmental hazard data shown in Figure 2-10 of the *Final Scope of the Risk Evaluation for DEHP; CASRN 117-81-7* (also called the "final scope") (U.S. EPA, 2020).

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) (also called "2021 Draft Systematic Review Protocol") and the *Risk Evaluation for Di-ethylhexyl Phthalate (DEHP) – Systematic Review Protocol* (U.S. EPA, 2025d). Studies were assigned an overall quality determination of high, medium, low, or uninformative.

Several international regulatory agencies, including the European Chemicals Agency (ECHA) and Environment and Climate Change Canada (ECCC), have investigated the environmental effects of DEHP. In the 2008 ECHA DEHP assessment, it was determined that although there was no concern from site-reported release information; however, generic exposure scenarios for high release sites/conditions of use indicated a potential concern for sediment-dwelling organisms and avian species consuming mussels (ECB, 2008). Further information was needed, though some of these concerns could be mitigated and eliminated through risk management actions. The 2020 ECCC assessment concluded that while DEHP *may* enter the environment at levels that could be harmful to biological diversity, it is *currently not* entering the environment in a sufficient quantity to cause harm (Health Canada, 2020). In the same assessment, DEHP was determined to not meet persistence or bioaccumulation criteria set forth by ECCC. EPA has confidence in conclusions drawn by these authorities based on study results and summaries. The Agency reviewed and summarized hazard thresholds from these reports and included them in the weight of scientific evidence supporting the hazard effects characterization (Section 5).

No studies on the effects of DEHP on terrestrial wildlife mammalian species were available; therefore, mammalian studies from human health model organisms (mice and rats) were used to calculate a hazard value for mammals, which is expressed as doses in units of mg/kg-bw-day. Although the hazard value for DEHP is derived from laboratory rat and mouse studies, this value can be used as surrogate information for ecologically relevant wildlife species to evaluate risk from chronic dietary exposure to DEHP.

3 AQUATIC SPECIES HAZARD

Toxicity to Aquatic Organisms

EPA reviewed 82 aquatic toxicity studies rated high-/medium-quality to determine hazard to aquatic organisms. Some studies included multiple endpoints, species, and test durations. Studies that received an overall quality determination of low, unacceptable, or did not meet systematic review criteria were not considered quantitatively to develop hazard thresholds. Of the 82 studies, 73 either demonstrated no acute or chronic effects at any concentration tested, or the reported hazard values exceeded the limit of solubility of 3.0 µg/L selected by EPA to be representative of non-colloidal water solubility (U.S. EPA, 2025c). Because negative data indicating no effects are just as important as data showing effects, these 73 studies were considered qualitatively in the weight of evidence as they relate to exposure—though EPA was unable to use these studies quantitatively to develop hazard thresholds (Table 3-1).

Aquatic Vertebrates

No acute aquatic vertebrate studies with definitive values less than the limit of solubility were available to determine a hazard threshold for DEHP. Chronic fish hazard data for DEHP were identified in five studies representing four fish species (Japanese medaka [*Oryzias latipes*]; guppy fish [*Poecilia reticulata*]; goldfish [*Carassius auratus*]; and zebrafish [*Danio rerio*]).

Two medium-quality chronic fish studies evaluated the effects of DEHP at nominal concentrations of 0, 0.01, 0.1, 1.0, and 10 µg/L in water for a duration of over 21 days on Japanese medaka (*O. latipes*) embryo and fry stage (Chikae et al., 2004a; Chikae et al., 2004b). In embryos, mortality was the most sensitive endpoint, with significant effects observed starting at the lowest concentration tested, 0.01 µg/L; however, the magnitude of this finding was not concentration-dependent and was not significantly different than controls at the highest concentration of 10 µg/L (Chikae et al., 2004a). Mortality in the fry stage was not significant at any concentration of DEHP (Chikae et al., 2004b). In both studies, DEHP had a significant effect on body weight. In embryos, body weight in males was significantly different from controls starting at 0.1 µg/L. Specifically, body weight was reduced by 15.3 percent at this concentration compared to controls, resulting in a 21-day male embryo body weight no-observed-adverse-effect concentration/lowest-observed-adverse-effect concentration (NOAEC/LOAEC) of 0.01/0.10 µg/L. Similarly in the female fry stage, body weight was significantly reduced starting at 0.1 µg/L DEHP, with a decrease of 23.6 percent at this concentration compared to controls, resulting in a 21-day female fry body weight NOAEC/LOAEC of 0.01/0.10 µg/L. Both NOAEC/LOAECs were used to calculate the chronic aquatic COC. Body weight was not significant at any DEHP concentration in female embryos, and while male fry body weight was significantly lower than controls at 0.01 and 10 µg/L, a clear concentration-response relationship was not observed for this sex and life stage. Additionally, significant mechanistic endpoints were also observed for the gonadosomatic index (GSI) at the fry stage of male fish in which GSI was reduced at 0.01, 1.0, and 10 µg/L (but not at 0.1 µg/L). Lastly, in medaka embryos, time to hatch was significantly increased at DEHP concentrations of 0.1 and 1.0 µg/L.

A chronic fish study, which received a medium-quality ranking, was conducted on 1-week old guppy fish (*P. reticulata)* over 91 days to measure effects of DEHP at water concentrations of 0.1, 1.0, and 10 µg/L (Zanotelli et al., 2010). Metrics of growth, including length, weight, and Fulton's condition factor (a measure of length to weight relationship), were assessed. After day 14, guppies exposed to 10 µg/L DEHP displayed shorter length compared to control fish, and by the end of the study, both length and weight were significantly less than controls at 1.0 and 10 µg/L (resulting in a NOAEC/LOAEC of 0.1/1.0 µg/L). Fulton's condition factor, defined as weight over length (cubed), was unaffected. In that study, the solubility of DEHP may have been increased by the use of a solvent (dimethyl sulfoxide [DMSO]); however, the study authors stated that at the highest tested concentration (10 µg/L), DEHP

may have separated, creating a surface layer film, and thus limiting oxygen exchange on the surface. Additionally, the nominal concentrations of DEHP used in that study were not analytically verified, and it was noted that the maximum reported nominal concentration might not have been reached due to the saturation of water with DEHP (Zanotelli et al., 2010).

A chronic fish study that received a high-quality ranking was conducted on mature goldfish (*C. auratus)* following a 30-day DEHP exposure at 1, 10, and 100 µg/L to evaluate reproductive parameters (Golshan et al., 2015). Although some of the study concentrations exceeded the DEHP limit of solubility, the authors noted the use of a solvent (acetone) in all groups. However, the concentrations of DEHP are nominal and were not analytically verified. Following the exposure period, sperm motility and velocity at 15s post-sperm activation were significantly decreased at 10 and 100 µg/L compared to controls. Additionally, 11- ketotestosterone (11-KT) was significantly decreased after the 30-day exposure at all DEHP concentrations; luteinizing hormone was significantly decreased at all concentrations after 15 days at concentrations of 1.0 and 100 µg/L after 30 days; and StAR (steroidogenic acute regulatory) mRNA levels for steroidogenesis were significantly decreased at 1, 10, and 100 µg/L following a 30-day exposure in males (Golshan et al., 2015).

A chronic fish study that received a medium-quality ranking was conducted with DEHP on zebrafish (*D. rerio*) over 21 days to measure reproductive effects at 0.2 and 20 µg/L (Corradetti et al., 2013). At the end of the study, significant increases in GSI and decreases in embryo number and hatching rate percentage were observed at both concentrations tested. The study authors concluded that exposure to DEHP at environmentally relevant concentrations could negatively affect fish reproduction (Corradetti et al., 2013).

Aquatic Invertebrates

Hazard data for DEHP acute invertebrate exposures were identified in a medium quality study representing one species. In this study, the marine copepod (*Parvocalanus crassirostris*) was exposed to DEHP at concentrations of 0.06, 0.48, 3.81, 20.52, 244.14, and 1,953.13 ng/L for 48 hours (Heindler et al., 2017). Although there may be concerns regarding the analytical verification of concentrations used in this study, the investigators determined the LC50 to be 1.04 ng/L (0.000001 mg/L). The study authors concluded that *P. crassirostris* nauplii were highly sensitive to DEHP with effects on mortality at low concentrations at this early life stage. In the same study, a subchronic 5-day evaluation was conducted using concentrations of 0.3, 1.0, and 3.0 ng/mL to determine reproductive effects in *P. crassirostris* (Heindler et al., 2017). At test termination, a reduction in the number of eggs per female was identified at every concentration tested. The study authors also examined the effects on population size at day 24 following exposure to 0.11 ng/L for 6 days (followed by an 18-day recovery period) or following exposure for 24 days. At 24 days, the authors noted a similar significant reduction in population size from DEHP exposure to 0.11 ng/L for 6 days and for 24 days and stated that the concentrations of DEHP affected egg production within levels found in the natural environment (Heindler et al., 2017).

Chronic invertebrate hazard data were identified in one study which evaluated reproduction in one freshwater invertebrate species (water flea [*D. magna*]). In a 21-day study that received a medium-quality ranking, freshwater daphnids were exposed to nominal concentrations of 0, 3, 10, and 30 µg/L in an intermittent-flow system that provided a constant concentration of DEHP (Mayer Jr et al., 1973). A significant reduction in offspring was observed at 3 µg/L and above. As concentrations of DEHP increased, the production of offspring was reduced by 60, 70, and 83 percent compared to controls (Mayer Jr et al., 1973).

Sediment-Dwelling Invertebrates
No acute sediment-dwelling organism studies with definitive endpoint values below the limit of solubility were available for the quantitative hazard assessment of DEHP. Chronic hazard data for sediment-dwelling organisms for DEHP was identified in one study represented by one insect species (midge [*Chironomus riparius*]).

A chronic study with nominal DEHP concentrations of 0.3, 1, 10, and 30 µg/L in water (combined with M4 at ≤0.2% acetone) evaluated growth (body length, weight, and volume) and emergence of *C. riparius* in 300-milliliter crystallizing dishes (Kwak and Lee, 2005). At the end of the 32-day treatment period, significant differences were observed in female emergence at 0.3 µg/L and male emergence at 1.0 µg/L compared to controls. The study authors reported there was no clear relationship for emergence period because only one of the four concentrations had effects (no significant differences were observed at concentrations of 10 or 30 µg/L for either sex. Male body length was significantly decreased at 0.3 and 10 µg/L, but not at 1.0 and 30 µg/L. Negative and solvent controls for male body length were also significantly different, but this result was not explained by the study authors. However, male and female body volume and male body width were significantly different than controls at every test concentration (Kwak and Lee, 2005).

Amphibians
Available amphibian hazard studies suggest no hazard from DEHP below the limit of water solubility (see Table_Apx A-1).

Aquatic Plants and Algae
Available aquatic plant and algae hazard studies suggest no hazard from DEHP below the limit of solubility (Table_Apx A-1).

Table 3-1. Aquatic Organism Environmental Hazard Studies Used for DEHP

Study Type	Test Organism (Species)	Hazard Value (NOAEC/ LOAEC or LC50)	Duration	Endpoint(s)	Citation (Study Quality)
Aquatic vertebrates					
Chronic	Guppy Fish (*Poecilia reticulata*)	0.1/1.0 µg/L	91-day NOAEC / LOAEC	Growth	(Zanotelli et al., 2010) (Medium)
	Japanese medaka (*Oryzias latipes*)	<0.01/0.01 µg/L	21-day NOAEC / LOAEC	Mortality	(Chikae et al., 2004a) (Medium)
		0.01/0.1 µg/L	21-day NOAEC / LOAEC	Development	
	Japanese medaka (*Oryzias latipes*)	0.01/0.1 µg/L	21-day NOAEC / LOAEC	Growth/ Development	(Chikae et al., 2004b) (Medium)
	Goldfish (*Carassius auratus*)	1.0/10 µg/L	30-day NOAEC / LOAEC	Reproduction	(Golshan et al., 2015) (High)
	Zebrafish (*Danio rerio*)	<0.2/0.2 µg/L	21-day NOAEC / LOAEC	Reproduction/ Development	(Corradetti et al., 2013) (Medium)
Aquatic invertebrates					
Acute	Marine copepod (*Parcovalanus crassirostris*) (nauplii)	0.001 µg/L	48-hour LC50	Mortality	(Heindler et al., 2017) (Medium)
Chronic	Water flea *(Daphnia magna)*	<3.0/3.0 µg/L	21-day NOAEC / LOAEC	Reproduction	(Mayer Jr et al., 1973) (Medium)

Study Type	Test Organism (Species)	Hazard Value (NOAEC/ LOAEC or LC50)	Duration	Endpoint(s)	Citation (Study Quality)
	Marine copepod (*Parvocalanus crassirostris*)	<0.3/0.3 µg/L	5-day NOAEC / LOAEC	Reproduction	(Heindler et al., 2017) (Medium)
Sediment-dwelling invertebrates					
Chronic	Midge (*Chironomus riparius*)	<0.3/0.3 µg/L	32-day NOAEC / LOAEC	Growth	(Kwak and Lee, 2005) (High)
LC50 = Lethal concentration at which 50% of test organisms die; LOAEC = lowest-observed-adverse-effect concentration; NOAEC = no-observed-adverse-effect concentration					

4 TERRESTRIAL SPECIES HAZARD

EPA assigned an overall quality level of high or medium to 46 studies of terrestrial species. The Agency used studies from the human health animal model data set (terrestrial mammals) and considered only studies with ecologically-relevant hazard endpoints (*e.g.*, survival, growth, development, and reproduction). Studies with lowest-observed-adverse-effect levels (LOAELs) based on reproductive endpoints were further considered for selection of hazard value for terrestrial species, over that of survival/mortality, given that these endpoints were more sensitive. Four terrestrial toxicity studies were included for the quantitative DEHP risk evaluation and are presented in Table 4-1. These studies contained relevant DEHP terrestrial toxicity data for terrestrial mammals, including the following: F344/N rats; avian species including chicken (*Gallus gallus domesticus*), male and female quail (*Coturnix C. coturnix* and *Coturnix japonica*); and terrestrial plants including cucumber (*Cucumis sativus*), mungbean (*Vigna radiata*), perennial ryegrass (*Lolium perenne*), radish (*Raphanus sativus*), alfalfa (*Medicago sativa*), common oat (*Avena sativa*), common onion (*Allium cepa*), and bread wheat (*Triticum aestivum*).

Terrestrial Mammals

EPA considered 26 studies to evaluate hazard to terrestrial mammals from the human health animal model data set. From this data set, EPA selected the study with the best available LOAEL value to represent hazard to terrestrial mammals. The selected study evaluated effects of DEHP on mouse pup survival during lactation (Tanaka, 2002). DEHP was administered via diet to the F0 generation 4-weeks before mating, during five days of mating, all of gestation, and all of lactation. The F1 generation was administered DEHP via diet after weaning and through week 9. In male mice, the concentration of DEHP administered during pre-mating ranged from 15.59 to 142.08 mg/kg-day and ranged from 19.86 to 168.17 mg/kg-day in females. During mating, the concentration of DEHP administered to both males and females ranged from 14.67 to 125.77 mg/kg-day. During gestation, female rats were administered DEHP concentration of 16.84 to 140.15 mg/kg-day and 59.89 to 493 mg/kg-day during lactation. From post-weaning through week nine, male and female mice were given DEHP concentration of 15.85 to 144.59 mg/kg-day and 19 to 170.50 mg/kg-day, respectively. The lowest dose available from pre-mating, gestation, and lactation for females was used to establish a hazard value. From this study, the lowest value for which a significant effect was observed resulted from doses administered during gestation, which resulted in a lactation (birth to weaning) NOAEL/LOAEL of 46.58/140.15 mg/kg-day for a reduced pup survival during lactation.

A second study was also considered but not selected to evaluate DEHP hazard to terrestrial mammals (Lamb et al., 1987). That study compared reproductive toxicity of DEHP and other phthalates to COBS CD-1 mice over a 98-day cohabitation period to observe the number of litters per breeding pair, number of live pups, pup weight, and offspring survival. Evaluation at the end of the study indicated dose-dependent decreases in fertility and in the number of live pups in DEHP-exposed mice. However, that study was not selected to represent terrestrial vertebrate hazard due to uncertainties regarding the achieved dose. Although the investigators reported the analytical concentrations in the diet, achieved doses (in mg/kg-day) were not reported and could not be calculated because body weights and food consumption data were not adequately reported across all dose groups.

Terrestrial Invertebrates

Available studies received through systematic review administered DEHP as a 20, 10, or 1 mg/L test solution that exceeded the limit of solubility. The study authors indicated that 100 µL of DEHP solution was “uniformly dripped” into the 24-well plates containing the test organisms (nematodes *Caenorhabditis elegans*) (Yin et al., 2018). As a result, it is uncertain if the administration of aqueous solutions of DEHP above solubility resulted in appropriate DEHP concentrations in the culture media,

and final concentrations were not analytically determined. Therefore, a hazard threshold could not be established for terrestrial invertebrates because of the uncertainty regarding exposure concentrations.

Terrestrial Avian

One avian study using the chicken (*Gallus gallus domesticus*) examined the effects of pre-hatch egg injections with single dose of 0, 5, 20, 50, and 100 mg DEHP per kg of egg administered on incubation day zero (Abdul-Ghani et al., 2012). Percent hatching (out of eggs incubated) was lower in the DEHP treated groups (62–68%) compared to controls (80%); however, these decreases were not dose-related. Furthermore, of those eggs that hatched, there were no effects of treatment on percent late hatchings (1 day delay) at any dose. Upon examination, gross developmental malformations (gastroschisis and omphalocele) were observed in the DEHP-treated animals at 20 mg/kg of egg and above (13–33% of those that hatched) compared to controls (0%), resulting in a NOAEL of 5 mg/kg of egg and a LOAEL of 20 mg/kg of egg.

This study (Abdul-Ghani et al., 2012) also evaluated the effects of a single dose of 100 mg/kg (via egg injection) on imprinting in juvenile chicks. Significant effects were observed in juvenile imprinting (assessed as a decrease in imprinting preference scores) when eggs were injected with a single dose of 100 mg DEHP/kg of egg, resulting in a behavioral change (imprinting) LOAEL of 100 mg/kg of egg; however, a NOAEL was not established for this endpoint because it was not evaluated at lower doses. Additionally, elevated alkaline phosphatase and 8-hydroxydeoxyguanosine were reported in chicks exposed to DEHP at 100 mg/kg of egg (Abdul-Ghani et al., 2012).

Another study examined the effects of DEHP on feed consumption, growth, and reproduction in the chicken (*Gallus gallus domesticus*), where individual animals were fed a single concentration of 1 percent DEHP (10,000 mg/kg feed) incorporated into their diet for 4 weeks (Wood and Bitman, 1980). Food consumption was reported graphically with group mean body weight detailed for each week of the 28-day study. Graphical representation of mean feed intake (grams/hens/day) and mean final weight of treatment groups allowed for the derivation of an achieved DEHP dose of approximately 578 mg/kg-day. Overall, feed consumption was significantly decreased by 10 percent compared to controls over the 4-week period. This effect was most prominent during the first 3 weeks of the study, whereby differences in mean feed consumption of the DEHP-treated feed was 6, 20, and 9 percent at days 7, 14, and 21, respectively. Egg production in the DEHP treated group was decreased by 5 percent compared to controls over the 4-week period with no differences in egg weight, percent shell, white or yolk. Although there was an increase in liver lipids and cholesterol in the DEHP treated group compared to controls, no significant effects were observed in chicken growth. This study was excluded from quantitative use in hazard determination due to significant food aversion occurring in chicken exposed to an achieved DEHP dose of approximately 578 mg/kg-day.

One study investigated the effects of DEHP on heat shock proteins and heat shock transcription factors of juvenile male quail (*Coturnix C. coturnix*) at 0, 250, 500, and 750 mg/kg-day via gavage for 45 days. (Wang et al., 2019). At the end of the treatment period, histological changes occurred including cardiac muscle fiber dilation (expansion) and cell necrosis, which was accompanied by myocardial disorganization at the 500 and 700 mg/kg treatment groups. At 250 mg/kg-day there was swelling of cells, dilation of muscle fibers, and pale staining, whereas abnormal myocardial cells were seen in the 500 mg/kg concentration. Additionally, mRNA expression of HSP60 was significantly reduced at 750 mg/kg and HSP70 was significantly reduced at 500 and 700 mg/kg. HSP10, HSP40, and HSP90 were significantly induced at 500 mg/kg only, HSP25 at 250 and 750 mg/kg, HSP27 at 250 mg/kg only, HSP47 at 250 and 500 mg/kg, and HSP110 at all concentrations. HSF1 and HSF3 expression was significantly increased at 250 and 500 mg/kg, HSF2 was increased at 500 and 750 mg/kg, and HSF4 was

significantly reduced at 500 and 750 mg/kg. Expression of HSP10, HSP25, HSP27, HSP40, HSP47, HSP90, HSP110 had different levels of induction. The NOAEL and LOAEL were less than 250 and 250 mg/kg-day based on effects on swelling and dilation of cardiac cells (Wang et al., 2019).

Another study by the same laboratory evaluated the effects of DEHP nephrotoxicity on juvenile female quail (*Coturnix japonica*) at concentrations of 0, 250, 500, and 1,000 mg/kg-day via gavage for 45 days (Wang et al., 2020). At the end of the treatment period, histological changes occurred at all concentrations including a disorganized renal structure, a partially dilated glomerulus, renal interstitial congestion, and an atrophied Bowman's space at 250 mg/kg. Renal tubular epithelial cells were unclear, and the study authors observed swelling of columnar epithelial cells. Cytochrome P450 (CYP450) enzymatic activity significantly increased for CYP1A1 at all concentrations, increased at the highest two concentrations for CYP1A2, CYP1A4, and CYTB5, 250 mg/kg only for CYP1A5, and significantly decreased at all concentrations for CYP1B1. AHR significantly decreased at the 250 and 500 mg/kg concentration before significantly increasing at 750 mg/kg, ERND significantly increased at all concentrations, and APND significantly increased at the highest concentration only. The expression of other nuclear receptors was increased compared to negative controls as well, PXR, CYP2C18, CYP2J3, and CYP3A4 at all concentrations, CAR and CYP2D6 decreased at 500 mg/kg only, CYP 3A12 at 250 and 750 mg/kg only, and CYP3A9 increased at 500 mg/kg but decreased at 700 mg/kg. Total CYP450 activity was significantly increased at the 500 and 750 mg/kg concentrations. The NOAEL and LOAEL were less than 250 and 250 mg/kg-day based on effects on renal structure (Wang et al., 2020).

Terrestrial Plants

For terrestrial plant species, one medium- and one high-quality study were identified by EPA as relevant for quantitative assessment. A study on the effects of DEHP on mungbean (*V. radiata*) shoot and root length identified 72-hour EC50s (effect concentration at which 50 percent of test organisms exhibit an effect; analyzed by regression analysis) of 16,500 and 3,969 mg/kg dry soil, respectively (Ma et al., 2014). Another study looked at the effects of DEHP on growth in perennial ryegrass (*L. perenne*), radish (*R. sativus*), alfalfa (*M. sativa*), and bread wheat (*T. aestivum*) (Ma et al., 2015). In perennial ryegrass, root elongation and seedling growth significantly decreased by 9 and 22 percent, respectively, at 20 mg/kg DEHP resulting in 72-hour NOAEC/LOAEC of 5.0/20 mg/kg soil (dry weight). However, both root elongation and seedling growth increased at higher concentrations of DEHP (100 and 500 mg/kg DEHP). In the radish, root elongation and seedling growth were found to be significantly increased, compared to controls, at all tested concentrations. In alfalfa, root elongation and seedling growth were both significantly decreased at all treated concentrations (5 mg/kg soil and above). In wheat, root elongation was decreased in all treated groups (5 mg/kg soil and above), but seedling growth was only decreased at the low concentration (5 mg/kg soil). At 5.0 mg/kg soil DEHP, alfalfa root length and seedling growth decreased by 25 and 7 percent, respectively, and by 10 and 6 percent, respectively, in bread wheat (Ma et al., 2014).

Table 4-1. Terrestrial Organism Environmental Hazard Studies Used for DEHP

Test Organism	Hazard Value (NOAEL/LOAEL or EC50)	Duration	Endpoint	Citation (Study Quality)
Terrestrial vertebrates				
Mice	46.58/140.15 (80.79) [a] mg/kg-day	Lactation (birth to weaning) NOAEL/ LOAEL	Reproduction	(Tanaka, 2002)
Terrestrial avian				
Chicken (*Gallus gallus*)	5/20 mg/kg of egg	Egg to juvenile NOAEL/ LOAEL	Development	(Abdul-Ghani et al., 2012) (Medium)
Male quail (*Coturnix C. coturnix*)	<250/250 mg/kg-d	45-day	Histological effects on heart	(Wang et al., 2019) (Medium)
Female Quail (*Coturnix japonica*)	<250/250 mg/kg-d	45-day	Histological effects on kidney	(Wang et al., 2020) (Medium)
Terrestrial plants				
Mungbean (*Vigna radiata*) shoot	16,550 mg/kg soil	72-hour EC50	Growth	(Ma et al., 2014) (Medium)
Mungbean (*Vigna radiata*) root	3,969 mg/kg soil			
Perennial ryegrass (*Lolium perenne*)	5.0/20 mg/kg soil	72-hour NOAEC/ LOAEC		(Ma et al., 2015) (High)
Radish (*Raphanus sativus*)	<5.0/5.0 mg/kg soil			
Alfalfa (*Medicago sativa*)				
Bread wheat (*Triticum aestivum*)				

LOAEC = lowest-observed-adverse-effect concentration; NOAEC = no-observed-adverse-effect concentration; LOAEL = lowest-observed-adverse-effect level; NOAEL = no-observed-adverse-effect level
[a] Represents a geometric mean

5 WEIGHT OF SCIENTIFIC EVIDENCE FOR ENVIRONMENTAL HAZARD

EPA uses several considerations when weighing and weighting the scientific evidence to determine confidence in the environmental hazard data. These considerations include the quality of the database, consistency, strength and precision, biological gradient/dose response, and relevance. This approach aligns with the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021) regarding the evaluation of these considerations for the determination of each environmental hazard threshold. Criteria for assessing confidence is provided in Appendix B.1.

Quality of the Database; Consistency; Strength (Effect Magnitude), and Precision

All studies that factored into the confidence section received an overall quality determination of high or medium. Based on systematic review data quality evaluation of studies, two studies with an overall quality determination of high and seven studies with an overall quality determination of medium were considered for the aquatic environmental hazard assessment. Studies with an overall quality determination of low or uninformative were not used for aquatic or terrestrial hazard characterization.

Several aquatic and terrestrial studies evaluated multiple endpoints, species, and durations, adding to the overall strength of the database (Appendix A). Aquatic studies were considered quantitatively for acute and chronic hazards if the effect was demonstrated at equal to or less than the limit of DEHP solubility in water (3.0 µg/L). Five aquatic studies showed effects with an unbounded LOAEC (Heindler et al., 2017; Corradetti et al., 2013; Kwak and Lee, 2005; Kim and Lee, 2004; Mayer Jr et al., 1973). The remaining studies showed definitive effects less than the limit of solubility ((Heindler et al., 2017) (acute); (Zanotelli et al., 2010; Chikae et al., 2004a; Chikae et al., 2004b)). These studies reported effects on mortality, growth, reproduction, and development at reported concentrations ranging from less than 0.01 up to 3.0 µg/L.

All studies considered for the mammalian assessment demonstrated effects following dietary exposure for chronic durations (Appendix A). The study with the most sensitive endpoint was selected to represent the mammalian hazard threshold (Tanaka, 2002). Of the four representative avian studies considered, one was selected with developmental abnormality endpoints to represent the avian hazard threshold (Abdul-Ghani et al., 2012). Although the two other studies showed histological effects from DEHP exposure, the thresholds needed to achieve effects were higher than the study selected for the avian hazard threshold (Wang et al., 2020; Wang et al., 2019). Most terrestrial invertebrate studies demonstrated no effects, and remaining terrestrial invertebrate studies conducted exposures in aqueous media using concentrations of DEHP that exceed 3.0 µg/L, the value selected by EPA to be most representative of non-colloidal water solubility. However, effects were observed in mammalian vertebrates over a chronic duration when exposed through the dietary route (Aviles et al., 2019; Chen et al., 2018). Significant effects were also observed in all but one of the terrestrial plant studies.

Confidence in the quality of the database, consistency, and strength and precision of the database for terrestrial vertebrates (mammals) were all considered to be robust. Confidence in the quality of the database, consistency, and strength and precision of the database for avian species were all considered moderate. Confidence in the quality of the database, consistency, and strength and precision of the database for terrestrial invertebrates is considered robust, slight, and slight, respectively. Confidence in the quality of the database, consistency, strength and precision of the database for terrestrial plants is considered robust, robust, and moderate, respectively (Table_Apx B-2).

Biological Gradient/Dose-Response: Most aquatic hazard studies reviewed by EPA incorporated

concentrations exceeding the DEHP limit of water solubility (3.0 µg/L).

In the chronic fish and aquatic invertebrate studies considered for hazard threshold determination, effects from DEHP were observed as low as 0.01 µg/L. In both studies by Chikae (2004a; 2004b) a dose-response gradient was established using nominal concentrations of 0.01, 0.1, 1.0, and 10.0 µg/L with definitive NOAEC/LOAEC values established. A dose-response relationship was not observed in the study on sediment-dwelling organisms since the LOAEC was unbounded (*i.e.*, effects were observed at the lowest concentration tested, so a NOAEC was not established). Confidence in the biological gradient/dose-response is considered slight for all aquatic taxa.

For terrestrial organisms, all chronic studies of rodents considered for quantitative assessment of mammalian hazard demonstrated a dose-response relationship, including the study from which the hazard value was derived (Tanaka, 2002).

For avian taxa, a NOAEL and LOAEL were determined in a dose series from an egg injection study (Abdul-Ghani et al., 2012) resulting in a hazard threshold for DEHP within an egg of 10 mg/kg of egg, leading to developmental deformities at hatch. The study authors noted that the concentrations used in this experiment were very high and unlikely to reflect expected environmental exposures to DEHP.

Chronic exposures of DEHP to avian taxa are represented by two studies with 45-day oral administration of DEHP (Wang et al., 2020; Wang et al., 2019). Both studies on kidney and cardiac effects were conducted at non-lethal concentrations and were designed to specifically elicit possible target organ effects from chronic oral doses. The authors indicate that a 45-day DEHP oral dose of 500 mg/kg-d induced myocardial injury, while the corresponding 250 mg/kg-d treatment resulted in histological observations swelling of cells, dilation of muscle fibers, and pale staining in addition to significant increases in heat-shock factor and heat-shock protein expression within the heart (Wang et al., 2019). While the results from both studies included molecular, enzymatic, and histological endpoints, authors did not report any corresponding deleterious effects at the organ level and beyond (*i.e.*, survival, growth, reproduction). These studies on Japanese quail indicate an unbounded LOAEL of 250 mg/kg-d, but given the effects are subapical, the NOAEL is likely not much lower.

A wide range of terrestrial invertebrate studies were considered. However, many of these studies exposed organisms to concentrations of DEHP that exceeded the limit of solubility and/or found no effects at the highest concentration tested. Terrestrial plant studies demonstrated effects at multiple test concentrations in multiple species. Some studies showed effects at the lowest concentration tested while others showed no effects at the highest concentration tested (Gao et al., 2018; Ma et al., 2015). Confidence in the biological gradient/dose-response is considered as follows: (1) robust for terrestrial mammals; (2) moderate for avian taxa; and (3) moderate for terrestrial invertebrate and terrestrial plants.

Biological, Physical/Chemical, Environmental Relevance: The 48-hour mortality endpoint evaluated in an acute aquatic invertebrate hazard study is a relevant endpoint for ecological hazard (Heindler et al., 2017). Growth, development, and reproduction endpoints in the remaining chronic studies are also relevant endpoints for biological and ecological hazard (Heindler et al., 2017; Golshan et al., 2015; Corradetti et al., 2013; Zanotelli et al., 2010; Chikae et al., 2004a; Chikae et al., 2004b; Kim and Lee, 2004; Mayer Jr et al., 1973). Growth and emergence of the midge *C. riparius* is a biologically relevant endpoint for sediment-dwelling organisms (Kwak and Lee, 2005). Most acute fish and aquatic invertebrate hazard studies considered the low solubility/high hydrophobicity of DEHP within the experimental design and incorporated a solvent. Although these studies incorporated test concentrations less than the limit of solubility in the experimental design, all studies considered for hazard threshold

determination incorporated the solvent ethanol to enhance DEHP solubility (Heindler et al., 2017; Corradetti et al., 2013; Chikae et al., 2004a; Chikae et al., 2004b; Mayer Jr et al., 1973), or solvents acetone (Golshan et al., 2015; Kwak and Lee, 2005) or DMSO (Zanotelli et al., 2010).

DEHP is expected to partition to the benthos and impact sediment-dwelling organisms to a greater extent compared to pelagic organisms within the water column. Most studies where sediment-dwelling organisms were exposed to DEHP via bulk sediment demonstrated no hazard (Appendix A). However, two sediment-dwelling invertebrate studies did demonstrate hazard in aqueous exposures (Kwak and Lee, 2005; Kim and Lee, 2004). Test concentrations in the study conducted by Kim and Lee (2004) however, exceeded the limit of solubility. In the benthic environment, several chronic studies not considered for hazard threshold determination listed an unbounded NOAEC. Therefore, there is uncertainty regarding the actual hazard value, especially to sensitive or early life stages of aquatic organisms that reside in these habitats. Conversely, Kwak and Lee (2005) did demonstrate an unbounded LOAEC that was used for the determination of the hazard threshold. Confidence in biological, physical/chemical, and environmental relevance is considered robust for all aquatic organism studies considered for hazard threshold determination. In the terrestrial environment, the main exposure pathway would be soil exposure or through DEHP ingestion. Animal studies considered for quantitative terrestrial hazard endpoints were all dietary based where the low solubility of DEHP is less of a factor. In a mechanistic avian study, rapid metabolism and excretion of DEHP in avian taxa is expected (Ishida, 1993). More information on absorption, distribution, metabolism, and excretion can be found in the *Environmental Media and General Population and Environmental Exposure for Diethylhexyl Phthalate (DEHP*) (U.S. EPA, 2025b).

Studies in the mammalian, avian, terrestrial invertebrate, and terrestrial plant database considered DEHP exposure in the study design. Multiple species across multiple taxa were identified with acceptable hazard endpoints, thereby emphasizing biological relevance. Confidence in biological, physical/chemical, and environmental relevance is considered robust for all terrestrial organisms.

Overall, EPA has robust confidence in the evidence for acute aquatic species and aquatic plants that DEHP has low hazard potential in these taxa (Table_Apx A-1). EPA has robust confidence in the evidence for chronic aquatic hazard for DEHP and moderate confidence in the evidence for chronic sediment-dwelling organisms (Table_Apx B-2). Within the terrestrial environment, EPA has robust confidence in the evidence for terrestrial mammalian hazard and terrestrial plants, moderate confidence in the evidence for avian hazard, and no reasonably available data to determine confidence to terrestrial invertebrates (Table_Apx B-2). Therefore, the weight of scientific evidence leads EPA to have moderate confidence in the overall conclusion that DEHP has potential hazards to wild organism populations. EPA does, however, have uncertainty and less confidence in the number (2 studies) and quality of the studies in the avian taxa and terrestrial invertebrate database as well as strength and precision of that data, and does not have sufficient data to establish a dose-response relationship for those taxa. A more detailed explanation of the weight of scientific evidence, uncertainties, and overall confidence is presented in Appendix A.

Although EPA reviewed over 90 studies, no consistent effects of DEHP on aquatic organism survival, growth, reproduction, or development were observed across taxonomic groups, habitats, exposure type, and exposure duration—other than within the chronic hazard data set (vertebrates and sediment-dwelling invertebrates). Chronic effects were consistently observed in vertebrates at levels less than the limit of solubility, affecting survival, growth, development, and reproduction. One study demonstrated effects on sediment-dwelling organisms with an unbounded LOAEC. Appendix A depicts studies that either demonstrated no effects or showed effects to fish, invertebrates, amphibians, as well as aquatic plants

and algae at reported concentrations higher than the limit of solubility of 3 µg/L. No acute toxicity was observed below the DEHP limit of water solubility of 3.0 µg/L. Unbounded effects were observed in some aquatic studies affecting reproduction and development in vertebrates and invertebrates as identified above in Table 3-1.

Although DEHP is expected to partition to sediment, no effects were observed in sediment-dwelling organisms. For acute exposures to DEHP, most studies and endpoints that exposed fish, amphibians, invertebrates, and algae via water in the aquatic environment reported no effects up to the highest concentration tested. Additionally, most studies tested concentrations that exceed the DEHP limit of water solubility. To achieve target doses, most studies were conducted with a solvent to enhance solubility. However, these reported values exceed expected environmental conditions.

Within the terrestrial environment, EPA has robust confidence in the evidence and hazard potential for terrestrial mammalian and terrestrial plants, and moderate confidence for avian taxa (see Table 4-1 above). EPA has robust confidence in terrestrial mammalian and terrestrial plants hazard values due to the high number of high-quality rodent studies with ecologically relevant endpoints used as human health models and well-represented terrestrial plant data.

Environmental 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. Table 5-1 summarizes the concentrations of concern identified for DEHP. See Section 5 and Appendix A for more details about how EPA weighed the scientific evidence.

In aquatic species, EPA uses probabilistic approaches (*e.g.*, species sensitivity distribution [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. However, no reasonably available acute aquatic vertebrate or invertebrate studies with definitive values less than the 3.0 µg/L limit of solubility or studies that showed effects up to the limit of solubility were available for quantitative assessment of DEHP. For DEHP, a deterministic approach was used to assess hazard in aquatic taxa, and hazard values were assigned for terrestrial taxa. 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, 2013, 2012).

Equation 5-1.

$$COC = toxicity\ value \div AF$$

For terrestrial species, EPA estimates hazard by calculating a toxicity reference value (TRV) or by assigning the hazard value as the hazard threshold in the case of mammals, avian taxa, and terrestrial plants.

5.1 Aquatic Species COCs

EPA reviewed 82 studies categorized as high or medium quality rated studies for toxicity to aquatic organisms. Of these studies, 73 demonstrated no acute/chronic effects up to or exceeding the highest concentration tested, or the effects occurred at concentrations greater than the limit of solubility (3.0 µg/L). EPA typically does not consider unbounded NOAEC/LOAEC values in the calculation of COCs. These studies were not considered for quantitative risk evaluation but can be found in Appendix A.

Studies that received an overall quality determination of low, unacceptable, or did not meet systematic review criteria were likewise not considered quantitatively for determination of hazard values. The remaining one acute and four chronic studies found in Table 3-1 were considered by EPA for COC calculations.

Acute Aquatic Threshold

One 48-hour acute toxicity study with the marine copepod *P. crassirostris* was considered quantitatively (Heindler et al., 2017). *P. crassirostris* were exposed to DEHP at 0.06, 0.48, 3.81, 20.52, 244.14, and 1953.13 ng/mL, and the LC50 was determined to be 1.04 ng/mL (1.04 µg/L). However, that study was excluded from the final quantitative assessment due to low confidence in the measured hazard value. In addition to the lack of analytical verification of the low DEHP concentrations used in the study, the materials, such as the mesh screen used to filter-out adult copepods and the polycarbonate carboys in the culturing system, may have contributed to background concentration of DEHP. Furthermore, that study represented an outlier in comparison to the other available acute aquatic data in which toxicity was not observed at concentrations below DEHP water solubility. Therefore, that study was not considered for COC calculations.

EPA did not identify any other reasonably available data with definitive hazard values to be used in deriving a hazard threshold for acute aquatic species, including sediment-dwelling organisms. The data suggest that DEHP has low acute toxicity, as no definitive effects were observed below the limit of water solubility.

Chronic Aquatic Vertebrate Threshold

The DEHP chronic aquatic COC was derived from the chronic value (ChV) from the two 21-day NOAEC/LOAEC studies of 0.01/0.1 µg/L for the aquatic vertebrate Japanese medaka (*O. latipes*) with the application of an AF of 10. The ChV for *O. latipes* was the most sensitive chronic endpoint represented in Table 3-1 for aquatic vertebrates and invertebrates representing effects of growth and development of embryo and fry of *O. latipes* (Chikae et al., 2004a; Chikae et al., 2004b). The ChV was determined to be 0.032 µg/L based on the geometric mean of the NOAEC/LOAEC values for growth and development; thus, the COC (ChV ÷ adjustment factor [AF]) was 0.0032 µg/L.

Amphibian Threshold

No studies with definitive values below the limit of solubility were available to assess the hazard of DEHP to amphibians. Therefore, a hazard threshold could not be established.

Aquatic Plants and Algae Threshold

No studies with definitive values below the limit of solubility were available to assess the hazard of DEHP to aquatic plants or algae. Therefore, a hazard threshold could not be established.

Acute Sediment-Dwelling Threshold

No studies with definitive values below the limit of solubility were available to assess the hazard of DEHP to sediment-dwelling taxa on an acute exposure basis. Therefore, a hazard threshold could not be established.

Chronic Sediment-Dwelling Threshold

One study was submitted to evaluate DEHP toxicity to sediment-dwelling organisms *C. riparius* (Kwak and Lee, 2005). The DEHP chronic sediment-dwelling COC was derived based on significant reduction in male body width and male body volume and significant increase female body volume at every concentration tested, resulting in a LOAEC of 0.3 µg/L and a NOAEC not established. EPA chose the

LOAEC of 0.3 µg/L as the chronic sediment-dwelling hazard threshold.

COC for Aquatic Toxicity
EPA did not identify any reasonably available data with definitive hazard values below the limit of solubility to be used in deriving a hazard threshold for acute aquatic vertebrates, acute and chronic invertebrates and amphibians, and aquatic plants and algae.

The chronic sediment-dwelling organism COC was derived from an unbounded LOAEC at 0.3 µg/L from a *C. riparius* 30-day DEHP exposure resulting in significant effects on male body width and male and female body volume (Kwak and Lee, 2005). The LOAEC ÷ AF of 10 resulted in a chronic COC of 0.03 µg/L.

5.2 Terrestrial Species Hazard Values

Terrestrial Mammal Threshold
For terrestrial vertebrate species exposed to DEHP, EPA estimated hazard using a deterministic approach. Twenty-six laboratory rat and mouse studies were assessed with the most sensitive and ecologically relevant reproductive endpoint value chosen to represent the terrestrial mammalian hazard threshold. Phthalates are endocrine disrupters and therefore studies were filtered to identify those with reproductive effects as the most sensitive endpoints. The terrestrial mammalian hazard threshold was derived from the NOAEL/LOAEL of 48.58/140.15 mg/kg-day (representing the maternal achieved intake during lactation), which resulted in a geometric mean of 80.79 mg/kg-day as the hazard value for terrestrial mammals. This was the most sensitive hazard value from the dataset, with the LOAEL based on a decrease in pup survival during lactation (Tanaka, 2002).

Avian Threshold
The avian hazard threshold was derived from developmental malformations upon examination including gastroschisis and omphalocele in the chicken (*Gallus gallus domesticus*) resulting in a NOAEL/LOAEL of 5/20 mg/kg from DEHP injected into the albumen of an egg (Abdul-Ghani et al., 2012). EPA is using the geometric mean of the NOAEL/LOAEL of 10 mg/kg of egg for the avian hazard threshold.

Terrestrial Invertebrate Threshold
Available invertebrate studies identified through systematic review showed no effects of DEHP. Other studies administered DEHP as an aqueous test solution that exceeded the limit of solubility, and the amount of DEHP administered to test organisms was unclear. Therefore, a hazard threshold could not be established.

Terrestrial Plant Threshold
The terrestrial plant hazard threshold was derived from the DEHP 72-hour NOAEC/LOAEC of 5.0/20 mg/kg soil, which resulted in a geometric mean of 10 mg/kg soil for decreased root elongation and seedling growth of perennial ryegrass (*Lolium perenne*) (Ma et al., 2015).

Calculations

- The DEHP hazard threshold for mammals is 80.79 mg/kg-bw/day.
- The DEHP hazard threshold for avian taxa is 10 mg/kg of egg
- The DEHP hazard threshold for terrestrial plants is 10 mg/kg soil.

Table 5-1. Environmental Hazard Thresholds for Environmental Toxicity

Environmental Assessment	Assessment Medium	Hazard Threshold
Acute Aquatic Assessment	Surface water	ND
Chronic Aquatic Vertebrate Assessment	Surface water	0.0032 µg/L
Chronic Sediment-Dwelling Invertebrate Assessment	Sediment porewater	0.03 µg/L
Algal Assessment	Surface water	ND
Mammal: Hazard Value	Dietary	80.79 mg/kg-day
Terrestrial Invertebrate	Soil	ND
Avian: Hazard Value	Egg injection	10 mg/kg of egg
Terrestrial Plants: Hazard value	Soil	10 mg/kg soil
ND = not determined		

6 CONCLUSIONS FOR ENVIRONMENTAL HAZARD: STRENGTHS, LIMITATIONS, ASSUMPTIONS, AND KEY SOURCES OF UNCERTAINTY

EPA determined that DEHP poses no acute exposure effects on aquatic organisms because the available evidence indicates that there were no acute effects up to the limit of water solubility (3.0 µg/L). Most of the available studies tested concentrations that exceed the DEHP limit of water solubility. To achieve target doses, most studies were conducted with a solvent to enhance DEHP solubility in water. However, these reported values exceed expected environmental conditions. EPA determined that DEHP poses potential chronic hazard to aquatic organisms based on data from two studies Chikae et al. (2004a) and Chikae et al. (2004b) from which a COC of 0.0032 µg/L was derived.

EPA determined that DEHP poses a hazard to terrestrial mammals at a dietary dose of 80.79 mg/kg-day, which is supported by laboratory rodent studies. This terrestrial hazard value is limited by uncertainties surrounding the lack of available studies for wild animal and/or plant populations, as well as uncertainties regarding whether laboratory rodent results may translate to wild populations. Additionally, DEHP was also found to pose a hazard to terrestrial avian and plant species based on two studies in which terrestrial hazard values of 10 mg DEHP/kg of egg for the avian threshold (Abdul-Ghani et al., 2012) and 10 mg/kg soil for the plant threshold (Ma et al., 2015) were identified.

EPA has robust confidence that DEHP poses little to no hazard to aquatic vertebrates in the environment on an acute exposure basis, and no hazard to aquatic invertebrates on an acute or chronic basis. This robust confidence is supported by reasonably available data that consistently found that acute DEHP exposure poses no hazard up to and exceeding the limit of water solubility.

Conversely, though the extensive database of studies indicate that DEHP does not impact survival of aquatic species from acute exposure durations, exposure to DEHP for a longer period of time at lower concentrations impacts more sensitive endpoints of growth, development, and reproduction. EPA has robust confidence that DEHP poses potential hazard to aquatic vertebrates on a chronic basis below the limit of water solubility. This robust confidence is supported by two studies in which effects on mortality, growth, and development were observed in Japanese medaka fish exposed to 0.1 µg/L DEHP for 21-day (Chikae et al., 2004a; Chikae et al., 2004b) as well as studies by Golshan et al. (2015), Corradetti et al. (2013), and Zanotelli et al. (2010). These studies reported effects on mortality, growth, reproduction, and development at concentrations ranging from 0.01 up to 10 µg/L. There is uncertainty however, in chronic aquatic vertebrate data since the majority of the studies either only used DEHP concentrations above the limit of water solubility or found no effects up to the limit of solubility—even when a solvent was incorporated.

EPA has moderate confidence that DEHP has effects on growth and development to sediment-dwelling invertebrate species below the limit of water solubility. This moderate confidence is supported by one study in which effects on growth were observed in midge exposed to 0.3 µg/L DEHP (Kwak and Lee, 2005). However, because a LOAEC was used in the COC, there is uncertainty regarding the actual hazard value for this group. Although not used for COC determination, a pelagic invertebrate study with the marine copepod (*Parvocalanus crassirostris*) also showed effects around a similar threshold of less than 0.3 µg/L (Heindler et al., 2017). This study was not considered for COC calculations due to analytical measurement concerns and background concentrations of DEHP.

EPA has robust confidence that DEHP poses little to no acute exposure hazard to aquatic algae. This robust confidence is supported by reasonably available data indicating DEHP poses no risk to aquatic

algae below the limit of water solubility. The approach to EPA's consideration of the strengths, limitations, assumptions, and key sources of uncertainty for environmental hazard is outlined in Appendix A.

EPA acknowledges the aquatic hazard conclusions are limited by the low number of studies to assess DEHP quantitatively below the limit of water solubility. EPA does not have acute data on vertebrates or acute or chronic data on aquatic invertebrates, amphibians, and/or aquatic plants and algae, which leads to further uncertainty of the effects of DEHP on these organisms.

In the terrestrial environment, EPA has robust confidence that DEHP poses potential hazard to mammals and terrestrial plants. The conclusion that DEHP poses hazard to terrestrial mammals at a dietary dose of 80.79 mg/kg-day is supported by evidence obtained from laboratory rodent studies used as human health models. Furthermore, nearly all other studies of rats and mice considered for hazard threshold determination were within an order of magnitude of the selected value. Utilizing human health rodent models as a surrogate for terrestrial models introduces uncertainty into the terrestrial hazard characterization because these species may not be fully representative of effects in a more diverse array of wild animal populations.

The conclusion that DEHP poses hazard to terrestrial plants is supported by two terrestrial plant studies that identified effects of DEHP on plant growth in six plant species (Ma et al., 2015; Ma et al., 2014). For avian taxa, EPA has uncertainty in the hazard characterization that the dose reached by the embryo is representative of concentrations that would be depurated to the embryo in the egg development process. The study design and data reporting did not allow for dose-response analysis for mechanistic endpoints because only control and high dose were reported for these endpoints. EPA identified no studies within the reasonably available database to assess risk to terrestrial invertebrates.

The aquatic vertebrate and sediment-dwelling COCs and terrestrial hazard values identified in this technical support document will be used in the *Environmental Hazard Assessment for Diethylhexyl Phthalate (DEHP)* (U.S. EPA, 2025a) to characterize environmental risk.

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APPENDICES

Appendix A ENVIRONMENTAL HAZARD TABLE OF STUDIES

Table_Apx A-1. List of Aquatic Studies Not Considered for Quantitative Assessment

Study Type	Test Organism (Species)	Hazard Values	Duration	Endpoint(s)	Citation (Data Evaluation Rating)
Acute	Acute aquatic vertebrates				
	Japanese medaka (*Oryzias latipes*)	>0.67 mg/L	96-hour LC50	Mortality	(Defoe et al., 1990) (High)
	Fathead minnow (*Pimephales promelas*)	>0.32 mg/L	96-hour LC50	Mortality	(Defoe et al., 1990) (High)
	Rainbow trout (*Oncorhynchus mykiss*)	>19.5 mg/L	96-hour LC50	Mortality	(Defoe et al., 1990) (High)
	Rainbow trout (*Oncorhynchus mykiss*)	>0.32 mg/L	96-hour LC50	Mortality	(EG&G Bionomics, 1983b) (High)
	Sheepshead minnow (*Cyprinodon variegatus*)	>0.17 mg/L	96-hour LC50	Mortality	(Adams et al., 1995) (High)
	Fathead minnow (*Pimephales promelas*)	>0.16 mg/L	96-hour LC50	Mortality	(Adams et al., 1995) (High)
	Bluegill (*Lepomis macrochirus*)	>0.20 mg/L	96-hour LC50	Mortality	(Adams et al., 1995) (High)
	Fathead minnow (*Pimephales promelas*)	>0.67 mg/L	96-hour LC50	Mortality	(Adams et al., 1995) (High)
	Rainbow trout (*Oncorhynchus mykiss*)	>0.32 mg/L	96-hour LC50	Mortality	(Adams et al., 1995) (High)
	Fathead minnow (*Pimephales promelas*)	>0.67 mg/L	96-hour LC50	Mortality	(EG&G Bionomics, 1984a) (High)
	Fathead minnow (*Pimephales promelas*)	>0.24 mg/L	96-hour LC50	Mortality	(EG&G Bionomics, 1983a) (High)
	Fathead minnow (*Pimephales promelas*)	>0.1 mg/L	48-hour LC50	Mortality	(Wood et al., 2015) (High)
	Danio rerio (*Zebra Danio*)	>0.5 mg/L	72-hour LC50	Mortality	(Chen et al., 2014) (Medium)
	Bluegill (*Lepomis macrochirus*)	>770 mg/L	96-hour LC50	Mortality	(Buccafusco et al., 1981) (Medium)
	Sheepshead minnow (*Cyprinodon variegatus*)	>550 mg/L	96-hour LC50	Mortality	(Heitmuller et al., 1981) (Medium)
	Bluegill (*Lepomis macrochirus*)	>0.32 mg/L	96-hour LC50	Mortality	(EG&G Bionomics, 1983c) (High)
	Sheepshead minnow (*Cyprinodon variegatus*)	>0.17 mg/L	96-hour LC50	Mortality	(Springborn Bionomics, 1984b) (High)
	Zebra fish (*Danio rerio*)	<2.03/ 2.03 mg/L	24-hour NOAEC/LOAEC	Growth/ development	(Kinch et al., 2016) (High)
	Common carp (*Cyprinus carpio*)	37.95 mg/L	96-hour LC50	Mortality	(Zhao et al., 2014) (Medium)
	Acute aquatic invertebrates				
	Water flea (*Daphnia magna*)	2.0 mg/L	48-hour EC50	Mortality	(Monsanto, 1983a) (High)
	Harpacticoid copepod (*Nitrocra spinipes*)	>300 mg/L	96-hour LC50	Mortality	(Linden et al., 1979) (Medium)
	Midge (*Paratanytarsus*	>0.24 mg/L	96-hour LC50	Mortality	(EG&G Bionomics, 1984d)

Study Type	Test Organism (Species)	Hazard Values	Duration	Endpoint(s)	Citation (Data Evaluation Rating)
Acute	*parthenogeneticus*)				(High)
	Opossum shrimp (*Americamysis bahia*)	>0.44 mg/L	96-hour LC50	Mortality	(EG&G Bionomics, 1984b) (High)
	Water flea (*Daphnia magna*)	>0.32 mg/L	48-hour LC50	Mortality	(Springborn Bionomics, 1984a) (Medium)
	Water flea (*Daphnia magna*)	>0.16 mg/L	48-hour EC50	Immobilization	(Adams et al., 1995) (High)
	Midge (*Paratanytarsus parthenogeneticus*)	>0.18 mg/L	96-hour LC50	Mortality	(Adams et al., 1995) (High)
	Opossum shrimp (*Americamysis bahia*)	>0.37 mg/L	96-hour LC50	Mortality	(Adams et al., 1995) (High)
	Water flea (*Daphnia magna*)	>0.32 mg/L	48-hour LC50	Mortality	(Brown and Thompson, 1982) (Medium)
	Water flea (*Daphnia magna*)	2.0 mg/L	48-hour EC50	Mortality	(Monsanto, 1983a) (High)
	Water flea (*Daphnia magna*)	13.9 mg/L	48-hour EC50	Mortality	(Monsanto, 1983b) (High)
	Copepod (*Parcovalanus crassirostris*)	>5.1 mg/L	48-hour LC50	Mortality	(Heindler et al., 2017) (Medium)
	Water flea (*Daphnia magna*)(juvenile)	0.56 mg/L	48-hour LC50	Mortality	(Wang et al., 2018) (High)
	Water flea (*Daphnia magna*)	0.35 mg/L	48-hour LC50	Mortality	(Wang et al., 2018) (High)
	Midge (*Chironomus tentans*)	0.05 mg/L	48-hour NOEC	Growth/ development	(Lee et al., 2006) (Medium)
	Taiwan abalone (*Haliotis diversicolor*)	0.0188/ 0.204 mg/L	96-hour NOAEC/LOAEC	Growth/ development	(Liu et al., 2009) (Medium)
	Taiwan abalone (*Haliotis diversicolor*)	20/ >20 mg/L	96-hour NOAEC/LOAEC	Growth/ development	(Yang et al., 2009) (Medium)
	Rotifer (*Brachionus calyciflorus*)	>2 mg/L	96-hour NOEC	Reproduction	(Cruciani et al., 2015) (Medium)
	Midge (*Chironomus tetans*)	>10.0 mg/L	48-hour LC50	Mortality	(Monsanto, 1983c) (Medium)
	Water flea (*Daphnia magna*)	2.69/ >2.69 mg/L	72-hour NOEAC/LOAEC	Growth	(Jordão et al., 2015) (Medium)
	Calanoid copepod (*Eurytemora affinis*)	0.5 mg/L	96-hour LC50	Mortality	(Forget-Leray et al., 2005) (High)
	Water flea (*Daphnia magna*)	>3.9 mg/L	24-hour LOAEC	Mortality	(Seyoum and Pradhan, 2019) (Medium)
	Water flea (*Daphnia magna*)	2.1 mg/L	24-hour EC50	Mortality	(Huang et al., 2016) (High)
	Midge (*Chironomus plumosus*)	>18 mg/L	48-hour LC50	Emergence and reproduction	(Streufort, 1978) (High)
Subchronic / chronic	Chronic aquatic vertebrate				
	Fathead minnow (*Pimephales promelas*)	0.012/ >0.012 mg/L	28-day NOAEC/LOEC	Reproduction	(Crago and Klaper, 2012) (Medium)
	Chinese rare minnow (*Gobiocypris rarus*)	4.2/ 13.3 µg/L	6-month NOAEC/LOAEC	Reproduction	(Guo et al., 2015) (High)
	Japanese medaka (*Oryzias latipes*)	0.39/ >0.39 mg/L	14-day NOAEC/LOAEC	Reproduction	(Shioda and Wakabayashi, 2000) (Medium)
	Zebrafish (*Danio rerio*)	0.5/ 5 mg DEHP/kg diet	10-day NOAEC/LOAEC	Reproduction	(Uren-Webster et al., 2010) (High)

Study Type	Test Organism (Species)	Hazard Values	Duration	Endpoint(s)	Citation (Data Evaluation Rating)
Subchronic/ chronic	Japanese medaka (*Oryzias latipes*)	1.0/ 10.0 µg/L	3-month NOAEC/LOAEC	Growth/ development	(Kim et al., 2002) (Medium)
	Japanese medaka (*Oryzias latipes*)	5/ >5 mg/L	21-day NOAEC/LOAEC	Growth	(Metcalfe et al., 2001) (Medium)
	Bagrid catfish (*Pseudobagrus fulvidraco*)	100/ 500 mg/kg diet	4/8-week NOAEC/LOAEC	Growth	(Jee et al., 2009) (High)
	Marine medaka (*Oryzias melastigma*)	<0.1/ 0.1 mg/L	6-month NOAEC/LOAEC	Reproduction	(Ye et al., 2014) (Medium)
	Rainbow trout (*Salmo gairdneri*)	5/14 µg/L	24-day NOAEC/LOAEC	Survival	(Mehrle and Mayer, 1976) (Medium)
	Rainbow trout (*Salmo gairdneri*)	50/ >50 mg DEHP/kg	10-day NOAEC/LOAEC	Reproduction	(Ahmadivand et al., 2016) (High)
	Japanese medaka (*Oryzias latipes*)	<20/ 20 µg/L	7-day NOAEC/LOAEC	Growth	(Yang et al., 2018) (High)
	Yellowhead catfish (*Aeromonas hydrophila*)	0.1/ 0.5 mg/L	57-day NOAEC/LOAEC	Growth/ development	(Yuan et al., 2017) (High)
	African sharptooth catfish (*Clarias gariepinus*)	>100 µg/L	14-day NOAEC	Survival	(Wood et al., 2015) (High)
	African sharptooth catfish (*Clarias gariepinus*)	400/ >400 µg/L	14-day NOAEC/LOAEC	Growth	(Adeogun et al., 2018) (High)
	Zebrafish (*Danio rerio*)	<0.5/ 0.5 µg/L	6-month NOAEC/LOAEC	Growth/ reproduction	(Muhammad et al., 2018) (Medium)
	Zebrafish (*Danio rerio*)	4.0/ <4.0 mg/kg diet	7-week NOAEC/LOAEC	Growth/ reproduction	(Buerger et al., 2019) (High)
	Zebrafish (*Danio rerio*)	33/ 100 µg/L	3-month NOAEC/LOAEC	Reproduction	(Ma et al., 2018) (High)
	Atlantic salmon (*Salmo salar*)	300/ 1,500 mg/kg	28-day NOAEC/LOAEC	Growth	(Norrgren et al., 1999) (Medium)
	Atlantic salmon (*Salmo salar*)	1,634–1,661 mg/kg diet	28-day NOAEC/LOAEC	Population	(Norman et al., 2007) (High)
	Japanese medaka (*Oryzias latipes*); Rainbow trout (*Salmo gairdneri*)	0.496/ <0.496 mg/L	90-day NOAEC/LOAEC	Growth	(Defoe et al., 1990) (High)
	Chronic aquatic invertebrates				
	Water flea *(Daphnia magna)*	107/ >107 µg/L	21-day NOAEC/LOAEC	Reproduction	(Brown and Thompson, 1982) (Medium)
	Water flea *(Daphnia magna)*	0.39/ >0.39 mg/L	14-day NOAEC/LOAEC	Growth/ reproduction	(Seyoum and Pradhan, 2019) (Medium)
	Water flea *(Daphnia magna)*	0.077/ 0.16 mg/L	14-day NOAEC/LOAEC	Survival	(Springborn Bionomics, 1984c) (High)
	Water flea *(Daphnia magna)*	0.077/ 0.16 mg/L	21-day NOAEC/LOAEC	Survival	(Rhodes et al., 1995) (High)
	Water flea *(Daphnia magna)*	158/ >811 µg/L	21-day NOAEC/LOAEC	Survival and reproduction	(Knowles et al., 1987) (High)
	Abalone (*Haliotis diversicolor*)	2/ 10 µg/L	9, 120-hour NOAEC/LOAEC	Reproduction and development	(Zhou et al., 2011) (High)
	Copepod (*Eurytemora affinis*)	109/ 245 µg/L	10-day NOAEC/LOAEC	Reproduction	(Forget-Leray et al., 2005) (High)

Study Type	Test Organism (Species)	Hazard Values	Duration	Endpoint(s)	Citation (Data Evaluation Rating)
Subchronic / chronic	Copepod (*Eurytemora affinis*)	109/ 245 µg/L	10-day NOAEC/LOAEC	Survival	(Forget-Leray et al., 2005) (High)
	Penaeid shrimp (*Penaeus vannamei*)	60,000/ >60,000 ppm	21-day NOAEC/LOAEC	Mortality	(Hobson et al., 1984) (Medium)
	Freshwater rotifer (*Brachionus calyciflorus*)	5,000/ >5,000 µg/L	6-day NOAEC/LOAEC	Reproduction and mortality	(Zhao et al., 2009) (Medium)
	Freshwater amphipod (*Gammarus pulex*)	100/ 500 µg/L	25-day NOAEC/LOAEC	Behavior	(Thurén and Woin, 1991) (Medium)
	Grass shrimp (*Palaemonetes pugio*)	0.39/ 0.51 mg/L	28-day NOAEC/LOAEC	Mortality and growth/ development	(Laughlin RB et al., 1978) (Medium)
	Mud crab (*Macrophthalmus japonicus*)	10/ 30 µg/L	7-day NOAEC/LOAEC	Survival	(Park et al., 2019) (Medium)
	Water flea *(Daphnia magna)*	1.0/ >1.0	21-day NOAEC/LOAEC	Mortality	(Brown et al., 1998) (High)
	Aquatic sediment-dwelling invertebrates				
	Scud (*Hyalella azteca)*	>3,170 mg/kg dw bs	10-day LC50	Mortality	(Call et al., 2001a) (High)
	Scud (*Hyalella azteca*	>0.273 mg/L	10-day LC50	Mortality	(Call et al., 2001a) (High)
	Midge (*Chironomus tentans*)	>3,070 mg/kg dw bs	10-day LC50	Mortality	(Call et al., 2001a) (High)
	Midge (*Chironomus tentans*)	>0.382 mg/L	10-day LC50	Mortality	(Call et al., 2001a) (High)
	Scud (*Hyalella azteca*	>0.059 mg/L	10-day LC50	Mortality	(Call et al., 2001b) (High)
	Midge (*Chironomus tentans*)	>0.047 mg/L	10-day LC50	Mortality	(Call et al., 2001b) (High)
	Worm (*Lumbriculus variegatus*)	>0.069 mg/L	10-day LC50	Mortality	(Call et al., 2001b) (High)
	Scud (*Gammarus pulex*)	0.1/ >0.5 mg/L	20-day NOAEC/ LOAC	Behavior	(Thurén and Woin, 1991) (Medium)
	Midge (*Chironomus riparius*)	4,300/ >4,300 mg/kg	28-day NOAEC/LOAEC	Emergence	(Brown et al., 1996) (High)
	Midge (*Paratanytarsus parthenogenica*)	>0.24 mg/L	48-hour LC50	Mortality	(EG&G Bionomics, 1984c) (High)
	Midge (*Chironomus plumosus*)	>144/ 144 µg/L	40-day LOAEC/NOAEC	Emergence and reproduction	(Streufort, 1978) (High)
	Midge (*Chironomus plumosus*)	0.36/ >0.36 mg/L	35-day NOAEC/LOAEC	Emergence and reproduction	(Streufert et al., 1980) (Medium)
	Midge (*Chironomus riparius*)	<0.01/ 0.01 mg/L (ppm)	30-day NOAEC/ LOAEC	Reproduction	(Kim and Lee, 2004) (Medium)
Amphibians					
	Chinese brown frog (*Rana chensinensis*)	0.039/ 0.39 mg/L	80-day NOAEC/LOAEC	Growth/ development	(Zhang et al., 2018) (Medium)
	Moorfrog (*Rana arvalis*)	8.8–800 µg/g wet weight	60-day NOAEC/LOAEC	Survival, growth, development	(Larson and Thuren, 1987) (Medium)
Aquatic plants and algae					
	Green algae (*Raphidocelis subcapitata*)	>0.1 mg/L	14-day EC50	Growth and chlorophyll	(Springborn Bionomics, 1984d) (High)

Study Type	Test Organism (Species)	Hazard Values	Duration	Endpoint(s)	Citation (Data Evaluation Rating)
	Green algae (*Raphidocelis subcapitata*)	>0.1 mg/L	96-hour EC50	Growth and chlorophyll	(Adams et al., 1995) (High)

EC50 = effect concentration at which 50% of test organisms exhibit an effect; LOAEC = lowest-observed-adverse-effect concentration; LC50 = lethal concentration at which 50% of test organisms die; NOAEC = no-observed-adverse-effect concentration
Study type is not listed for terrestrial species as the duration for determining acute or chronic is more variable in terrestrial species as compared to aquatic species.

Table_Apx A-2. List of Terrestrial Studies Not Considered for Quantitative Assessment

Test Organism	Hazard Values	Duration	Endpoint	Citation(s) (Study Quality)
Mice	14/ 138 mg/kg-day	18-week NOAEC/ LOAEC	Reproduction	(Lamb et al., 1987)
	138/ 414 mg/kg-day			
	70/ 90 mg/kg-day	GD 0–18 NOAEC/ LOAEC		(Shiota et al., 1980) (Shiota and Nishimura, 1982)
	190/ 410 mg/kg-day			
	91/ 191 mg/kg-day	GD 0–17 NOAEC/ LOAEC		(RTI International, 1984) (Tyl et al., 1988)
	191/ 292 mg/kg-day			
	169/ 537 mg/kg-day			
	20/ 200 mg/kg-day	10-day NOAEC/ LOAEC		(Chiang et al., 2020)
	150/ 200 mg/kg-day	GD 7–14 NOAEC/ LOAEC		(Quinnies et al., 2015)
	5/ 250 mg/kg-day	GD 7–16 NOAEC/ LOAEC		(Ungewitter et al., 2017)
	172/ 493 mg/kg-day	2-generation		(Tanaka, 2002)
	5/ 500 mg/kg-day	8-week NOAEC/ LOAEC		(Schmidt et al., 2012)
	5/ 500 mg/kg-day	GD 0.5–PND 21 NOAEC/ LOAEC		(Pocar et al., 2012)
	250/ 500 mg/kg-day	E6.5–14.5 NOAEC/ LOAEC		(Tang et al., 2018)
	500/ 750 mg/kg-day	GD 11 to birth NOAEC/ LOAEC		(Barakat et al., 2017)
	500/ 1,000 mg/kg-day	GD 1–6 NOAEC/ LOAEC		(Li et al., 2012)
	500/ 1,000 mg/kg-day	GD 7–9 NOAEC/ LOAEC		(Shiota and Mima, 1985)
	1,000/ 2,000 mg/kg-day			
Rats	93/ 272 mg/kg-day	2-generation NOAEC/ LOAEC		(BASF, 2001)
	145/ 400 mg/kg-day			
	148/ 451 mg/kg-day			
	271/ 792 mg/kg-day			
	272/ 999 mg/kg-day			
	451/ 1,128 mg/kg-day			
	136/ 409 mg/kg-day	PND 1–22 NOAEC/ LOAEC		(Marsman, 1995)
	1,381/ 2,762 mg/kg-day	GD 0–20		
	357/ 666 mg/kg-day	GD 0–20 NOAEC/ LOAEC		(Wolkowski-Tyl et al., 1983) (Tyl et al., 1988)
	422/ 767 mg/kg-day			
	856/ 1,055 mg/kg-day			
	767/ 1,168 mg/kg-day			
	300/ 750 mg/kg-day	GD 7 to PND 17 NOAEC/ LOAEC		(Jarfelt et al., 2005)
	284/ 820 mg/kg-day	Two-generation NOAEC/ LOAEC		(BASF AG, 1999)

Test Organism	Hazard Values	Duration	Endpoint	Citation(s) (Study Quality)
Rats	277/ 820 mg/kg-day		Reproduction	
	504/ 1,131 mg/kg-day			
	300/ 1,000 mg/kg-day	5-week NOAEC/ LOAEC		(Takai et al., 2009)
	1,000/ 3,000 mg/kg-day			
	284/ 1,156 mg/kg-day	60-day NOAEC/LOAEC		(Agarwal et al., 1986)
	974/ 1,461 mg/kg-day	GD 6–15 NOAEC/ LOAEC		(Morrissey et al., 1989)
	5,000/ 10,000 mg/kg-day	4-week NOAEC/ LOAEC		(Dalgaard et al., 2000)
Chicken (*Gallus gallus*)	100/ <100 mg/kg	5-day NOAEL/LOAEL	Behavior	(Abdul-Ghani et al., 2012)
Fruit fly (*Drosophila melanogaster*)	>7.8 mg/L	N/A	Mortality	(Vogel and Nivard, 1993) (Rating)
Earthworm (*Eisenia fetida*)	3,140 µg/cm^2	48-hour LC50		(Neuhauser et al., 1985) (Medium)
Nematode (*Caenorhabditis elegans*)	22.55 mg/L	24-hour LC50		(Roh et al., 2007) (Medium)
	>100 mg/L	24-hour LC50		(Yin et al., 2018) (Medium)
	1.0/ 10 mg/L	75-hour NOAEC/LOAEC	Reproduction – fecundity	
	1.0/ 2.0 mg/L	24-hour NOAEC/LOAEC	Behavior	(Tseng et al., 2013) (High)
	<0.2/ 0.2 mg/L	72-hour NOAEC/LOAEC		(Li et al., 2018) (Medium)
	<0.1/ 0.1 mg/L			(How et al., 2019) (Medium)
	0.1/ 1.5 mg/L	48-hour NOAEC/LOAEC	Reproduction – brood size	
Springtail (*Folsomia fimetaria*) Adult	5,000/ >5,000 mg/kg	50-day NOAEC/ LOAEC	Mortality	(Jensen et al., 2001) (Medium)
	1,000/ >1,000 mg/kg	30-day NOAEC/ LOAEC		
Fruit fly (*Drosophila melanogaster*)	78.11/ >78.11 mg/L	7-day post-hatch	Behavior	(Cao et al., 2016) (Medium)
Nematode (*Caenorhabditis elegans*)	<1.5/ 1.5 mg/L	28-day NOAEC/ LOAEC	Survival	(How et al., 2019) (Medium)
Fruit fly (*Drosophila melanogaster*)	0.2/0.4% diet	60-day NOAEC/ LOAEC	Mortality	(Chen et al., 2018) (High)
Black garden ant (*Lasius niger*)	<2.0/ 2.0 mg/L	5-week NOAEC/ LOAEC	Reproduction	(Cuvillier-Hot et al., 2014) (High)
Cucumber (*Cucumis sativus*)	30/ 50 mg/L	7-day NOAEC/ LOAEC	Growth	(Zhang et al., 2014) (Medium)
Common oat (*Avena sativa*)	500/ >500 mg/kg soil	72-hour NOAEC/ LOAEC		(Ma et al., 2015) (High)
Common onion (*Allium cepa*)				
Bread wheat (*Triticum*	43.2 (53) mg/L	72-hour IC50		(Gao et al., 2017) (High)
	<10/ 10 mg/kg soil	N/A		(Gao et al., 2018)

Test Organism	Hazard Values	Duration	Endpoint	Citation(s) (Study Quality)
aestivum)				(Medium)
EC50 = effect concentration at which 50% of test organisms exhibit an effect; GD = gestational day; IC = inhibition effect concentration; LOAEC = lowest-observed-adverse-effect concentration; LC50 = lethal concentration at which 50% of test organisms die; NOAEC = no-observed-adverse-effect concentration; PND = post-natal day				

Appendix B ENVIRONMENTAL HAZARD DETAILS

B.1 Evidence Integration

Data integration includes analysis, synthesis, and integration of information for the risk evaluation. During data integration, EPA considers quality, consistency, relevancy, coherence, and biological plausibility to make final conclusions regarding the weight of scientific evidence. As stated in the 2021 Draft Systematic Review Protocol (U.S. EPA, 2021), data integration involves transparently discussing the significant issues, strengths, and limitations as well as the uncertainties of the reasonably available information and the major points of interpretation.

The general analytical approaches for integrating evidence for environmental hazard is discussed in Section 7.4 of the 2021 Draft Systematic Review Protocol.

The organization and approach to integrating hazard evidence is determined by the reasonably available evidence regarding routes of exposure, exposure media, duration of exposure, taxa, metabolism and distribution, effects evaluated, the number of studies pertaining to each effect, as well as the results of the data quality evaluation.

The environmental hazard integration is organized around effects to aquatic and terrestrial organisms as well as the respective environmental compartments (*e.g.*, pelagic, benthic, soil). Environmental hazard assessment may be complex based on the considerations of the quantity, relevance, and quality of the available evidence.

For DEHP, environmental hazard data from toxicology studies identified during systematic review have used evidence that characterizes apical endpoints; that is, endpoints that could have population-level effects such as reproduction, growth, and/or mortality. Additionally, mechanistic data that can be linked to apical endpoints will add to the weight of scientific evidence supporting hazard thresholds.

B.1.1 Weight of Scientific Evidence

After calculating the hazard thresholds that were carried forward to characterize risk, a narrative describing the weight of scientific evidence and uncertainties was completed to support EPA's decisions. The weight of 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 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 using evidence for environmental hazard (Table_Apx B-2). 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 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.

Confidence Levels

- Robust (+ + +) confidence suggests thorough understanding of the scientific evidence and uncertainties. The supporting weight of 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 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.

B.1.2 Data Integration Considerations Applied to Aquatic and Terrestrial Hazard Representing the DEHP Environmental Hazard Database

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_Apx B-2):

- *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_Apx B-1 summarizes the weight of 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 B-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. • 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	• 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. • 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

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)
	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).	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.		

Table_Apx B-2. DEHP 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 assessment	+++	+++	+++	+	+++	Robust
Chronic aquatic assessment	+++	+	++	+	+++	Robust
Chronic sediment-dwelling assessment	++	++	++	+	+++	Moderate
Algal assessment	++	+++	++	+	+++	Robust
Terrestrial						
Chronic mammalian assessment	+++	+++	+++	+++	+++	Robust
Chronic avian assessment	++	++	++	++	+++	Moderate
Terrestrial invertebrate assessment	++	+++	++	+	+++	Robust
Terrestrial plant assessment	+++	+++	++	++	+++	Robust

[a] Relevance includes biological, physical/chemical, and environmental relevance

+++ Robust confidence suggests thorough understanding of the scientific evidence and uncertainties. The supporting weight of 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 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.

Appendix C SUPPLEMENTAL SUBMITTED DATA CONSIDERED FOR FINAL RISK EVALUATION

On July 10, 2024, EPA received supplemental information from DEHP Consortium member companies related to ecotoxicity data supporting the risk evaluation for DEHP. The Agency was unable to incorporate this data into the draft DEHP ecological hazard assessment due to its late submission in the draft risk evaluation development process but has considered these submissions in the development of the final risk evaluation for DEHP. Furthermore, EPA received supplemental environmental hazard information from public comments on the draft risk evaluation and supporting documents (Docket ID: EPA-HQ-OPPT-2018-0433) and considered these submissions in the development of the final risk evaluation for DEHP.

Supplemental environmental hazard information was evaluated for quantitative inclusion in the final risk evaluation by applying an updated PECO (Population, Exposure, Comparator, Outcome) criteria according to the *Risk Evaluation for Di-ethylhexyl Phthalate (DEHP) – Systematic Review Protocol* (U.S. EPA, 2025d). The updates to the PECO criteria specified that studies that included exposures potentially indicating adverse apical effects below the underlying exposure level (LOEC/LOEL, ChV, EC10, *etc.*) that underpinned the draft concentration of concern (COC) or hazard value (HV) for a taxonomic group would be considered for data extraction and quantitative inclusion in the final risk evaluation, because such studies had the potential to change the COC or HV. Studies that passed PECO screening, but did not have any exposures potentially indicating adverse apical effects below the underlying exposure levels for each COC/HV, were tagged as follows: "Supplemental, Updated literature search: Meets original PECO criteria but does not fill a critical data gap"

EPA identified three studies in this submission that passed PECO (Pu et al., 2020; Thomas et al., 2019; Truong et al., 2014); however, these studies were rated as uninformative when evaluated through systematic review. Although these studies were not considered for quantitative assessment, they were used to support the overall weight of evidence for ecological hazard.