EPA Document #EPA-740-R-25-028
December 2025
Office of Chemical Safety and
Pollution Prevention

United States
Environmental Protection Agency

Technical Support Document for the Cumulative Risk Analysis of Di(2-ethylhexyl) Phthalate (DEHP), Dibutyl Phthalate (DBP), Butyl Benzyl Phthalate (BBP), Diisobutyl Phthalate (DIBP), Dicyclohexyl Phthalate (DCHP), and Diisononyl Phthalate (DINP) Under the Toxic Substances Control Act (TSCA)

CASRNs: 17-81-7 (DEHP), 84-74-2 (DBP), 85-68-7 (BBP), 84-69-5 (DIBP), 84-61-7 (DCHP), 28553-12-0 (DINP), 68515-48-0 (DINP)

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KEY ABBREVIATIONS AND ACRONYMS

AIC	Akaike information criterion
AGD	Anogenital distance
BBP	Butyl benzyl phthalate
BMD	Benchmark dose
BMDL	Benchmark dose (lower confidence limit)
BMR	Benchmark response
CASRN	Chemical Abstracts Service registry number
CDR	Chemical Data Reporting
COU	Condition of use
CPSC	Consumer Product Safety Commission (U.S.)
CRA	Cumulative risk assessment
DBP	Dibutyl phthalate
DCHP	Dicyclohexyl phthalate
DEHP	Di(2-ethylhexyl) phthalate
DIBP	Diisobutyl phthalate
DIDP	Diisodecyl phthalate
DINP	Diisononyl phthalate
DMR	Discharge Monitoring Report
EPA	Environmental Protection Agency (U.S.)
GD	Gestation day
MNG	Multinucleated gonocyte
MOA	Mode of action
MOE	Margin of exposure
NASEM	National Academies of Sciences, Engineering, and Medicine
NEI	National Emissions Inventory
NR	Nipple/areolae retention
OCSPP	Office of Chemical Safety and Pollution Prevention
OES	Occupational exposure scenario
OEV	Occupational exposure value
OPPT	Office of Pollution Prevention and Toxics
POD	Point of departure
PESS	Potentially Exposed or Susceptible Subpopulations(s)
PV	Production volume
RPF	Relative potency factor
SACC	Science Advisory Committee on Chemicals
SD	Sprague-Dawley (rat)
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
UF	Uncertainty factor
U.S.	United States

ACKNOWLEDGEMENTS

The Assessment Team gratefully acknowledges the participation, input, and review comments from the U.S. Environmental Protection Agency (EPA or the Agency) Office of Pollution Prevention and Toxics (OPPT) and Office of Chemical Safety and Pollution Prevention (OCSPP) senior managers and science advisors, as well as intra-agency reviewers including the Office of Research and Development (ORD). The Agency is also grateful for assistance from EPA contractors ERG (Contract No. 68HERD20A0002 and GS-00F-079CA); ICF (Contract No. 68HERC23D0007); and SRC, Inc. (Contract No. 68HERH19D0022).

Docket
Supporting information can be found in the public dockets Docket IDs (EPA-HQ-OPPT-2018-0504, EPA-HQ-OPPT-2018-0434, EPA-HQ-OPPT-2018-0503, EPA-HQ-OPPT-2018-0433, and EPA-HQ-OPPT-2018-0501).

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SUMMARY

The U.S. Environmental Protection Agency (EPA) has developed this technical support document (TSD) for the cumulative risk assessment (CRA) of six toxicologically similar phthalates being evaluated under Section 6 of the Toxic Substances Control Act (TSCA): di(2-ethylhexyl) phthalate (DEHP), butyl benzyl phthalate (BBP), dibutyl phthalate (DBP), dicyclohexyl phthalate (DCHP), diisobutyl phthalate (DIBP), and diisononyl phthalate (DINP). EPA previously issued a *Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the Toxic Substances Control Act* (U.S. EPA, 2023b) which was subsequently peer-reviewed by the Science Advisory Committee on Chemicals (SACC) (U.S. EPA, 2023c). In the 2023 proposed approach, EPA identified a cumulative chemical group and potentially exposed or susceptible subpopulations (PESS) [15 U.S.C. § 2605(b)(4)].

As each chemical substance was prioritized or requested individually, EPA is required to evaluate the health and environmental risks of each individual phthalate and determine for each chemical substance whether it presents unreasonable risk or injury to health or the environment. Aspects of this TSD are used to inform EPA's individual phthalate risk determinations, pending completion of the individual phthalate risk evaluations. Specifically, this TSD provides the following for reference in the individual chemical substance risk evaluations and for consideration in any subsequent risk management:

- ***Common Hazard Assessment via Relative Potency Factors (RPFs):*** Section 2 calculates RPFs for phthalate syndrome based on the shared endpoint and pooled dataset for assessing fetal testicular testosterone health endpoint for each of the six chemical substances using DBP as an index chemical. For all the assessed phthalates, RPFs have been applied to convert exposures into equivalent units for summation across phthalates.
- ***Scenario-Based Phthalate Exposure:*** Section 3 frames the relevant frequency and duration of exposures and provides qualitative analysis of where co-exposures are expected with exposures assessed within the individual TSCA risk evaluations under specific conditions of use (COUs) for workers and consumers. Section 3 also provides a quantitative analysis of cumulative risk from indoor dust using monitoring data and a general update to the literature regarding non-TSCA exposures from diet.
- ***National Cumulative Exposure and Risk:*** Average aggregate exposures to the assessed phthalates for the U.S. population are presented in Section 4 using reverse dosimetry from urinary biomonitoring in the National Health and Nutrition Examination Survey (NHANES). This NHANES reverse dosimetry, combined with the RPFs, provides a common understanding of non-attributable exposures and risks to the U.S. population, including the susceptible subpopulations of women of reproductive age and male children, which can augment specific acute exposure scenarios described further in individual risk evaluations.
- ***Examples for Calculating Cumulative Risk:*** This TSD also elaborates two examples of cumulative risk calculations for combining exposures from individual chemical substance risk evaluations, from monitoring data, or in support of decision making using the RPFs (Section 5). Notably, an option is elaborated for considering a cumulative occupational exposure value (OEV) (Appendix E). The calculated value was provided for public comment and transparency and may be considered during risk management efforts for some or all of the six toxicologically similar phthalates under TSCA section 6(a), 15 U.S.C. §2605.

This TSD concludes with an overview of two approaches used by EPA demonstrating how the RPFs can supplement the hazard values for each individual phthalate and then be used in combination with the NHANES data for risk characterization within the individual phthalate risk evaluations (Section 5).

1 INTRODUCTION AND SCOPE

The U.S. Environmental Protection Agency (EPA or the Agency) is individually evaluating the health and environmental risks of several phthalates under section 6 of the Toxic Substances Control Act (TSCA) as separate chemical substances. Phthalates are a group of chemicals used in many industrial and consumer products, including building and construction materials, and polyvinyl chloride products, to make plastics more flexible and durable. Some phthalates are used in cosmetic, as well as food contact materials and have been measured in food. Studies investigating human exposure to phthalates have demonstrated widespread exposure to some phthalates and that humans may become co-exposed to multiple phthalates at the same time. Further, some phthalates have been shown to cause common adverse effects on the developing male reproductive system, sometimes referred to as "phthalate syndrome." TSCA requires EPA, in conducting risk evaluations pursuant to section 6 to consider the reasonably available information, consistent with the best available science, and make decisions based on the weight of scientific evidence [15 U.S.C. § 2625(h), (i), (k)]. EPA recognizes that for some chemical substances undergoing risk evaluation, the best available science may require analysis of cumulative risk to ensure that any risks to human health are adequately characterized in support of TSCA risk evaluations.

In 2023, EPA issued a *Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the Toxic Substances Control Act* (draft 2023 approach) which outlined an approach for cumulative risk assessment (CRA) of six toxicologically similar phthalates being evaluated under TSCA (U.S. EPA, 2023b). EPA's proposal was subsequently peer-reviewed by the Science Advisory Committee on Chemicals (SACC) in May 2023 (U.S. EPA, 2023c). In this approach, EPA identified a cumulative chemical group and potentially exposed or susceptible subpopulations (PESS) [15 U.S.C. § 2605(b)(4)]. Based on toxicological similarity and induced effects on the developing male reproductive system consistent with a disruption of androgen action and phthalate syndrome, EPA proposed a cumulative chemical group of di(2-ethylhexyl) phthalate (DEHP), butyl benzyl phthalate (BBP), dibutyl phthalate (DBP), dicyclohexyl phthalate (DCHP), diisobutyl phthalate (DIBP), and diisononyl phthalate (DINP), but not diisodecyl phthalate (DIDP). DIDP was not included in the cumulative chemical group because it does not induce effects consistent with phthalate syndrome. This approach emphasizes a uniform measure of hazard for sensitive subpopulations, namely women of reproductive age and/or male infants and children; however additional health endpoints are known for broader populations and described in the individual non-cancer human health hazard assessments for DEHP (U.S. EPA, 2025x), DBP (U.S. EPA, 2025v), DIBP (U.S. EPA, 2025y), BBP (U.S. EPA, 2025u), DCHP (U.S. EPA, 2025w), and DINP (U.S. EPA, 2025z), including hepatic, kidney, and other developmental and reproductive toxicity.

While additional groups and subpopulations may be susceptible to health effects from phthalate exposure, EPA identified groups with higher susceptibility to phthalate syndrome due to lifestage as (1) pregnant women/women of reproductive age, and (2) male infants, male toddlers, and male children.

Sections 1.1 through 1.7 further outline the scope of this CRA TSD.

This CRA TSD was released for public comment and peer-review by the SACC during the August 4–8, 2025 SACC meeting (U.S. EPA, 2025ag). Following SACC peer-review and public comment, this TSD was revised to incorporate recommendations from the SACC and public commenters. Readers are directed to EPA's response to public comments summary document and EPA's response to the 2025 phthalates SACC meeting report for further details.

1.1 Phthalate Syndrome Mode of Action

EPA has previously described the mode of action (MOA) for phthalate syndrome in the *Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the Toxic Substances Control Act* (draft 2023 approach) (U.S. EPA, 2023b), as well as in its non-cancer hazard assessments for DEHP (U.S. EPA, 2025x), DBP (U.S. EPA, 2025v), DIBP (U.S. EPA, 2025y), BBP (U.S. EPA, 2025u), DCHP (U.S. EPA, 2025w), and DINP (U.S. EPA, 2025z). A brief description of the MOA for phthalate syndrome is provided in this section. Readers are directed to EPA's draft 2023 approach and the non-cancer hazard assessments cited above for more detailed MOA information.

Although the MOA underlying phthalate syndrome has not been fully established, key cellular-, organ-, and organism-level effects are generally understood (Figure 1-1). Studies have demonstrated that gestational exposure to certain phthalate diesters, and their subsequent hydrolysis to monoester metabolites, which occur during a critical window of development (*i.e.*, the masculinization programming window) can lead to antiandrogenic effects on the developing male reproductive system (NRC, 2008). In rats, the masculinization programming window in which androgen action drives development of the male reproductive system occurs between days 15.5 to 18.5 of gestation, while the mouse critical window corresponds to gestational days 14 to 16, and the human masculinization programming window is between gestational weeks 8 to 14 (MacLeod et al., 2010; Welsh et al., 2008; Carruthers and Foster, 2005).

In vivo pharmacokinetic studies with rats have demonstrated that the monoester metabolites of DEHP, DBP, BBP, and DINP can cross the placenta and be delivered to the target tissue, the fetal testes (Clewell et al., 2013a; Clewell et al., 2010). *In utero* phthalate exposure can affect both Leydig and Sertoli cell function in the fetal testes. Histologic effects observed following phthalate exposure include Leydig cell aggregation and/or altered tissue distribution, as well as reductions in Leydig cell numbers. Functional effects on Leydig cells have also been reported. Leydig cells are responsible for producing hormones required for proper development of the male reproductive system, including insulin-like growth factor 3 (INSL3), testosterone, and dihydrotestosterone (DHT) (Scott et al., 2009). Phthalate exposure during the critical window reduces mRNA and/or protein levels of INSL3, as well as genes involved in steroidogenesis, sterol synthesis, and steroid and sterol transport (Figure 1-1) (Gray et al., 2021; Hannas et al., 2012). Decreased steroidogenic mRNA expression leads to decreased fetal testicular testosterone production, as well as reductions in DHT levels, which is produced from testosterone by 5α-reductase in the peripheral tissues. Because DHT is required for growth and differentiation of the perineum and for normal regression of nipple development in male rats, reduced DHT levels can lead to phenotypic changes (*i.e.*, nipple/areolae retention [NR] and reduced anogenital distance [AGD] in males) indicative of reduced Leydig cell function and androgen action.

Gestational exposure to certain phthalate diesters can also affect Sertoli cell function, development, and interactions with germ cells contributing to seminiferous tubule degeneration (Boekelheide et al., 2009). Immature Sertoli cells secrete Anti-Müllerian hormone and play an essential role in gonadal development (Lucas-Herald and Mitchell, 2022). Reported Sertoli cell effects include decreased cell numbers, changes in mRNA and/or protein levels of genes involved in Sertoli cell function, their development and altered Sertoli-germ cell interactions. Because proper Sertoli cell function is necessary for germ cell proliferation and development, altered Sertoli cell function can contribute to increased germ cell death, decreased germ cell numbers, and increased formation of multinucleated gonocytes (MNGs) (Arzuaga et al., 2019).

At the organ level, a disruption of androgen action can lead to reduced testes and accessory sex gland (*e.g.*, epididymis, seminal vesicle [SV], prostate, etc.) weight; agenesis of accessory organs; delayed preputial separation (PPS); testicular pathology (*e.g.*, interstitial cell hyperplasia); and severe reproductive tract malformations such as hypospadias. INSL3 is crucial for gubernacular cord development and the initial transabdominal descent of the testes to the inguinal region (Adham et al., 2000), while androgen action is required for the inguinoscrotal phase of testicular descent. Thus, reduced INSL3 and testosterone levels following gestational phthalate exposure can prevent gubernaculum development and testicular descent into the scrotum. Collectively, these effects can lead to reduced spermatogenesis, increased sperm abnormalities, and reduced fertility and reproductive function (Gray et al., 2021; Arzuaga et al., 2019; NASEM, 2017; Howdeshell et al., 2016; NRC, 2008).

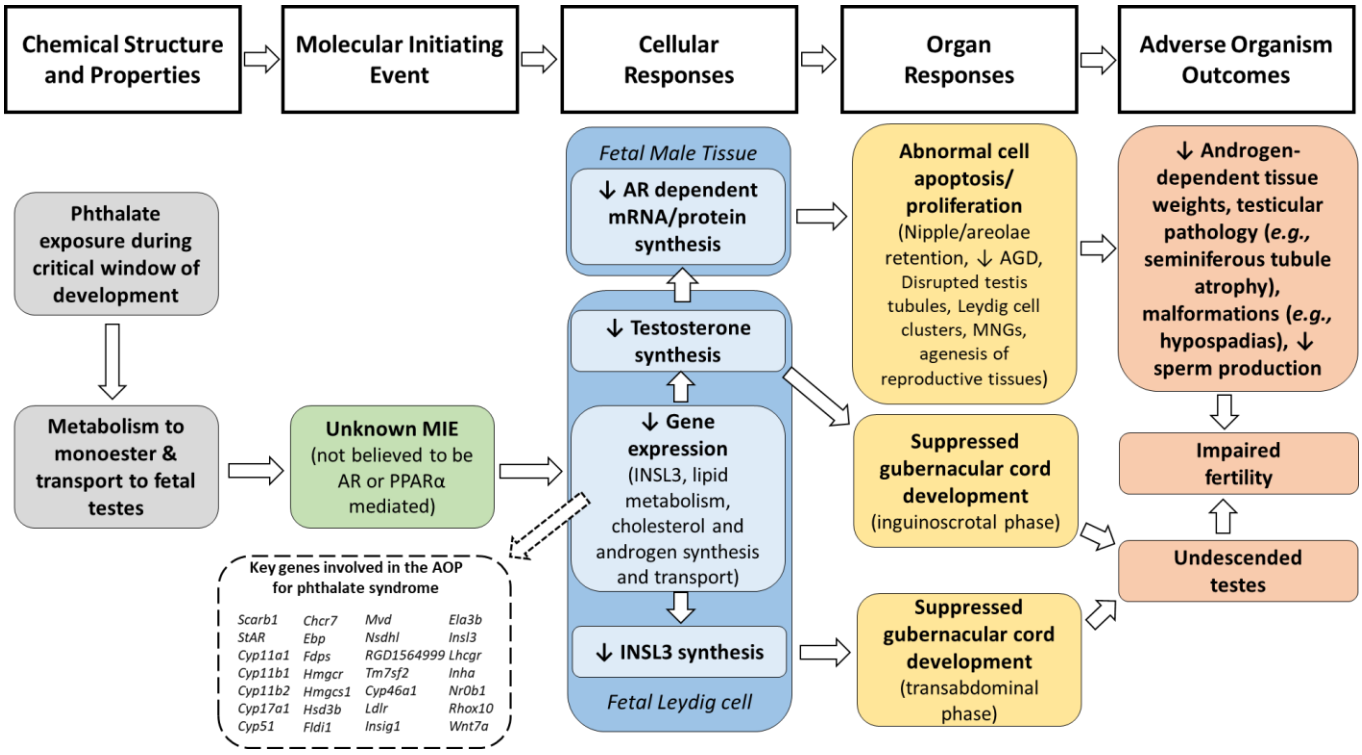


Figure 1-1. Phthalate Syndrome Mode of Action Following Gestational Exposure
Figure adapted from (Conley et al., 2021; Gray et al., 2021; Schwartz et al., 2021; Howdeshell et al., 2016). AR = androgen receptor; INSL3 = insulin-like growth factor 3; MNG = multinucleated gonocyte; PPARα = peroxisome proliferator-activated receptor alpha.

1.2 Phthalates Included in the Cumulative Chemical Group Based on Toxicologic Similarity

In the draft 2023 approach (U.S. EPA, 2023b), EPA evaluated the MOA for phthalate syndrome consistent with modified Bradford Hill criteria (*i.e.*, temporal and dose-response concordance; strength, consistency and specificity; biological plausibility) outlined in EPA and other international guidance documents (IPCS, 2007; U.S. EPA, 2005). Additional phthalates could be included based on this toxicological similarity but were not evaluated during this phase of risk evaluation under TSCA. For example, Health Canada (Health Canada, 2020) recently conducted a CRA of phthalates, which included the 6 high-priority and manufacturer-requested phthalates (DIBP, DCHP, DINP, BBP, DBP, DEHP) as

well as 10 phthalates not undergoing risk evaluation at EPA, including: butyl cyclohexyl phthalate (BCHP, CASRN 84-64-0), dibenzyl phthalate (DBzP, CASRN 523-31-9), cyclohexyl isobutyl phthalate (CHIBP, CASRN 5334-09-8), benzyl 3-isobutyryloxyl-1-isopropyl-2,2-dimethylpropyl phthalate (B84P, CASRN 16883-83-3), benzyl isooctyl phthalate (BIOP, CASRN 27215-22-1), bis(methylcyclohexyl)phthalate (DMCHP, CASRN 27987-25-3), benzyl octyl phthalate (B79P, CASRN 68515-40-2), diisoheptyl phthalate (DIHepP, CASRN 71888-89-6), diisooctyl phthalate (DIOP, CASRN 27554-26-3), and dihexyl ester phthalate (DnHP, CASRN 84-75-3).

Overall, EPA concluded that DEHP, BBP, DBP, DCHP, DIBP, and DINP, but not DIDP, are toxicologically similar and can induce effects on the developing male reproductive system consistent with a disruption of androgen action and phthalate syndrome. Overall, this conclusion was supported by the SACC in its the final peer-review report to EPA (U.S. EPA, 2023c). Briefly, SACC stated:

> "The committee concluded that there is an extensive database of animal studies to support EPA's preliminary conclusions that di(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), diisobutyl phthalate (DIBP), dicyclohexyl phthalate (DCHP), butyl benzyl phthalate (BBP), and diisononyl phthalate (DINP) are toxicologically similar, while diisodecyl phthalate (DIDP) is not. Epidemiological studies were considered by most of the committee to be generally consistent with the animal data. In addition, a majority of the committee concluded that, while there are some inconsistencies in the data, there is sufficient evidence that DINP is toxicologically similar to the other active phthalates but is less potent. Based upon their toxicological similarity, the committee noted the grouping of the chemicals is supported by available evidence."

Therefore, EPA is including DEHP, BBP, DBP, DCHP, DIBP, and DINP in its CRA. DIDP was not included in the cumulative chemical group because it does not induce effects on the developing male reproductive system consistent with phthalate syndrome.

During the 2023 peer-review of the CRA proposed approach, SACC also recommended that EPA consider adding a second endpoint in addition to phthalate syndrome for demonstrating toxicological similarity and conducting CRA (U.S. EPA, 2023c). Specifically, SACC recommended including liver toxicity, developmental neurotoxicity, or female reproductive effects. While EPA acknowledges that there are varying amount of data demonstrating that certain phthalates can cause these effects, EPA did not consider these effects as the basis for a CRA for several reasons. First, although DEHP, BBP, DBP, DCHP, DIBP, DINP, and DIDP have all been shown to cause liver toxicity, most of the observed liver effects in experimental animal models are mechanistically linked to peroxisome proliferator-activated receptor alpha (PPARα) activation, which can vary between species raising questions about human relevance. Additionally, the non-cancer POD based on phthalate syndrome-related effects is a more sensitive outcome than liver toxicity for most phthalates (with DINP and DIDP being exceptions). Further, there are limited data demonstrating female reproductive effects or developmental neurotoxicity for DCHP and DIBP, while data for other phthalates varies in quality and quantity such that definitive conclusions about exposure-response relationships cannot be established. *Therefore, EPA did not consider liver toxicity, developmental neurotoxicity, or female reproductive effects further as the basis for a CRA.* However, these effects are discussed further, as relevant, in the cancer human health hazard assessment of phthalates (U.S. EPA, 2025a) and each individual non-cancer human health hazard assessments for DEHP (U.S. EPA, 2025x), DBP (U.S. EPA, 2025v), DIBP (U.S. EPA, 2025y), BBP (U.S. EPA, 2025u), DCHP (U.S. EPA, 2025w), DINP (U.S. EPA, 2025z), and DIDP (U.S. EPA, 2024d).

1.3 Endpoints and Options Considered for Relative Potency Factor Derivation

To conduct its cumulative risk assessment of phthalates, EPA is using a relative potency factor (RPF) approach. In the draft 2023 approach (U.S. EPA, 2023b), EPA outlined six potential options for deriving RPFs that considered use of data from two gestational outcomes (*i.e.*, altered expression of steroidogenic genes in the fetal testis and decreased fetal rat testicular testosterone) and four postnatal outcomes (*i.e.*, reduced anogenital distance (AGD), increased nipple retention, seminiferous tubule atrophy, and hypospadias). Options 1 through 4 involve benchmark dose (BMD) modeling of fetal outcomes associated with the MOA underlying phthalate syndrome (*i.e.*, reduced fetal testicular testosterone content and/or reduced testicular steroidogenic gene expression), and involve BMD modeling of data from individual studies (Options 1 and 3) or combining data from studies of similar design prior to BMD modeling (Options 2 and 4). Similarly, Options 5 and 6 involve BMD modeling of postnatal outcomes (*i.e.*, reduced AGD, increased nipple/areolae retention, seminiferous tubule atrophy, hypospadias), and involve BMD modeling of data from individual studies (Option 5) or combining data from studies of similar design prior to BMD modeling (Option 6). Section 4.4 of the draft 2023 approach (U.S. EPA, 2023b) provides further details regarding the six options considered by EPA for deriving RPFs.

In its final peer-review report to EPA (U.S. EPA, 2023c), SACC did not endorse any single option to derive RPFs, but instead concluded:

> "In terms of options to calculate RPFs, the committee was in consensus that it prefers any approach which uses as much of the data as possible assuming the dose-response aspects are considered in the process for selecting endpoints. Option 2 and 4 that incorporate dose-response data are preferable to not using some of the data. Option 6 is similar except it uses postnatal outcomes instead of fetal ones. In an attempt to use the greatest amount of data, the committee suggests a combination of prenatal and postnatal outcomes would provide the best of both approaches."

Strengths, limitations, and uncertainties of the available datasets for each of the six key outcomes considered for RPF derivation are discussed in detail in Section 4.4 of the draft 2023 approach (U.S. EPA, 2023b) and discussed briefly below.

Overall, EPA noted several factors that increased its confidence in using the fetal testicular testosterone dataset to derive RPFs, including:

- Reduced testosterone production in the fetal testis plays an early role in the phthalate syndrome MOA.
- Androgen action has a conserved role in the development of the male reproductive system across mammalian species, including humans.
- There are dose-response data available for all six of the toxicologically similar phthalates from multiple studies that are similar in design to support RPF derivation (*i.e.*, utilize the same species/strain of rat, same route/method of exposure, similar exposure durations, similar timing and method (*i.e.*, *ex vivo* testosterone production via radioimmunoassay or fetal testicular testosterone content) of measurement.
- During the 2023 peer-review meeting, SACC supported fetal testosterone production as an outcome for phthalate syndrome (U.S. EPA, 2023c). Briefly, SACC stated "[t]he committee

endorsed fetal testosterone production due to the availability of dose-response data on selected phthalate esters in the same species and strain via the same route of administration and during the same window of vulnerability. The committee noted that transient reductions in the rate of testosterone synthesis at the critical period of development do have permanent effects (e.g., structural, functional) on male reproductive organs (Hannas et al. 2011; Gray et al. 2016). Therefore, the rate of testosterone production, rather than plasma or testicular levels, may be a more relevant predictor of downstream effects."

In contrast, EPA noted several factors that decreased its confidence in using postnatal outcomes to derive RPFs, including:

- ***Anogenital distance (AGD):*** AGD is the measured distance between the anus to the base of the penis, and decreased AGD is considered a biomarker of a disruption of androgen action and male reproductive health. There is variability in how studies report decreased male AGD. Changes in AGD are sometimes but not always normalized to body weight. Per OECD guidance (OECD, 2013), AGD should be normalized to body weight (preferably the cubic root of body weight) since animal size can influence AGD. Further, in the case of DIBP only one dose-response study is available, and this study only reports absolute AGD. Another source of uncertainty stems from the DINP dataset. In contrast to DEHP, BBP, DBP, DCHP, and DIBP where consistent effects on AGD are reported, statistically significant effects on AGD are less consistently reported for DINP across studies that test comparable doses (*i.e.,* DINP reduced AGD in two of six studies). Variability in AGD reporting, limited data for DIBP, and inconsistency in the DINP dataset reduces EPA's confidence in deriving RPFs based on this postnatal outcome. Although SACC noted that there are some limitations of phthalate studies of AGD (*e.g.,* some studies do not report AGD normalized to body weight), SACC ultimately concluded that AGD is a "robust outcome" and supported reduced rat AGD as an outcome for phthalate syndrome (U.S. EPA, 2023c).
- ***Nipple/Areolae Retention:*** Across available studies, there is variability in how nipple/areolae retention is reported. For example, sometimes this outcome is reported as mean number of nipples/areolas per male, incidence of males with nipples, or mean percent of litters including males with nipples. Variability in data reporting makes comparisons across studies difficult. Additionally, although male pup nipple/areolae retention is a biomarker of disrupted androgen action in rodents, it is not directly a human relevant effect. This uncertainty reduces EPA's confidence in deriving RPFs based on nipple/areolae retention in male pups. During the 2023 peer-review meeting, SACC did not support use of nipple/areolae retention as an outcome for phthalate syndrome, however, SACC did not provide a reason for this (U.S. EPA, 2023c).
- ***Seminiferous Tubule Atrophy:*** Seminiferous tubule atrophy, associated with infertility, testicular atrophy, and pain, has been reported consistently for DEHP, DBP, DIBP, BBP, and DCHP; however, available studies reporting seminiferous tubule atrophy are of varying design and durations. For example, seminiferous tubule atrophy has been reported in two-generation studies of DCHP and BBP, while for DIBP seminiferous tubule atrophy has only been reported in one study in which rats were exposed throughout gestation. Additionally, effects on seminiferous tubular atrophy are less consistently reported in studies of DINP that test comparable doses. Differences in study design and exposure duration across available studies and inconsistency in the DINP dataset reduces EPA's confidence in deriving RPFs based on this outcome. During the 2023 peer-review meeting, SACC did not comment on whether or not it supports seminiferous tubule atrophy as an outcome for phthalate syndrome (U.S. EPA, 2023c).

- ***Hypospadias:*** Hypospadias, birth defects of abnormal urethral opening on the penis, have been reported consistently in studies of DEHP, DBP, DIBP, BBP, and DCHP; however, significant increases in hypospadias have not been reported in studies of DINP. Further, available studies reporting hypospadias are of varying design and duration. For example, hypospadiases have been reported in a single study of BBP (a two-generation reproductive study) and a single study of DIBP (a gestational exposure study). Differences in study design and exposure duration and inconsistency in the DINP dataset reduces EPA's confidence in deriving RPFs based on this outcome. Further, SACC recommended against including hypospadias as an outcome because "a threshold of exposure must be reached prior to the outcome being manifested. It would be very challenging to model this outcome in the lower dose range" (U.S. EPA, 2023c).

Given the strengths, limitations, and uncertainties of each key outcome discussed above and in Section 4.4. of (U.S. EPA, 2023b), *EPA has selected reduced fetal testicular testosterone as the basis for deriving RPFs*.

EPA considered deriving candidate RPFs using the one postnatal outcome supported by SACC (*i.e.*, reduced AGD). However, given the limitations and uncertainties discussed above, EPA considered there to be too much uncertainty associated with the dataset to derive candidate RPFs for all six of the phthalates included in the CRA. Further, reduced rat AGD is a less sensitive outcome than reduced rat fetal testicular testosterone. This is demonstrated by the 2017 NASEM meta-analysis and BMD analysis of reduced fetal rat testicular testosterone and reduced rat AGD for DEHP, DBP, and BBP, which provides BMD_5 estimates of 15 (reduced fetal testis testosterone) and 270 (reduced AGD) mg/kg-day for DEHP; 12 (reduced fetal testis testosterone) and 150 (reduced AGD) mg/kg-day for DBP; 23 (reduced fetal testis testosterone) and 250 (reduced AGD) mg/kg-day for BBP (NASEM, 2017). Further, NASEM judged the animal database for AGD to not be amenable to meta-analysis for DIBP and DINP. EPA did not identify any new information that would change the conclusions drawn from the NASEM meta-analysis.

Consistent with the SACC's recommendation that it prefers any option for deriving RPFs that makes use of as much of the available data as possible (U.S. EPA, 2023c), *EPA selected Option 2 for deriving RPFs. This option involves combining fetal testicular testosterone data from studies of similar design prior to conducting BMD modeling*. EPA's BMD modeling approach of fetal testicular testosterone data to derive RPFs is discussed further in Section 2.

1.4 Relevant Populations

Gestational exposure to DEHP, BBP, DBP, DIBP, DCHP and DINP can disrupt testicular steroidogenesis and cause adverse effects on the developing male reproductive system consistent with phthalate syndrome. Postnatal phthalate exposure can also cause male reproductive toxicity; however, the perinatal and peripubertal lifestages are believed to be the most sensitive to phthalate exposure (NRC, 2008). In the draft 2023 approach (U.S. EPA, 2023b), EPA proposed to focus its CRA for phthalates on two groups that may be more susceptible to phthalate syndrome due to lifestage:

- pregnant women/women of reproductive age, and
- male infants, male toddlers, and male children.

While additional populations may experience health effects, these populations are considered the most susceptible for phthalate syndrome. Overall, SACC agreed with EPA that these lifestages "should certainly be considered susceptible populations given the abundant data from hazard assessment studies,"(U.S. EPA, 2023c). *EPA is focusing its CRA on pregnant women/women of reproductive age, and male infants, male toddlers, and male children*.

1.5 Relevant Durations

As described in the non-cancer human health hazard assessment for DINP (U.S. EPA, 2025z), DEHP (U.S. EPA, 2025x), DBP (U.S. EPA, 2025v), BBP (U.S. EPA, 2025u), DIBP (U.S. EPA, 2025y), and DCHP (U.S. EPA, 2025w), there is evidence that effects on the developing male reproductive system consistent with a disruption of androgen action can result from a single exposure during the critical window of development (*i.e.*, gestation day (GD) 14 to 18). Therefore, EPA considers effects on fetal testicular testosterone relevant as an acute effect associated with higher, acute exposures. Notably, SACC agreed with EPA's decision to consider effects on the developing male reproductive system consistent with a disruption of androgen action to be relevant for setting a point of departure (POD) for acute durations during the July 2024 peer-review meeting of the DINP human health hazard assessment (U.S. EPA, 2024e) and during the August 2025 phthalate peer-review meeting (U.S. EPA, 2025ag). In addition, phthalates have relatively rapid elimination kinetics with half-lives on the order of several hours before being quickly excreted from the body (ATSDR, 2022; EC/HC, 2015). Thus, unlike chemical substances with more bioaccumulative potential, historical exposures are not as relevant as concurrent or recent exposures particularly in relation to critical windows of development. Taken together, *EPA is focusing the application of its phthalate CRA on acute exposure durations* which are expected to represent the highest relevant exposures for the common health effect for susceptible populations. Notably, protecting for acute exposure durations will be protective of longer duration exposures, since acute exposures are higher than longer duration exposures.

1.6 Exposure Evaluations

In the draft 2023 approach (U.S. EPA, 2023b), EPA proposed both a reverse-dosimetry method for estimating cumulative non-attributable phthalate exposure from NHANES urinary biomonitoring and the development of scenarios for combining exposures from multiple sources in conjunction with the individual phthalate risk evaluations (U.S. EPA, 2023b). The proposed scenario-based approach included estimating and combining reasonable combinations of exposure attributable to TSCA COUs, to non-TSCA sources (*e.g.*, diet, food packaging cosmetics, etc.), and any other non-attributable exposures to determine cumulative risk.

Overall, the SACC supported the use of reverse dosimetry for estimating exposure using biomonitoring, over the use of modeling, where monitoring represents exposed sub-populations. However, the SACC noted that highly exposed subpopulations, including workers with occupational exposures, would not likely be represented by a national survey. Nonetheless, NHANES data do provide total exposure, including non-attributable and non-TSCA exposures, which could be aggregated with any scenario-specific estimates.

Exposures and risks for each individual phthalate under its conditions of use (COUs) continue to be evaluated in individual risk evaluations in accordance with TSCA.[1] EPA assesses exposure for consumers, workers, and general population exposed to environmental releases for each individual phthalate. Within these exposed populations, there are PESS with increased susceptibility to the developmental and reproductive effects associated with phthalate syndrome, including pregnant women/women of reproductive age, male infants, male toddlers, and male children. The 2023 proposal laid out a multi-step approach and conceptual model which suggested the results of the individual phthalate risk evaluations could be combined into a single cumulative risk assessment.

[1] Conditions of use (COUs) are defined as "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." (15 U.S.C. 2602(4))

These individual assessments represent a mix of deterministic and probabilistic methods as well as differing tiers of analyses (*i.e.* screening through more refined approaches). In its review, the SACC specifically expressed "concern" about mixing these estimates in an approach that combines estimates from these individual assessments and stated "EPA should conduct deterministic OR (fully) probabilistic analyses and avoid blending of these techniques" (U.S. EPA, 2023c). In addition, credible exposure scenario-based approaches would need to be informed by site specific data and "laborious" to construct (if even possible) with reasonably available data.

Therefore, *EPA is using NHANES data to supplement, not substitute, evaluations for exposure scenarios for TSCA COUs to provide non-attributable, total exposure for addition to the relevant scenarios presented in the individual risk evaluations*. Section 5 provides this quantitative approach to be tabulated in each individual relevant risk evaluation for evaluating cumulative risk resulting from aggregate exposure to a single phthalate from an exposure scenario or COU plus non-attributable cumulative risk from NHANES.

Finally, the SACC recommended more discussion and analyses related to exposure, specifically related to emphasis on the importance of indoor dust exposures, updates to estimates of phthalates in diet given the highly diverse U.S. population, and specific emphasis on potential risk to arctic communities from exposures to environmental releases (U.S. EPA, 2023c). The SACC also recommended that EPA provide the physical-chemical and fate parameters for consideration across the group. These recommendations are addressed in Section 3 in a qualitative or semi-quantitative manner.

1.7 Risk Cup Concept in Cumulative Risk Assessment

The analogy of a "risk cup" is used throughout this document to describe cumulative exposure estimates. The "risk cup" term is used to help conceptualize the contribution of various phthalate exposure routes and pathways to overall cumulative risk estimates and serves primarily as a communication tool. The "risk cup" concept describes exposure estimates where the full cup represents the total exposure that leads to risk (cumulative margin of exposure (MOE)) and each chemical substance contributes a specific amount of exposure that adds a finite amount of risk to the cup.

To estimate non-cancer cumulative risks from exposure to phthalates, EPA is using a cumulative MOE approach. As discussed further in Section 5.1, the cumulative MOE is a ratio of the index chemical POD to the cumulative exposure estimate expressed in index chemical equivalent units. The MOE is then compared to the benchmark MOE (*i.e.,* the total uncertainty factor associated with the assessment) to characterize risk. The MOE estimate is interpreted as a human health risk of concern if the MOE estimate is less than the benchmark MOE (*i.e.,* the total UF). On the other hand, if the MOE estimate is equal to or exceeds the benchmark MOE, the risk is not considered to be of concern and mitigation is not needed. Typically, the larger the MOE, the more unlikely it is that a non-cancer adverse effect occurs relative to the benchmark. When determining whether a chemical substance presents unreasonable risk to human health or the environment, calculated risk estimates are not "bright-line" indicators of unreasonable risk, and EPA has the discretion to consider other risk-related factors in addition to risks identified in the risk characterization.

A full risk cup indicates that the cumulative MOE has dropped below the benchmark MOE of 30, whereas cumulative MOEs above the benchmark indicate that only a percentage of the risk cup is full. For example, a cumulative MOE of 120 would indicate that the risk cup is 25 percent full, since the benchmark MOE is 30 (empirical examples of the risk cup approach are provided in Section 5).

2 RELATIVE POTENCY FACTORS

This section describes the approach used by EPA to derive relative potency factors (RPFs) for the six phthalates (*i.e.*, DEHP, DBP, BBP, DIBP, DCHP, DINP) that EPA is including in its CRA. These RPFs are used to scale each phthalate exposure by potency and to calculate risk in common units of index chemical (DBP) equivalents for cumulative assessment.

The remainder of this hazard chapter is organized as follows:

- Section 2.1 – Describes the general principles of the RPF approach.
- Section 2.2 – Describes the benchmark dose (BMD) modeling approach used by EPA for deriving RPFs.
- Section 2.3 – Describes selection of the index chemical used as a point of reference to standardize the potency of each phthalate.
- Section 2.4 – Describes the RPFs derived by EPA for each phthalate included in the CRA.
- Section 2.5 – Describes the uncertainty factors selected by EPA for use as the cumulative benchmark margin of exposure (benchmark MOE).
- Section 2.6 – Describes the applicability of the RPFs.
- Section 2.7 – Describes EPA's weight of scientific evidence conclusions.

2.1 Relative Potency Factor Approach

As described in the draft 2023 approach (U.S. EPA, 2023b), EPA proposed to use a RPF approach to characterize risk from cumulative exposure to phthalates under TSCA. Overall, SACC was "generally supportive of the approach," but noted several uncertainties (*e.g.*, issues with dose-response curves having differing slopes and shapes depending on the outcome being evaluated) (U.S. EPA, 2023c), which are addressed by EPA in Section 2.4. Consistent with its initial proposal (U.S. EPA, 2023b), *EPA is using a RPF approach for its CRA of phthalates under TSCA.*

For the RPF approach, chemical substances being evaluated require data that support toxicologic similarity (*e.g.*, components of a mixture share a known or suspected common mode of action or share a common apical endpoint/effect) and have dose-response data for the effect of concern over similar exposure ranges (U.S. EPA, 2023a, 2000, 1986). RPF values account for potency differences among chemicals in a mixture and scale the dose of one chemical to an equitoxic dose of another chemical (*i.e.*, the index chemical). The chemical selected as the index chemical is often among the best characterized toxicologically and considered to be representative of the type of toxicity elicited by other components of the mixture. Implementing an RPF approach requires a quantitative dose-response assessment for the index chemical and pertinent data that allow the potency of the mixture components to be meaningfully compared to that of the index chemical. In the RPF approach, RPFs are calculated as the ratio of the potency of the individual component to that of the index chemical using either (1) the response at a fixed dose; or (2) the dose at a fixed response (Equation 2-1).

Equation 2-1. Calculating RPFs

$$RPF_i = \frac{BMD_{R-IC}}{BMD_{R-i}}$$

Where:

- *BMD* = benchmark dose (mg/kg/day)

- R = magnitude of response (*i.e.*, benchmark response)
- i = i^{th} chemical
- IC = index chemical

After scaling the chemical component doses to the potency of the index chemical, the scaled doses are summed and expressed as index chemical equivalents for the mixture (Equation 2-2).

Equation 2-2. Calculating index chemical equivalents

$$Index\ Chemical\ Equivalents_{MIX} = \sum_{i=1}^{n} d_i \times RPF_i$$

Where:

- Index chemical equivalents = dose of the mixture in index chemical equivalents (mg/kg-day)
- d_i = dose of the i^{th} chemical in the mixture (mg/kg-day)
- RPF_i = relative potency factor of the i^{th} chemical in the mixture (unitless)

Non-cancer risk associated with exposure to the mixture can then be assessed by calculating a MOE, which in this case is the ratio of the index chemical's non-cancer benchmark dose lower confidence limit (BMDL) to an estimate of mixture exposure expressed in terms of index chemical equivalents. The MOE is then compared to the benchmark MOE (*i.e.*, the total uncertainty factor associated with the assessment) to characterize risk.

2.2 Benchmark Dose Modeling of Fetal Testicular Testosterone to Determine Toxic Potency

In 2017, the National Academies of Sciences, Engineering, and Medicine (NASEM) demonstrated the utility of a meta-analysis and meta-regression approach to combine fetal rat testicular testosterone data from multiple studies of similar design prior to conducting BMD modeling (NASEM, 2017). Meta-analysis is a statistical procedure that can be used to summarize outcomes from several studies and can be used to explore sources of heterogeneity in the data through use of random effects models. Therefore, meta-analysis can help overcome limitations associated with results from individual studies and provide a more robust dataset across the chemicals for modeling dose-response of a common endpoint.

To derive RPFs for DEHP, DBP, BBP, DIBP, DCHP, and DINP based on reduced fetal testicular testosterone, EPA used the same meta-analysis and BMD modeling approach used by NASEM (2017), with several notable updates. First, EPA identified new fetal testicular testosterone data that were not included in the 2017 NASEM analysis. These new data were included in EPA's updated meta-analysis and BMD analysis. Table 2-1 provides a summary of studies included in the updated analysis. EPA's updated analysis also utilized the most up-to-date version of the Metafor meta-analysis package for R (https://wviechtb.github.io/metafor/index.html; accessed December 17, 2025) available at the time of the updated analysis (*i.e.*, Version 4.6.0). However, EPA also conducted the updated analysis using the same version of Metafor originally used by NASEM (2017) (*i.e.*, Version 2.0.0) so that results could be compared. As part of its updated analysis, EPA also evaluated benchmark responses (BMRs) of 5, 10, and 40 percent based on biological and statistical considerations (comparatively, NASEM evaluated BMRs of 5 and 40%).

Results of EPA's updated meta-analysis and BMD analysis are provided in Section 2.2.1. Readers are directed to EPA's *Meta-Analysis and Benchmark Dose Modeling of Fetal Testicular Testosterone for Di(2-ethylhexyl) Phthalate (DEHP), Dibutyl Phthalate (DBP), Butyl Benzyl Phthalate (BBP), Diisobutyl Phthalate (DIBP), and Dicyclohexyl Phthalate (DCHP)* (U.S. EPA, 2025t) and *Non-Cancer Human*

Health Hazard Assessment for Diisononyl Phthalate (DINP) (U.S. EPA, 2025z) for a more thorough discussion of the methodology and results of EPA's updated analysis.

Table 2-1. Summary of Studies Included in EPA's Updated Meta-Analysis and BMD Modeling Analysis

Reference	Study Details					Phthalate					
	Strain/ Species	**Exposure Route (Method)**	**Exposure Window**	**Measured Outcome (Timing of Measure)**	**TSCA Study Quality Rating**	**DEHP**	**DBP**	**DIBP**	**BBP**	**DCHP**	**DINP**
(Martino-Andrade et al., 2008)	Wistar rat	Oral (gavage)	GD 13-21	Fetal testis testosterone content (GD 21)	Medium confidence	X[a]	X[a]				
(Furr et al., 2014)	SD rat	Oral (gavage)	GD 14-18	*Ex vivo* fetal testicular testosterone production (3-hour incubation) (GD 18)	High confidence	X[a]	X[a]		X[a]	X[b]	X[b]
(Howdeshell et al., 2008)	SD rat	Oral (gavage)	GD 8-18	*Ex vivo* fetal testicular testosterone production (2-hour incubation) (GD 18)	High confidence	X[a]	X[a]	X[a]	X[a]		
(Gray et al., 2021)	SD rat	Oral (gavage)	GD 14-18	*Ex vivo* fetal testicular testosterone production (3-hour incubation) (GD 18)	High (DEHP, DBP, BBP, DCHP) or Medium (DIBP) confidence	X[b]	X[b]	X[b]	X[b]	X[b]	
(Hannas et al., 2011)	SD rat	Oral (gavage)	GD 14-18	*Ex vivo* fetal testicular testosterone production (3-hour incubation) (GD 18)	Medium confidence	X[a]		X[a]			X[a]
	Wistar rat	Oral (gavage)	GD 14-18	*Ex vivo* fetal testicular testosterone production (3-hour incubation) (GD 18)	Medium confidence	X[a]					
(Kuhl et al., 2007)	SD rat	Oral (gavage)	GD 18	Fetal testis testosterone content (GD 19)	Low confidence		X[a]				
(Struve et al., 2009)	SD rat	Oral (gavage)	GD 12-19	Fetal testis testosterone content (GD 19; 4 or 24 hours post-exposure)	Medium confidence		X[a]				
(Johnson et al., 2011)	SD rat	Oral (gavage)	GD 12-20	Fetal testis testosterone content (GD 20)	Medium confidence		X[a]				

Reference	Study Details					Phthalate					
	Strain/ Species	**Exposure Route (Method)**	**Exposure Window**	**Measured Outcome (Timing of Measure)**	**TSCA Study Quality Rating**	**DEHP**	**DBP**	**DIBP**	**BBP**	**DCHP**	**DINP**
(Johnson et al., 2007)	SD rat	Oral (gavage)	GD 19	Fetal testis testosterone content (GD 19)	Medium confidence		X[a]				
(Lin et al., 2008)	Long-Evans rat	Oral (gavage)	GD 2-20	Fetal testis testosterone content (GD 21)	Medium confidence	X[a]					
(Culty et al., 2008)	SD rat	Oral (gavage)	GD 14-20	*Ex vivo* fetal testicular testosterone production (24-hour incubation) (GD 21)	Medium confidence	X[a]					
(Saillenfait et al., 2013)	SD rat	Oral (gavage)	GD 12-19	*Ex vivo* fetal testicular testosterone production (3-hour incubation) (GD 19)	High confidence	X[a]					
(Boberg et al., 2011)	Wistar rat	Oral (gavage)	GD 7-21	*Ex vivo* fetal testicular testosterone production (GD 21) & fetal testis testosterone content (GD 21)	Medium confidence						X[a]
(Gray Jr et al., 2024)	SD rat	Oral (gavage)	GD 14-18	*Ex vivo* fetal testicular testosterone production (3-hour incubation) (GD 18)	Medium confidence						X[b]

[a] Data included in NASEM (2017) analysis.
[b] Cells highlighted in gray indicate data not included in the 2017 NASEM analysis. However, these data were included in EPA's updated analysis.

2.2.1 Results: Benchmark Dose Estimation Using Metafor

Table 2-2 summarizes BMD modeling results of fetal testicular testosterone for DEHP, DBP, DIBP, BBP, DCHP, and DINP from EPA's updated meta-analysis using Metafor Version 4.6.0. Readers are directed to EPA's *Meta-Analysis and Benchmark Dose Modeling of Fetal Testicular Testosterone for Di(2-ethylhexyl) Phthalate (DEHP), Dibutyl Phthalate (DBP), Butyl Benzyl Phthalate (BBP), Diisobutyl Phthalate (DIBP), and Dicyclohexyl Phthalate (DCHP)* (U.S. EPA, 2025t) and *Non-Cancer Human Health Hazard Assessment for Diisononyl Phthalate (DINP)* (U.S. EPA, 2025z) for more detailed reporting and discussion of results.

Table 2-2. BMD Modeling Results of Fetal Testicular Testosterone for DEHP, DBP, DIBP, BBP, DCHP, and DINP using Metafor Version 4.6.0

Phthalate	Model Providing Best Fit [a]	BMD_5 Estimates (mg/kg-day) [95% Confidence Interval]	BMD_{10} Estimates (mg/kg-day) [95% Confidence Interval]	BMD_{40} Estimates (mg/kg-day) [95% Confidence Interval]
DBP	Linear Quadratic	14 [9, 27]	29 [20, 54]	149 [101, 247]
DEHP	Linear Quadratic	17 [11, 31]	35 [24, 63]	178 [122, 284]
DIBP	Linear Quadratic	–[b]	55 [NA, 266][b]	270 [136, 517]
BBP	Linear Quadratic	–[b]	–[b]	284 [150, 481]
DCHP	Linear Quadratic	8.4 [6.0, 14]	17 [12, 29]	90 [63, 151]
DINP	Linear Quadratic	74 [47, 158]	152 [97, 278]	699 [539, 858]

[a] Based on lowest Akaike information criterion (AIC) and visual inspection.
[b] BMD and/or BMDL estimate could not be derived.

2.3 Selection of the Index Chemical and the Index Chemical Point of Departure

As described in EPA mixture and cumulative risk assessment guidance documents (2023a, 2016, 2002a, 2000, 1986), for the RPF approach to be applied one chemical must be selected as the index chemical. The index chemical is used as the point of reference for standardizing the common toxicity of the other chemicals being evaluated as part of the cumulative chemical group. Once the index chemical is selected, RPFs are calculated (*i.e.*, the ratio of the toxic potency of one chemical to that of the index chemical). RPFs are used to convert exposures of all chemicals in the cumulative chemical group into exposure equivalents of the index chemical. Given that the RPF method portrays risk as exposure in terms of index chemical equivalents, it is preferred that the index chemical: 1) have the highest quality toxicological database of chemicals in the cumulative chemical group; 2) have high quality dose-response data; 3) be considered the most representative of the type of toxicity caused by other chemicals in the cumulative chemical group; and 4) be well characterized for the proposed mode of action (2023a, 2016, 2002a, 2000, 1986).

Table 2-3 provides a high-level comparison of the number of studies available for each phthalate that examined each outcome considered for RPF derivation. Of the six phthalates included in the cumulative chemical group (*i.e.*, DEHP, DBP, BBP, DIBP, DCHP, and DINP), *EPA considered DEHP and DBP as*

candidates for the index chemical because both phthalates have high quality toxicological databases demonstrating effects on the developing male reproductive system consistent with a disruption of androgen action and phthalate syndrome, demonstrate toxicity representative of all phthalates in the cumulative chemical group, and are well characterized for the MOA associated with phthalate syndrome. Compared to DEHP and DBP, other phthalates included in the cumulative chemical group (*i.e.*, BBP, DIBP, DCHP, DINP) have considerably smaller databases and fewer dose-response data (Table 2-3), and were not considered candidates for the index chemical.

Table 2-3. Comparison of the Number of Studies Supporting Key Outcomes Associated with Phthalate Syndrome[a]

Key Outcome	# of Studies Per Phthalate by Species					
	DEHP	**DBP**	**BBP**	**DIBP**	**DCHP**	**DINP**
↓ Steroidogenic gene and *Insl3* expression in fetal testis	7 (all rat)	9 (rat [8]; mouse [1])	2 (all rat)	6 (rat [5]; mouse [1])	2 (all rat)	5 (all rat)
↓ Fetal testicular testosterone	15 (rat [13]; mouse [2])	17 (rat [16]; mouse [1])	5 (all rat)	6 (rat [5]; mouse [1])	3 (all rat)	9 (all rat)
↓ Anogenital distance (AGD)	19 (rat [16]; mouse [3])	18 (all rat)	5 (all rat)	4 (rat [3]; mouse [1])	5 (all rat)	6 (all rat)
↑ Nipple retention (NR)	12 (all rat)	8 (all rat)	2 (all rat)	1 (all rat)	2 (all rat)	3 (all rat)
↑ Hypospadias	10 (rat [9]; mouse [1])	11 (rat [9]; rabbit [1]; marmoset [1])	3 (all rat)	1 (all rat)	1 (all rat)	3 (all rat)
↑ Seminiferous tubule atrophy	3 (all rat)	8 (all rat)	3 (all rat)	1 (all rat)	2 (all rat)	5 (all rat)
↑ Multinucleated gonocytes (MNGs)	7 (all rat)	11 (rat [9]; mouse [1]; marmoset [1])	1 (all rat)	1 (all rat)	2 (all rat)	4 (all rat)

[a] Data from Section 3.1.3.1 through Section 3.1.3.7 of EPA's draft proposed approach for CRA of phthalates under TSCA (U.S. EPA, 2023b).

The toxicological databases for DEHP and DBP are characterized elsewhere in EPA's non-cancer human health hazard assessments of DEHP (U.S. EPA, 2025x) and DBP (U.S. EPA, 2025v), as well as in the 2023 draft approach (U.S. EPA, 2023b), and are briefly summarized herein. Briefly, numerous studies of experimental rodent models are available that demonstrate that gestational exposure to DEHP and DBP during the critical window of development (*i.e.*, GD 15.5 to 18.5 in rats) can reduce steroidogenic gene and *Insl3* mRNA expression in the fetal testis and reduced fetal testis testosterone content and/or *ex vivo* fetal testis testosterone production. Consistent with a disruption of androgen action, studies have demonstrated that DEHP and DBP can reduce male offspring anogenital distance, increase nipple/areolae retention, and cause severe reproductive tract malformations such as hypospadias and cryptorchidism, as well as cause numerous other effects consistent with phthalate syndrome (*e.g.*, reduce weight of androgen sensitive tissues such as the prostate and testis; increase incidence of

testicular pathology such as seminiferous tubule atrophy; increase incidence of multinucleated gonocytes; cause various sperm effects; and decrease male fertility).

Because RPFs are being derived using fetal testicular testosterone data, EPA next compared the quantity and quality of available dose-response data for this outcome for DBP and DEHP. As can be seen from Table 2-1, EPA included fetal testicular testosterone data from 8 studies of DBP and 8 studies of DEHP in its updated meta-analysis and BMD analysis. As can be seen from Table_Apx A-1, most of the available fetal testicular testosterone data for DEHP are from studies of rats dosed with 100 mg/kg-day DEHP or higher. One study of DEHP provides testosterone data at a dose of 50 mg/kg-day (Saillenfait et al., 2013), while one other study of DEHP provides testosterone data at a dose of 10 mg/kg-day (Lin et al., 2008). Comparatively, more dose-response data are available for the low-end range of the dose-response curve for DBP. As can be seen from Table_Apx A-2, this includes two studies of DBP that provide testosterone data at 1 mg/kg-day DBP (Furr et al., 2014; Johnson et al., 2007), two studies that provide testosterone data at 10 mg/kg-day DBP (Furr et al., 2014; Johnson et al., 2007), two studies that provide testosterone data at 33 mg/kg-day DBP (Furr et al., 2014; Howdeshell et al., 2008), and two studies that provide testosterone data at 50 mg/kg-day DBP (Furr et al., 2014; Howdeshell et al., 2008).

As can be seen from Table 2-2, the BMD_5/$BMDL_5$ estimates for DEHP and DBP based on decreased fetal testicular testosterone are 17/11 mg/kg-day and 14/9 mg/kg-day, respectively, while the BMD_{10}/$BMDL_{10}$ estimates for DEHP and DBP are 35/24 mg/kg-day and 29/20 mg/kg-day, respectively (Table 2-2).

Overall, DBP has more dose-response data than DEHP in the low-end range of the dose-response curve where the BMD and BMDL estimates at the 5 and 10 percent response level are derived. *Therefore, EPA has selected DBP as the index chemical***.** Notably, the SACC agreed with EPA's selection of DBP as the index chemical during the August 2025 phthalate peer-review meeting (U.S. EPA, 2025ag). Readers are directed to EPA's response to public comments summary document and EPA's response to the 2025 phthalates SACC meeting report for further details regarding SACC and public recommendations and how they were addressed by EPA.

As with any risk assessment that relies on BMD analysis, the point of departure (POD) is the lower confidence limit used to mark the beginning of extrapolation to determine risk associated with human exposures. For the index chemical, DBP, EPA calculated $BMDL_5$, $BMDL_{10}$ and $BMDL_{40}$ values of 9, 20, and 101 mg/kg-day for reduced fetal testicular testosterone (Table 2-2). EPA selected the 95 percent lower confidence limit for the BMD_5 (*i.e.*, 14 mg/kg-day), the $BMDL_5$ (*i.e.*, 9 mg/kg-day DBP), which was derived via meta-analysis and BMD analysis of combined fetal testicular testosterone data from eight studies of DBP. EPA selected the $BMDL_5$ as the POD because, as discussed further in Appendix B, EPA does not consider BMRs of 10 or 40 percent health protective for all phthalates included in the cumulative chemical group. Notably, BMD analysis of individual fetal testicular testosterone data from the eight studies, all included in the meta-analysis, using EPA's BMD Software (BMDS Version 25.1) which includes more dose-response models than included in Metafor (*i.e.*, Exponential, Hill, Polynomial, Power, Linear models vs. linear and linear-quadratic models in Metafor) provided several similar $BMDL_5$ estimates ranging from 14 to 16 mg/kg-day, which further increases EPA's confidence in the selected POD (Table 2-6). Using allometric body weight scaling to the three-quarters power (U.S. EPA, 2011b), *EPA extrapolated a human equivalent dose (HED) of 2.1 mg/kg-day from the $BMDL_5$ of 9 mg/kg-day to use as the index chemical POD for the CRA of phthalates*.

2.4 Relative Potency Factors for the Cumulative Phthalate Assessment Based on Decreased Fetal Testicular Testosterone

As described in EPA mixture and cumulative risk assessment guidance documents (2023a, 2016, 2002a, 2000, 1986), RPFs are calculated using Equation 2-1 by taking the ratio of the toxic potency of one chemical to that of the index chemical. As described in Section 2.3, EPA has selected DBP as the index chemical and is using BMD_5, BMD_{10}, and BMD_{40} estimates from the best-fitting linear quadratic model derived using Metafor Version 4.6.0 (Table 2-2) to calculate RPFs based on decreased fetal testicular testosterone.

Table 2-4 shows calculated RPFs using BMD_5, BMD_{10}, and BMD_{40} estimates. As can be seen from Table 2-4, RPFs calculated using BMD_5, BMD_{10}, and BMD_{40} estimates for DEHP, DCHP, and DINP were nearly identical for each phthalate. RPFs ranged from 0.82 to 0.84 for DEHP, 1.66 to 1.71 for DCHP, and 0.19 to 0.21 for DINP. For DIBP, an RPF of 0.53 was calculated using both BMD_{10} and BMD_{40} estimates; however, no RPF could be calculated using a BMD_5 because a BMD could not be estimated for DIBP at the 5 percent response level. For BBP, an RPF of 0.52 was calculated using the BMD_{40} estimate. RPFs could not be estimated for BBP at the 5 or 10 percent response levels because BMD_5 and BMD_{10} values could not be estimated for BBP.

During the August 2025 phthalate peer-review meeting (U.S. EPA, 2025ag), SACC recommended that EPA consider use of Metafor Version 2.0.0 BMD modeling results to calculate alternative RPFs based on decreased fetal testicular testosterone because Metafor Version 2.0.0 allowed BMD_5, BMD_{10}, and BMD_{40} estimates to be derived for DEHP, DBP, BBP, DIBP, DCHP, and DINP. Table 2-5 shows these alternative RPFs calculated using Metafor Version 2.0.0 BMD_5, BMD_{10}, and BMD_{40} estimates. Similar to RPFs calculated using Metafor Version 4.6.0, RPFs calculated using Metafor Version 2.0.0 BMD were similar across response levels (*i.e.*, BMRs of 5, 10, 40%). As can be seen from Table 2-5, RPFs ranged from 0.86 to 0.88 for DEHP; 0.41 to 0.47 for DIBP; 0.48 to 0.56 for BBP; 1.75 to 1.83 for DCHP; and 0.19 to 0.22 for DINP.

*For input into the CRA of phthalates under TSCA, EPA is using RPFs calculated using BMD_{40} estimates using Metafor Version 4.6.0 shown in Table 2-4***.** There is some uncertainty in the applicability of the selected RPFs for DIBP and BBP at the low response levels (*i.e.*, 5% to 10% changes), since RPFs could not be estimated for BBP at the 5 or 10 percent response levels or for DIBP at the 5 percent response level using Metafor Version 4.6.0 BMD modeling results. However, the lack of variability in calculated RPFs for DEHP, DCHP, and DINP across response levels, and the fact that the RPF for DIBP was identical at the 10 and 40 percent response levels, increases EPA's confidence in the selected RPFs for BBP and DIBP. Furthermore, a comparison of the selected RPFs based on BMD_{40} estimates calculated using Metafor Version 4.6.0 (Table 2-4) to candidate RPFs calculated based on BMD_5 estimates calculated using Metafor Version 2.0.0 (Table 2-5) demonstrates that RPFs calculated at both response levels using different Versions of Metafor are similar. For example, the selected RPF for DEHP is 0.84 compared to a candidate RPF of 0.88 (4.8% difference); the selected RPF for DIBP is 0.53 compared to a candidate RPF of 0.42 (21% difference); the selected RPF for BBP is 0.52 compared to a candidate RPF of 0.48 (7.7% difference); the selected RPF for DCHP is 1.66 compared to a candidate RPF of 1.83 (10% difference); and the selected RPF for DINP is 0.21 compared to a candidate RPF of 0.19 (9.5% difference). The fact the selected RPFs based on BMD_{40} estimates calculated using Metafor Version 4.6.0 are similar to RPFs based on BMD_5 estimates calculated using Metafor Version 2.0.0 further increases EPA's confidence in the selected RPFs and indicates that the selected RPFs derived at the 40 percent response level are expected to provide reasonable estimates of potency at the 5 and 10 percent response levels.

Table 2-4. Comparison of Candidate Relative Potency Factors Based on BMD_5, BMD_{10}, and BMD_{40} Estimates Calculated using Metafor Version 4.6.0

Phthalate	RPF (Based on BMD_5)	RPF (Based on BMD_{10})	RPF (Based on BMD_{40}) (Selected RPFs)
DBP (Index Chemical)	1	1	1
DEHP	0.82	0.83	0.84
DIBP	--[a]	0.53	0.53
BBP	--[a]	--[a]	0.52
DCHP	1.67	1.71	1.66
DINP	0.19	0.19	0.21

[a] RPF could not be estimated because BMD_5 or BMD_{10} could not be estimated.

Table 2-5. Comparison of Candidate Relative Potency Factors Based on BMD_5, BMD_{10}, and BMD_{40} Estimates Calculated using Metafor Version 2.0.0

Phthalate	RPF[a] (Based on BMD_5)	RPF[a] (Based on BMD_{10})	RPF[a] (Based on BMD_{40})
DBP (Index Chemical)	1	1	1
DEHP	0.88	0.86	0.87
DIBP	0.42	0.41	0.47
BBP	0.48	0.48	0.56
DCHP	1.83	1.76	1.75
DINP	0.19	0.19	0.22

[a] RPFs calculated using BMD estimates derived using Metafor Version 2.0.0 reported in (U.S. EPA, 2025t).

2.4.1 Limitations, Uncertainties, and Additional Analyses

As noted by the SACC and several public commenters during the August 2025 phthalate peer-review meeting (U.S. EPA, 2025ag), there are several uncertainties and limitations associated with the current approach for BMD modeling of reduced fetal testicular testosterone to support derivation of RPFs, as well as the index chemical (DBP) POD. Uncertainties and limitations are discussed further below. Readers are directed to EPA's response to public comments summary document and EPA's response to the 2025 phthalates SACC meeting report for further details regarding SACC and public recommendations and how they were addressed by EPA.

One limitation associated with the current meta-analysis and BMD modeling approach is that the meta-analysis software (Metafor Version 4.6.0) only includes two models, including the linear and linear-quadratic models. SACC and several public commenters (EPA-HQ-OPPT-2024-0551-0137 and EPA-HQ-OPPT-2024-0551-0155) noted that the models included in Metafor might not be able to adequately

fit fetal testis testosterone dose-response data, which often displays a more sigmoidal shaped dose-response curve. To address this uncertainty, SACC recommended that EPA explore additional tools for BMD modeling and meta-analysis of reduced fetal testis testosterone, including use of EPA's BMD Software, as well as a Bayesian Hierarchical Modeling approach recommended by public commenters (EPA-HQ-OPPT-2024-0551-0137 and EPA-HQ-OPPT-2024-0551-0155). In response to SACC recommendations and public comments, EPA has conducted additional BMD analyses of fetal testicular testosterone data using EPA's BMD Software (Section 2.4.1.1), and has considered the Bayesian Hierarchical Modeling approach (Section 2.4.1.4).

SACC also noted uncertainty with combining fetal testicular testosterone concentration data with *ex vivo* fetal testicular testosterone production data for DBP and DEHP and recommended additional analyses to address this uncertainty. Uncertainty associated with combining data for these two measures of fetal testicular testosterone is discussed further in Section 2.4.1.2.

Finally, although SACC acknowledged that parallel dose-response curves are not required for application of RPFs, SACC recommended additional analyses to determine if phthalate dose-response curves are parallel. SACC recommended this because demonstration of parallel curves might increase confidence in EPA's derived RPFs. Further discussion of dose-response curves and parallelism is provided in Section 2.4.1.3.

2.4.1.1 BMD Modeling of Fetal Testis Testosterone Using EPA's BMD Software

To help address uncertainty associated with the limited number of models included in Metafor, EPA conducted additional BMD modeling of fetal testicular testosterone data from individual studies of DBP, DCHP, DIBP, and BBP using EPA's BMD Software (BMDS). This analysis was not conducted for individual studies of DEHP or DINP, because both approaches (*i.e.*, meta-analysis using Metafor and BMDS of individual data sets) generally provided similar results for DBP, DCHP, DIBP, and BBP. All studies included in this additional analysis were included in the meta-analysis and BMD analysis using Metafor. The primary benefit of this analysis is that EPA's BMD Software includes a broader suite of models compared to those included in the meta-analysis approach (*i.e.*, Exponential, Hill, Polynomial, Power, Linear models vs. linear and linear-quadratic models in Metafor). A comparison of BMD modeling results using Metafor and EPA's BMD Software for DBP, DCHP, DIBP, and BBP is provided below. More detailed results from this additional BMD modeling are provided in the individual non-cancer human health hazard assessments for DBP (U.S. EPA, 2025v), DIBP (U.S. EPA, 2025y), BBP (U.S. EPA, 2025u), and DCHP (U.S. EPA, 2025w).

- ***DBP:*** Using EPA's BMD Online Software (BMDS Version 25.1), EPA modeled fetal testicular testosterone content data from four publications (Struve et al., 2009; Martino-Andrade et al., 2008; Johnson et al., 2007; Kuhl et al., 2007) and *ex vivo* fetal testicular testosterone production data from three publications (Gray et al., 2021; Furr et al., 2014; Howdeshell et al., 2008), all of which were included in the combined meta-analysis and BMD analysis using Metafor. Data from one study (Johnson et al., 2011) were excluded from the analysis, as it only evaluated a single dose level of DBP. Adequate BMD model fits were obtained for data from three studies of fetal testicular testosterone content and three studies of *ex vivo* fetal testicular testosterone production (Table 2-6). However, for two studies of *ex vivo* fetal testicular testosterone production (Block 70 and 71 from Gray et al. (2021)), reliable BMD_5/$BMDL_5$ estimates could not be derived, as the BMD and BMDL estimates were greater than 10× below the lowest dose (300 mg/kg-day) included in each study. The Exponential 3 model provided the best fit for four of six datasets,

while the linear and polynomial degree 3 models each provided the best fit for one dataset (Table 2-6).

Notably, the linear model provided the best fit for one dataset and a viable fit for three other datasets (Table 2-6). This suggests that although the linear model does not frequently provide the best fit, it does frequently provide an adequate fit, suggesting the linear and linear-quadratic models in Metafor would be expected to provide reasonable BMD/BMDL estimates. Consistent with this, BMD_5 estimates (*i.e.*, 22, 24, 30, 49 mg/kg-day) from three of four individual studies were within approximately two-fold of the BMD_5 estimate of 14 mg/kg-day derived via meta-analysis of combined data from eight studies. Similarly, BMD_{10} (*i.e.*, 46, 48, 50, 61, 62, 98 mg/kg-day) and BMD_{40} (*i.e.*, 222, 231, 243, 244, 264, 385 mg/kg-day) estimates from five of six studies were similar and within approximately two-fold of the BMD_{10} (*i.e.*, 29 mg/kg-day) and BMD_{40} (*i.e.*, 149 mg/kg-day) estimates derived via meta-analysis of combined data from eight studies.

The similarity in BMD estimates between the two modeling approaches for DBP indicates that the linear-quadratic model in Metafor provides reasonable BMD/BMDL estimates, which increases EPA's confidence in use of Metafor for meta-analysis and BMD modeling of fetal testicular testosterone.

- ***DCHP:*** Using EPA's BMD Online Software (BMDS Version 25.1), EPA modeled *ex vivo* fetal testicular testosterone data from three studies of DCHP reported in two publications (Gray et al., 2021; Furr et al., 2014), all of which were included in the combined meta-analysis of DCHP. Adequate BMD model fits were obtained for two of three studies, and in both cases the Exponential 3 or Exponential 5 model provided the best-fit (Table 2-6). The linear model did not provide a viable fit for either dataset. Notably, BMD modeling of fetal testis testosterone data from individual studies provided similar BMD_5/$BMDL_5$, BMD_{10}/$BMDL_{10}$ and BMD_{40} /$BMDL_{40}$ estimates compared to the meta-analysis of combined data (*i.e.*, BMD estimates from individual studies were within two-fold of BMD estimates from the meta-analysis at all response levels). For example, BMD_5 estimates ranged from 9.0 to 14 mg/kg-day in the analysis of individual studies versus 8.4 mg/kg-day in the meta-analysis; BMD_{10} estimates ranged from 18 to 20 mg/kg-day in the analysis of individual studies versus 17 mg/kg-day in the meta-analysis; and BMD_{40} estimates ranged from 90 to 102 mg/kg-day in the analysis of individual studies versus 90 mg/kg-day in the meta-analysis.

  The similarity in BMD estimates between the two modeling approaches for DCHP indicates that the linear-quadratic model in Metafor provides reasonable BMD/BMDL estimates, which increases EPA's confidence in use of Metafor for meta-analysis and BMD modeling of fetal testicular testosterone.

- ***DIBP:*** Using EPA's BMD Software (BMDS Version 3.3.2), EPA modeled *ex vivo* fetal testicular testosterone data from three studies (Gray et al., 2021; Hannas et al., 2011; Howdeshell et al., 2008), all of which were included in the combined meta-analysis of DIBP. Adequate BMD model fits were obtained for two of three studies, with the Exponential 3 or Hill models providing the best fit (Table 2-6). The linear model also provided a viable fit for one study (Gray et al., 2021). As can be seen from Table 2-6, BMD_5/$BMDL_5$, BMD_{10}/$BMDL_{10}$, and BMD_{40}/$BMDL_{40}$ estimates were 63/24, 106/50, and 335/243 mg/kg-day from the best fitting Exponential 3 model (Gray et al., 2021) and 103/52, 136/82, and 298/236 mg/kg-day from the best fitting Exponential 3 model (Howdeshell et al., 2008). Comparatively, no BMD_5/$BMDL_5$ estimates could be derived via meta-analysis using Metafor Version 4.6.0, while the BMD_{10} estimate was 55 mg/kg-day (no $BMDL_{10}$ could be derived) and BMD_{40}/$BMDL_{40}$ estimates were

279/136 mg/kg-day. Notably, BMD_{40} estimates of 198 and 335 mg/kg-day from the analysis of individual studies are similar to the BMD_{40} estimate of 279 mg/kg-day from the meta-analysis of combined data (*i.e.*, within two-fold). Similarly, BMD_{10} estimates of 106 and 136 mg/kg-day from the analysis of individual studies are similar to the BMD_{10} estimate of 55 mg/kg-day from the meta-analysis of combined data (*i.e.*, within two- to three-fold). The similarity in BMD estimates between the two modeling approaches indicates that the linear-quadratic model in Metafor provides reasonable BMD/BMDL estimates, which increases EPA's confidence in use of Metafor for meta-analysis and BMD modeling of fetal testicular testosterone.

- ***BBP:*** Using EPA's BMD Software (BMDS Version 3.3.2), EPA modeled *ex vivo* fetal testicular testosterone data from four studies reported in three publications (Gray et al., 2021; Furr et al., 2014; Howdeshell et al., 2008), all of which were included in the combined meta-analysis of BBP. Adequate BMD model fits were obtained for one of four studies (Table 2-6). For this dataset (Howdeshell et al., 2008), the Exponential 3 model provided the best fit, however, the linear model also provided a viable fit. Because an adequate model fit was only obtained for one of four individual datasets, limited comparisons to BMD results obtained via meta-analysis and Metafor can be made. Briefly, for the one fetal testicular testosterone dataset with an adequate BMD model fit (Howdeshell et al., 2008), BMD_5/$BMDL_5$, BMD_{10}/$BMDL_{10}$, and BMD_{40}/$BMDL_{40}$ estimates were 138/81, 195/129, and 416/350 mg/kg-day, respectively, from the best-fitting Exponential 3 model (Table 2-6). Comparatively, BMD_5/$BMDL_5$ and BMD_{10}/$BMDL_{10}$ estimates could not be generated using Metafor Version 4.6.0 and the best-fitting linear-quadratic model, while the BMD_{40}/$BMDL_{40}$ estimate from was 284/150 mg/kg-day. The BMD_{40} of 416 mg/kg-day from Howdeshell et al. is similar (i.*e.*, withing two-fold) to the BMD_{40} of 284 mg/kg-day from the meta-analysis of combined data.

  Overall, fetal testicular testosterone data from individual studies of BBP did not model well as adequate model fits were only obtained for one of four datasets (U.S. EPA, 2025u). This is generally consistent with the meta-analysis approach using Metafor, where no BMD_5 or BMD_{10} estimates could be derived for BBP.

Across available studies with acceptable model fits, the Exponential 3 model provided the best fit for 8 of 11 datasets (Table 2-6), while the linear model provided the best-fit for one dataset and provided adequate fits for another five datasets. This suggests that although the linear model does not frequently provide the best fit, it can often provide an adequate fit, suggesting the linear and linear-quadratic models in Metafor would be expected to provide reasonable BMD/BMDL estimates. Consistent with this, BMD estimates across response levels were similar (generally within two-fold) across modeling approaches for each phthalate, supporting EPA's use of Metafor for meta-analysis and BMD analysis of fetal testicular testosterone.

Table 2-6. Comparison of BMD Results of Combined and Individual Fetal Testis Testosterone Data

Phthalate	BMD Modeling Approach	Dataset	Best-Fitting Model (Variance)	Linear Model Fit	BMD_5 (mg/kg-day) [95% CI]	BMD_{10} (mg/kg-day) [95% CI]	BMD_{40} (mg/kg-day) [95% CI]	Reference Document
DBP	Metafor Version 4.6.0	Meta-analysis of combined data	Linear-Quadratic	–	14 [9, 27]	29 [20, 54]	149 [101, 247]	(U.S. EPA, 2025t)
	BMD Online Version 25.1	Testis T Content (Martino-Andrade et al., 2008)	Exponential 3 (Constant)	Viable	24 [16, 86]	50 [32, 134]	244 [156, 405]	(U.S. EPA, 2025v)
		Testis T Content (Kuhl et al., 2007)	Exponential 3 (Constant)	Viable	22 [14, 97]	46 [29, 145]	222 [139, 372]	
		Testis T Content (Struve et al., 2009)	Linear (Non-constant)	Selected	30 [28, 34]	61 [56, 67]	243 [223, 268]	
		Ex vivo Testis T Production (Howdeshell et al., 2008)	Polynomial Degree 3 (Constant)	Viable	49 [39, 161]	98 [79, 232]	385 [314, 502]	
		Ex vivo Testis T Production (Gray et al., 2021) (Block 70)	Exponential 3 (Non-constant)	Questionable	–[a]	62 [41, 150]	264 [197, 409]	
		Ex vivo Testis T Production (Gray et al., 2021) (Block 71)	Exponential 3 (Non-constant)	Questionable	–[a]	48 [42, 69]	231 [206, 287]	
		Ex vivo Testis T Production (Furr et al., 2014)	No models adequately fit the dataset.					
		Testis T Content (Johnson et al., 2007)	No models adequately fit the dataset.					
DCHP	Metafor Version 4.6.0	Meta-analysis of combined data	Linear-Quadratic	–	8.4 [6.0, 14]	17 [12, 29]	90 [63, 151]	(U.S. EPA, 2025t)
	BMD Online Version 25.1	*Ex vivo* Testis T Production (Gray et al., 2021)	Exponential 3/5 (Constant)	Questionable	14 [10, 22]	20 [15, 41]	102 [75, 142]	(U.S. EPA, 2025w)
		Ex vivo Testis T Production (Furr et al., 2014) (Block 33)	Exponential 3 (Constant)	Questionable	9.0 [5.2, 9.2]	18 [11, 19]	90 [52, 92]	

Phthalate	BMD Modeling Approach	Dataset	Best-Fitting Model (Variance)	Linear Model Fit	BMD_5 (mg/kg-day) [95% CI]	BMD_{10} (mg/kg-day) [95% CI]	BMD_{40} (mg/kg-day) [95% CI]	Reference Document
DCHP		*Ex vivo* Testis T Production (Furr et al., 2014) (Block 23)	No models adequately fit the dataset.					
DIBP	Metafor Version 4.6.0	Meta-analysis of combined data	Linear-Quadratic	–	–	55 [NA, 266]	279 [136, 517]	(U.S. EPA, 2025t)
	BMDS Version 3.3.2	*Ex vivo* Testis T Production (Gray et al., 2021)	Exponential 3 (Constant)	Viable	63 [24, 137]	106 [50, 194]	335 [243, 439]	(U.S. EPA, 2025y)
		Ex vivo Testis T Production (Howdeshell et al., 2008)	Hill (Constant)	Questionable	103 [52, 185]	136 [82, 211]	298 [236, 362]	
		Ex vivo Testis T Production (Hannas et al., 2011)	No models adequately fit the dataset.					
BBP	Metafor Version 4.6.0	Meta-analysis of combined data	Linear-Quadratic	–	–	–	284 [150, 481]	(U.S. EPA, 2025t)
	BMDS Version 3.3.2	*Ex vivo* Testis T Production (Howdeshell et al., 2008)	Exponential 3 (Constant)	Viable	138 [81, 214]	195 [129, 275]	416 [350, 492]	(U.S. EPA, 2025u)
		Ex vivo Testis T Production (Gray et al., 2021)	No models adequately fit the dataset.					
		Ex vivo Testis T Production (Furr et al., 2014) (Block 36)	No models adequately fit the dataset.					
		Ex vivo Testis T Production (Furr et al., 2014) (Block 37)	No models adequately fit the dataset.					

Abbreviations: BMD = benchmark Dose; CI = confidence interval; T = Testosterone

[a] Reliable BMD_5/$BMDL_5$ estimates could not be derived. EPA's BMDS flagged the Exponential 3 model fit as 'Questionable' with BMD_5 and $BMDL_5$ estimates greater than 10× below the lowest dose (300 mg/kg-day) included in the study.

2.4.1.2 Combining Fetal Testicular Testosterone Concentration Data and *Ex Vivo* Fetal Testicular Testosterone Data

Another uncertainty noted by SACC during the August 2025 peer-review meeting was whether it was appropriate to combine fetal testicular testosterone concentration data with *ex vivo* fetal testicular testosterone production data as part of the meta-analysis and BMD analysis, as was done for DBP and DEHP. For example, the DEHP meta-analysis and BMD analysis included fetal testicular testosterone concentration data from two publications and *ex vivo* fetal testicular testosterone production data from six publications (Table 2-1), while the DBP meta-analysis and BMD analysis included fetal testicular testosterone concentration data from five publications and *ex vivo* fetal testicular testosterone production data from three publications (Table 2-1). In contrast, only *ex vivo* fetal testicular testosterone production data was included in the meta-analysis and BMD analysis for DIBP, BBP, and DCHP (Table 2-1).

As discussed above in Section 2.4.1.1, EPA conducted BMD modeling of individual fetal testicular testosterone datasets for DBP using EPA's BMD Software (BMDS Version 25.1). BMD_5, BMD_{10}, and BMD_{40} estimates were derived for three studies of fetal testicular testosterone content (Struve et al., 2009; Martino-Andrade et al., 2008; Kuhl et al., 2007), while BMD_5, BMD_{10}, and BMD_{40} estimates were derived for one, three, and three studies, respectively, of *ex vivo* fetal testicular testosterone production (Table 2-6) (Gray et al., 2021; Howdeshell et al., 2008). Reliable BMD_5 estimates could not be derived from two studies (Block 70 and Block 71 rats) of *ex vivo* fetal testicular testosterone production reported by Gray et al. (2021), as $BMDL_5$ estimates were greater than 10× lower than the lowest dose (*i.e.*, 300 mg/kg-day) included in the study and all BMD model fits at the 5 percent response level were flagged as 'Questionable' by EPA's BMD Software.

Across the 5, 10, and 40 percent response levels, BMD estimates for fetal testicular testosterone content and *ex vivo* fetal testicular testosterone production were similar (within approximately two-fold or less), indicating similar sensitivity in responses across the two measures of reduced fetal testicular testosterone. For example, BMD_5 estimates were 22, 24, and 30 mg/kg-day for reduced fetal testicular testosterone concentration versus 49 mg/kg-day for reduced *ex vivo* fetal testicular testosterone production (Table 2-6); BMD_{10} estimates were 46, 50, and 61 mg/kg-day for reduced fetal testicular testosterone concentration versus 48, 62, and 98 mg/kg-day for reduced *ex vivo* fetal testicular testosterone production; and BMD_{40} estimates were 222, 243, and 244 mg/kg-day for reduced fetal testicular testosterone concentration versus 231, 264, and 385 mg/kg-day for reduced *ex vivo* fetal testicular testosterone production (Table 2-6).

Given the similarity in BMD estimates across response levels for both measures of fetal testicular testosterone, EPA concludes that its current meta-analysis and BMD analysis approach that combines data for both measures of fetal testicular testosterone for DBP and DEHP remains appropriate.

2.4.1.3 Parallel Dose-Response Curves

As discussed by the National Research Council in 2008 (NRC, 2008), there may be challenges associated with the RPF approach because phthalate dose-response curves may lack "parallelism." For parallel dose-response curves the RPF is constant, regardless of the response level (that is, 5%, 10%, or 40%). However, different chemical dose-responses may have differing shape and slope dose-response curves leading to variability in RPFs across different BMRs. This concern was echoed by the SACC during the 2023 peer-review of EPA's *Draft Proposed Approach for Cumulative Risk Assessment (CRA) of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the Toxic Substances Control Act* (U.S. EPA, 2023c) and the August 2025 peer-review of this CRA TSD (U.S. EPA, 2025ag).

Although SACC noted that parallel dose-response curves are not required for estimating RPFs, they are preferred, and demonstrating parallel dose-response curves would increase confidence in EPA's derived RPFs (U.S. EPA, 2025ag).

Consistently, EPA's *Advances in Dose Addition for Chemical Mixtures: A White Paper* (U.S. EPA, 2023a) states "In the Agency-wide guidance on dose addition, there is an assumption of constant relative potency (U.S. EPA, 2000, 1987), but a demonstration of empirical evidence, such as similar DRC [dose-response curve] shapes, is not required.*"* Thus, RPFs can be applied for chemicals with dissimilar dose-response curves, as the establishment of a known or suspected common MOA shared by members of the class of compounds is considered more fundamental. It is common practice to estimate RPFs closer to the low-dose range of the dose-response function. This practice is intended to reduce possible high-dose influences on estimated RPFs that may arise due to saturation of certain kinetic processes (*e.g.*, receptor binding, metabolic elimination). However, this approach also carries an implicit assumption that dose-response curve shapes will be similar below the selected response level (U.S. EPA, 2023a).

For parallel dose-response curves, the RPF is constant regardless of the response level (that is, 5%, 10%, or 40%). As discussed earlier in Section 2.4, candidate RPFs calculated using BMD_5, BMD_{10}, and BMD_{40} estimates derived using Metafor Version 4.6.0 were nearly identical across response levels for DEHP (RPFs ranged from 0.82–0.84), DCHP (RPFs ranged from 1.66–1.71), and DINP (RPFs ranged from 0.19–0.21), providing evidence of parallel dose-response curves with the index chemical DBP. For DIBP, an RPF of 0.53 was calculated at both the 10 and 40 percent response levels, providing evidence of parallel dose-response curves with the index chemical; however, no RPF could be calculated at the 5 percent response level because a BMD_5 could not be estimated for DIBP. For BBP, an RPF of 0.52 was calculated using the BMD_{40} estimate. RPFs could not be estimated for BBP at the 5 or 10 percent response levels because BMD_5 and BMD_{10} values could not be estimated for BBP.

For use in the CRA, EPA selected RPFs based on BMD_{40} estimates calculated using Metafor Version 4.6.0, since this was the only the only response level at which a full set of RPFs could be derived for all phthalates included in the CRA (Table 2-4). Because candidate RPFs could not be derived for BBP or DBP at the 5 percent response level, or for BBP at the 10 percent response level, there is some uncertainty regarding constant proportionality for these two phthalates in the low-end range of the dose-response curve. However, this uncertainty was addressed by calculating candidate RPFs using BMD estimates derived via Metafor Version 2.0.0, which allowed BMD estimates to be calculated for all phthalates at all response levels. As discussed earlier in Section 2.4, there was little variability in candidate RPFs calculated using BMD_5, BMD_{10}, and BMD_{40} estimates derived using Metafor Version 2.0.0 (Table 2-5), providing evidence of parallel dose-response curves for DEHP, DBP, BBP, DCHP, DIBP, and DINP. Further, candidate RPFs calculated using BMD_5 estimates derived using Metafor Version 2.0.0, were similar to the selected RPFs calculated using BMD_{40} estimates derived using Metafor Version 4.6.0. This indicates that the selected RPFs derived from the 40 percent response level are expected to provide reasonable estimates of potency at the 5 and 10 percent response levels, and provides evidence of parallel dose-response curves for all the phthalates included in the CRA.

2.4.1.4 Bayesian Hierarchical Modeling Approach

During the August 2025 phthalate peer-review meeting (U.S. EPA, 2025ag), a public commentor (EPA-HQ-OPPT-2024-0551-0155) described a new method for estimation of RPFs that has recently been applied to dioxin-like compounds (Ring et al., 2023). A key concern addressed by the new RPF method

is the possibility of a lack of parallelism in the dose-response curves between the compound for which the RPF is being calculated and the index chemical.

The new RPF integration method (Ring et al., 2023) was developed to address a large body of knowledge about dioxin-like compounds comprising 604 RPFs of varying quality (Haws et al., 2006). To allow the new RPF method to be used, a machine learning model was developed and trained to assign study quality predictions to each RPF (Wikoff et al., 2023). The underlying dose-response dataset were available for approximately half the RPFs. Where the underlying dose-response datasets were available, the new method re-estimated the RPF as a function of response level. A Bayesian statistical framework allowed for weighting of each RPF based on the machine learning estimate of study quality and the uncertainty in the RPF estimate where available. The implementation of the new RPF method, while described in a peer-reviewed scientific publication, is not yet available as open-source software. A machine learning model is not available to determine the study quality of phthalate RPFs.

EPA recognizes that although the Bayesian Hierarchical Modeling approach may represent an alternative method to estimate BMD values and RPFs, the new method is not yet available as open-source software and is not reasonably available to EPA at this time. Under TSCA, reasonably available information means "information that EPA possesses or can reasonably generate, obtain, and synthesize for use in risk evaluations, considering the deadlines specified in TSCA section 6(b)(4)(G) for completing such evaluation [emphasis added]..." (40 CFR § 702.33).

Importantly, EPA considers its current analysis using Metafor to be scientifically valid and appropriate for deriving BMD estimates and RPFs. This is because EPA's current analysis (Table 2-4 and Table 2-5) demonstrates that for reduced fetal testicular testosterone, RPFs do not vary across a range of BMRs (*i.e.*, BMRs of 5, 10, and 40%). Further, similar BMD estimates across a range of response levels were derived using two BMD modeling approaches (*i.e.*, Metafor analysis of combined data and BMD analysis of individual datasets using EPA's BMD Software). The similarity in BMD estimates between the two modeling approaches indicates that the linear-quadratic model in Metafor provides reasonable BMD/BMDL estimates. All these reasons provide confidence that the current analysis with Metafor remains appropriate and consistent with the best available science and the tools and approaches reasonably available to EPA.

2.5 Uncertainty Factors and the Benchmark Margin of Exposure

Consistent with Agency guidance (U.S. EPA, 2022, 2002b), EPA selected an intraspecies uncertainty factor (UF_H) of 10, which accounts for variation in susceptibility across the human population and the possibility that the available data might not be representative of individuals who are most susceptible to the effect.

As described in Section 2.3, EPA used allometric body weight scaling to the three-quarters power to derive an HED of 2.1 mg/kg-day DBP from the $BMDL_5$ of 9 mg/kg-day for reduced fetal testicular testosterone, which accounts for species differences in toxicokinetics. Consistent with EPA Guidance (U.S. EPA, 2011b), the interspecies uncertainty factor (UF_A), was reduced from 10 to 3 to account for remaining uncertainty associated with interspecies differences in toxicodynamics.

EPA considered reducing the UF_A further to a value of 1 based on apparent differences in toxicodynamics between rats and humans. As discussed in Section 3.1.4 of the 2023 draft approach (U.S. EPA, 2023b), several explant (Lambrot et al., 2009; Hallmark et al., 2007) and xenograft studies (van Den Driesche et al., 2015; Spade et al., 2014; Heger et al., 2012; Mitchell et al., 2012) using human

donor fetal testis tissue have been conducted to investigate the antiandrogenicity of mono-2-ethylhexyl phthalate (MEHP; a monoester metabolite of DEHP), DBP, and monobutyl phthalate (MBP; a monoester metabolite of DBP) in a human model. Generally, results from human explant and xenograft studies suggest that human fetal testes are less sensitive to the antiandrogenic effects of phthalates, although effects on Sertoli cells and increased MNGs have been observed in available studies of donor fetal testis tissue. As discussed in EPA's 2023 draft approach (U.S. EPA, 2023b), the available human explant and xenograft studies have limitations and uncertainties, which preclude definitive conclusions related to species differences in sensitivity. For example, key limitations and uncertainties of the human explant and xenograft studies include: small sample size; human testis tissue was collected from donors of variable age and by variable non-standardized methods; and most of the testis tissue was taken from fetuses older than 14 weeks, which is outside of the critical window of development (*i.e.*, gestational weeks 8 to 14 in humans). Therefore, EPA did not reduce the UF_A from a value of 3 to 1.

Overall, a total uncertainty factor of 30 was selected for use as the benchmark margin of exposure for the cumulative risk analysis (based on an interspecies uncertainty factor [UF_A] of 3 and an intraspecies uncertainty factor [UF_H] of 10).

2.6 Applicability of Derived Relative Potency Factors (RPFs)

Exposure Route

EPA derived RPFs using data from gestational exposure studies in which pregnant rats were orally dosed with DEHP, DBP, BBP, DIBP, DCHP, or DINP. Because RPFs were derived from oral exposure studies, they are most directly applicable for the oral exposure route. As described in the non-cancer human health hazard assessment for DINP (U.S. EPA, 2025z) and non-cancer human health hazard assessments for DEHP (U.S. EPA, 2025x), DBP (U.S. EPA, 2025v), BBP (U.S. EPA, 2025u), DIBP (U.S. EPA, 2025y), and DCHP (U.S. EPA, 2025w), there are no dermal or inhalation exposure studies available that have evaluated fetal testicular testosterone in rats following gestational exposure during the critical window of development. Therefore, EPA could not derive route-specific RPFs. For the phthalate CRA, EPA is using the oral RPFs to scale inhalation and dermal phthalate exposures. This requires an inherent assumption of similar potency across exposure routes, which is a source of uncertainty. However, EPA cannot predict whether use of oral RPFs for the inhalation and dermal exposure routes will lead to an under- or overestimation of risk.

Population

Because the RPFs are based on reduced fetal testicular testosterone, EPA considers the RPFs most directly applicable to pregnant women, women of reproductive age, and male infants. Use of the RPFs for other lifestages (*i.e.*, adult males and women above reproductive age), who are not susceptible to the chosen health endpoint, may be overly conservative and protective for other lifestages.

2.7 Weight of Scientific Evidence: Relative Potency Factors and Index Chemical Point of Departure

EPA has selected an HED of 2.1 mg/kg-day ($BMDL_5$ of 9 mg/kg-day) as the index chemical (*i.e.*, DBP) POD. This POD is based on a meta-analysis and BMD modeling of decreased fetal testicular testosterone from eight studies of rats exposed to DBP during gestation. EPA has also derived RPFs of 1 for DBP (index chemical), 0.84 for DEHP, 0.53 for DIBP, 0.52 for BBP, 1.66 for DCHP, and 0.21 for DINP, respectively, based on a uniform measure (*i.e.*, reduced fetal testicular testosterone). Overall, EPA has *robust overall confidence in the index chemical (DBP) POD and the RPFs* based on the following weight of scientific evidence considerations:

- EPA has previously considered the weight of scientific evidence and concluded that oral exposure to DEHP, DBP, BBP, DIBP, DCHP, and DINP can induce effects on the developing male reproductive system consistent with a disruption of androgen action (see EPA's 2023 draft approach (U.S. EPA, 2023b)). Notably, EPA's conclusion was supported by the SACC (U.S. EPA, 2023c).
- EPA selected DBP as the index chemical because it has a high quality toxicological database demonstrating effects on the developing male reproductive system consistent with a disruption of androgen action and phthalate syndrome; demonstrates toxicity representative of all phthalates in the cumulative chemical group; is well characterized for the MOA associated with phthalate syndrome; and has the most fetal testicular testosterone dose-response data in the low-end range of the dose-response curve where the BMD and BMDL estimates at the 5 and 10 percent response level are derived.
- As discussed in the *Non-cancer Human Health Hazard Assessment for Dibutyl Phthalate (DBP)* (U.S. EPA, 2025v), EPA has also selected the HED of 2.1 mg/kg-day ($BMDL_5$ of 9 mg/kg-day) for calculation of risk from exposures to DBP in the individual chemical risk evaluation, which was derived via meta-analysis of fetal testicular testosterone data from eight studies. Notably, BMD analysis of individual fetal testicular testosterone data from the eight studies, all included in the meta-analysis, using EPA's BMD Software (BMDS Version 25.1) which includes more dose-response models than included in Metafor (*i.e.*, Exponential, Hill, Polynomial, Power, Linear models vs. linear and linear-quadratic models in Metafor) provided several similar $BMDL_5$ estimates ranging from 14 to 16 mg/kg-day, which further increases EPA's confidence in the selected POD. EPA has robust overall confidence in the POD selected for DBP. Overall, the same weight of scientific evidence considerations apply to the POD selected for the individual DBP risk evaluation and the CRA. Readers are directed to the *Non-cancer Human Health Hazard Assessment for Dibutyl Phthalate (DBP)* (U.S. EPA, 2025v) for a complete discussion of the weight of scientific evidence supporting the selected POD.
- In the MOA for phthalate syndrome, which has been described by EPA elsewhere (U.S. EPA, 2023b), decreased fetal testicular testosterone is an early, upstream event in the MOA that precedes downstream apical outcomes such as male nipple retention, decreased anogenital distance, and male reproductive tract malformations (*e.g.*, hypospadias and cryptorchidism). Decreased fetal testicular testosterone should occur at doses that are lower than or equal to doses that cause downstream apical outcomes associated with a disruption of androgen action.
- EPA derived RPFs using a meta-analysis and BMD modeling approach, which integrates fetal testicular testosterone data from 14 medium- and high-quality studies for DEHP, DBP, BBP, DIBP, DCHP, and DINP (Table 2-1). Notably, the statistical significance of the meta-analysis results were robust to leaving out individual studies as part of a sensitivity analysis (see updated meta-analysis technical support document (U.S. EPA, 2025t)).
- EPA derived candidate RPFs using BMD_5, BMD_{10}, and BMD_{40} estimates derived via Metafor Versions 4.6.0 (Table 2-2) to allow for a comparison of RPFs at the three evaluated BMR levels of 5, 10, and 40 percent. RPFs calculated using BMD_5, BMD_{10}, and BMD_{40} estimates for DEHP, DCHP, and DINP were nearly identical for each phthalate (Table 2-4). RPFs ranged from 0.82 to 0.84 for DEHP, 1.66 to 1.71 for DCHP, and 0.19 to 0.21 for DINP. For DIBP, an RPF of 0.53 was calculated using both BMD_{10} and BMD_{40} estimates; however, no RPF could be calculated using a BMD_5 because a BMD could not be estimated for DIBP at the 5 percent response level. For BBP, an RPF of 0.52 was calculated using the BMD_{40} estimate. RPFs could not be estimated for BBP at the 5 or 10 percent response levels because BMD_5 and BMD_{10} values could not be

estimated for BBP. There is some uncertainty in the applicability of the selected RPFs based on BMD_{40} estimates for DIBP and BBP at the low response levels (*i.e.,* 5% to 10% changes), since RPFs could not be estimated for BBP at the 5 or 10 percent response levels or for DIBP at the 5 percent response level. However, the lack of variability in calculated RPFs for DEHP, DCHP, and DINP across response levels, and the fact that the RPF for DIBP was identical at the 10 and 40 percent response levels, increases EPA's confidence in the selected RPFs for BBP and DIBP.

- EPA also derived candidate RPFs using BMD_5, BMD_{10}, and BMD_{40} estimates derived via Metafor Versions 2.0.0, since this version of Metafor allowed for BMD estimates to be derived for all response levels and all phthalates included in the CRA. RPFs calculated using Metafor Version 2.0.0 BMD were similar across response levels (*i.e.,* BMRs of 5, 10, 40%). RPFs ranged from 0.86 to 0.88 for DEHP; 0.41 to 0.47 for DIBP; 0.48 to 0.56 for BBP; 1.75 to 1.83 for DCHP; and 0.19 to 0.22 for DINP (Table 2-5). Further candidate RPFs derived using BMD_5 estimates from Metafor Version 2.0.0 were similar to the selected RPFs derived using BMD_{40} estimates from Metafor Version 4.6.0 (Section 2.4). This further increases EPA's confidence in the selected RPFs.

3 SCENARIO-BASED PHTHALATE EXPOSURE AND RISK

This section provides a qualitative analysis of co-exposures expected for workers (Section 3.1), consumers (Section 3.2), and general population (Section 3.3) exposed to environmental releases for each individual phthalate under their COUs. However, as discussed further in this section, EPA did not quantify cumulative phthalate exposures for these populations resulting from multiple COUs. Per TSCA, each evaluation must assess risks to human health and the environment under the chemical substance's COUs and determine whether the chemical substance presents unreasonable risk.[2]

3.1 Occupational Exposure for Workers

Occupational exposures to a combination of phthalates may occur in a variety of industrial and commercial settings. For instance, businesses may manufacture, import, process, or dispose of multiple phthalates within the same facility, which may lead to worker exposure to multiple phthalates. Also, some products used by workers may contain more than one phthalate, or workers may use multiple phthalate-containing products throughout a workday. Due to the workplace and task-specific nature of cumulative exposure scenarios that may exist in phthalate-containing workplaces, it was not possible to provide a full quantitative assessment of cumulative risk for workers who may be exposed to multiple phthalates. However, EPA was able to characterize the various businesses that use multiple phthalates and the products that contain multiple phthalates, and has developed one option for deriving an occupational exposure value (OEV) based on relative potency considerations. In addition to individual chemical OEVs, this cumulative option is intended to summarize the occupational exposure scenario and sensitive health endpoint into a single value. Similar to the individual OEVs, the calculated cumulative OEV may be used to support risk management efforts for these evaluated phthalates under TSCA section 6(a), 15 U.S.C. 6155 §2605.

This section provides an overview of the industrial and commercial products identified by EPA that contain multiple phthalates (Section 3.1.1), and the parent companies that report use of multiple phthalates and facilities that report release of multiple phthalates (Section 3.1.2). Section 3.1.3 provides a summary of EPA's conclusions, while Appendix E summarizes one option being considered by EPA for deriving an OEV based on relative potency considerations.

3.1.1 Industrial and Commercial Products Containing Multiple Phthalates

One way workers may be occupationally exposed to multiple phthalates being evaluated under TSCA (*i.e.*, DEHP, DBP, BBP, DIBP, DCHP, DINP) is through use of an industrial or commercial product that contains multiple phthalates. To assess the potential for co-exposure to multiple phthalates through the use of industrial and commercial products containing multiple phthalates, EPA reviewed product safety data sheets (SDSs) for products included in the occupational exposure assessments for DEHP (U.S. EPA, 2025q), DBP (U.S. EPA, 2025o), BBP (U.S. EPA, 2025n), DIBP (U.S. EPA, 2025r), DCHP (U.S. EPA, 2025p), and DINP (U.S. EPA, 2025s).

Overall, only 15 industrial and commercial products were identified that contained multiple phthalates (Table_Apx D-2). The majority of products identified that contain multiple phthalates are laboratory chemicals (13 out of 15 identified products with multiple phthalates are laboratory chemicals), except for one clay polymer product and one adhesive. Further, the laboratory chemical formulations shown in Table_Apx D-2 have low phthalate concentrations (generally less than 1% by weight fraction). The clay

[2] Conditions of use (COUs) are defined as "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." (15 U.S.C. 2602(4))

polymer product also has low phthalate concentrations (less than 2.5% by weight fraction) and solid physical form, and the material is commonly used in fashioning commercial pens, while the adhesive product also has low concentrations of two phthalates (*i.e.*, 1−5% DBP and 1−5% DCHP).

Given the small number of industrial and commercial products identified that contain multiple phthalates and given the low concentrations of phthalates in the identified products (Table_Apx D-2), *EPA does not expect these products to be a significant source of phthalate exposures contributing to cumulative risk under most occupational and commercial exposure scenarios*.

3.1.2 Multiple TSCA Phthalates at a Single Facility and/or Single Condition of Use

EPA acknowledges that there is potential for workers to be exposed to multiple phthalates being evaluated under TSCA at a single facility. This may occur if a single facility works with multiple phthalates. To provide an overview of potential phthalate co-exposures that may occur in the workplace, EPA relied on programmatic data from the Chemical Data Reporting (CDR) rule, Toxics Release Inventory (TRI), Discharge Monitoring Report (DMR), and the National Emissions Inventory (NEI). These databases provide manufacture, processing, and release data reported by businesses across the U.S.

3.1.2.1 Parent Companies Reporting Use of Multiple Phthalates

To better understand the landscape of parent companies that work with multiple phthalates, EPA first reviewed 2016 and 2020 CDR data and 2017 through 2022 TRI data to identify parent companies that report use of multiple phthalates. One limitation of this initial analysis is that only DEHP and DBP are reportable under TRI (DINP is reportable to TRI as of January 2024). Data from CDR provides manufacture and processing information from parent companies, including overall production volume and number of facilities, and all phthalates considered in this cumulative assessment are reported to CDR.

Table_Apx D-3 characterizes the various parent companies from CDR and TRI that report use of multiple phthalates. As can be seen from Table_Apx D-3, EPA identified 56 domestic parent companies that report use of multiple phthalates being evaluated under TSCA. Though these data provide a broad overview of the various businesses involved in the phthalate industry, the CDR data provide information about the parent company only and are not granular enough to determine if multiple phthalates are being processed within a singular facility. Therefore, there is uncertainty associated with assigning co-exposures based on parent company reporting data from CDR.

3.1.2.2 Facilities Reporting Releases of Multiple Phthalates

Data from TRI, DMR, and NEI provide release information for businesses that meet reporting thresholds. TRI provides data for releases to air, water, and land, while DMR provides data for releases to water, and NEI provides data for releases to air. However, since release reporting for some phthalates is not currently required by programmatic reporting standards (*i.e.*, for DIBP, DINP, and DCHP), TRI and NEI data are limited to businesses that release DEHP and DBP, while DMR data are limited to businesses that release DEHP, DBP, and BBP. Identified facilities from TRI (2017 to 2022), DMR (2017 to 2023), and NEI (2017 and 2020) that reported use of multiple phthalates considered in this cumulative assessment are provided in the *Summary of Facility Release Data for Di(2-ethylhexyl) Phthalate (DEHP), Dibutyl Phthalate (DBP), and Butyl Benzyl Phthalate (BBP)* (U.S. EPA, 2025ah).

Overall, EPA identified 1,922 unique facilities that report releases of DEHP, DBP, or BBP to TRI, DMR, and NEI (U.S. EPA, 2025ah). Of the identified facilities, 1,461 report environmental releases of a single phthalate, including 973, 483, and 5 facilities that report releases of DEHP, DBP, and BBP, respectively. Overall, 461 facilities were identified that reported releases of multiple phthalates, including the following combinations:

- 419 facilities report releases of DBP and DEHP;
- 15 facilities report releases of DEHP and BBP;
- 4 facilities report releases of DBP and BBP; and
- 23 facilities report releases of DBP, DEHP, and BBP.

This analysis indicates that there are approximately 461 facilities where workers may become co-exposed to multiple phthalates while working. It is important to note that TRI, DMR, and NEI often provide information from the release facility rather than the parent company, and this reduces uncertainty when assigning potential co-exposure for a particular chemical in a facility.

There are some limitations and uncertainties associated with the current analysis. First, it is important to re-iterate that because DIBP, DINP, and DCHP are not reportable to TRI, DMR, or NEI, specific facilities working with these phthalates were not identified by EPA and therefore the number of facilities identified by EPA as working with one or multiple phthalates is an underestimate. Another uncertainty with the current analysis is that facilities that work with multiple phthalates may run campaigns in which each phthalate is only used for part of the year. Further, these campaigns may not overlap and therefore workers may not actually be co-exposed to multiple phthalates at all the facilities identified by EPA. For example, Exxon runs continuous half-year operations dedicated to the manufacture of DINP and DIDP, which are staggered campaigns (ExxonMobil, 2022). This makes it difficult to determine if workers are actually co-exposed to multiple phthalates in the workplace, without conducting a facility-by-facility analysis, which is outside the scope of this cumulative assessment.

3.1.2.3 Overlap in Industrial and Commercial COUs

EPA acknowledges that there is overlap in industrial and commercial COUs, and that overlap in COUs may lead to worker co-exposure to multiple phthalates at facilities where multiple phthalates are handled. As part of the 2023 draft proposal (U.S. EPA, 2023b), COU tables from final scope documents were compared for DEHP, DBP, BBP, DCHP, DIBP, and DINP, demonstrating COU overlap (Table_Apx D-4).

As part of its cumulative approach, EPA considered combining phthalate exposures for COUs with overlap for multiple phthalates. For example, exposures for phthalates with the industrial use of adhesives and sealants COU could be combined to estimate occupational cumulative exposure and risk. However, this approach would require several assumptions that would likely lead to unrealistic cumulative exposure estimates that are not reflective of the complexity and wide range of cumulative exposure scenarios that may exist in phthalate-containing workplaces. For example, this approach would require the assumption that most facilities with industrial use of adhesives and sealants are working with multiple phthalates and that these facilities are working with multiple phthalates concurrently and not running staggered campaigns with each individual phthalate. As discussed in Section 3.1.2.2, not all facilities work with multiple phthalates. In fact, the majority of facilities may work with only one phthalate (*e.g.,* 1,461 of the 1,922 facilities identified in Section 3.1.2.2 report use of a single phthalate).

Given the complexity and wide range of cumulative exposure scenarios that may exist in phthalate-containing workplaces, EPA considers there to be too much uncertainty associated with combining phthalate exposures across COUs that apply to multiple phthalates.

3.1.3 Conclusions on Cumulative Occupational Phthalate Exposure

As discussed above in Sections 3.1.1 and 3.1.2, workers may be occupationally exposed to multiple phthalates through use of an industrial or commercial product containing multiple phthalates or through working at a facility that handles multiple phthalates. However, EPA identified a limited number of industrial and commercial products that contained multiple phthalates, and the products that were identified contained low concentrations of phthalates (Section 3.1.1). This indicates that industrial and commercial products containing multiple phthalates are not anticipated to be a major source of cumulative phthalate exposure for most workers.

As discussed in Section 3.1.2, EPA identified approximately 461 facilities that report working with multiple phthalates. However, these facilities report working with varying combinations of phthalates (*e.g.,* DEHP and DBP, DEHP and BBP, DBP and BBP, or DEHP, DBP, and BBP), and may run campaigns in which each phthalate is only used for part of the year. These campaigns may not overlap and therefore there is uncertainty as to whether workers are actually co-exposed to multiple phthalates at all of the facilities identified by EPA. For example, Exxon runs continuous half-year operations dedicated to the manufacture of DINP and DIDP, which are staggered campaigns (ExxonMobil, 2022).

Due to the wide range of cumulative exposure scenarios that may exist in phthalate-containing workplaces, it was not possible to provide a robust quantitative assessment of cumulative risk for workers who may be exposed to multiple phthalates based on reasonably available data. EPA did not have data on specific use patterns, facility campaigns, or quantitative estimates of co-exposure in an occupational setting necessary for development of probabilistic exposure models. Individual occupational exposure scenarios provided estimates of worker exposure using reasonably available data, but the development of cumulative occupational exposure scenarios that involve combining these deterministic exposure estimates across multiple COUs for multiple phthalates without data to support a coherent exposure profile of a worker may lead to unrealistic cumulative exposure estimates that may yield both large overestimation and underestimation of exposure scenarios according to the SACC. Instead, EPA developed an option for deriving an OEV that accounts for cumulative exposure and differences in relative potency based on air monitoring methods (Appendix E.1).

3.2 Consumer and Indoor Dust Exposure

Consumers may become co-exposed to multiple TSCA phthalates through a variety of potential exposure scenarios. Relevant consumer exposure scenarios that may lead to co-exposure to multiple TSCA phthalates include:

- Consumer use of a product that contains multiple phthalates, thus the consumer is directly exposed simultaneously;
- Consumer use of multiple products and/or articles with multiple phthalates in a relevant time frame (*e.g.,* same day); or
- Products and/or articles containing multiple phthalates contaminate indoor dust which is then inhaled or ingested.

This section provides a qualitative overview of consumer use scenarios could plausibly lead to co-exposure to multiple phthalates (Sections 3.2.1 and 3.2.2) and a quantitative assessment of cumulative exposure to indoor dust using available monitoring data (Section 3.2.3).

3.2.1 Consumer Products Containing Multiple Phthalates.

Most products previously identified by EPA only contain a single phthalate (see Table_Apx F-1 from 2023 CRA proposal (U.S. EPA, 2023b)). EPA identified a product (PSI PolyClay Canes and PSI PolyClay Bricks) that contains multiple phthalates (DEHP, BBP, DBP, and DINP), with each phthalate below 2.5 percent. EPA compared the source and manufacturer information for the consumer products and articles included in the consumer exposure assessments for DEHP (U.S. EPA, 2025c), DBP (U.S. EPA, 2025e), BBP (U.S. EPA, 2025d), DIBP (U.S. EPA, 2025f), DCHP (U.S. EPA, 2025b), and DINP (U.S. EPA, 2025g). This comparison identified one additional trade name, 3M™ Economy Vinyl Electrical Tape 1400, 1400C, as containing DEHP and DINP. A few other generic product and article categories contained multiple phthalates (*e.g.*, Car Mats (BBP, DBP, DEHP, DIBP, DINP); synthetic leather (DBP, DEHP, DIBP, DINP); adult toy (BBP, DBP, DEHP, DINP); garden hose and cutting board (DBP, DEHP, DIBP, DINP); footwear (BBP, DBP, DIBP); shower curtain, children toys compliant, football, wallpaper (DBP, DEHP, DIBP); children's toys (BBP, DBP, DINP); packaging (BBP, DBP, DEHP); work gloves, pet chew toys, 3M electrical vinyl tape (DEHP, DINP)); however, EPA is unable to confirm whether multiple phthalates are used concurrently in each of these items, or if the phthalates are used interchangeably.

3.2.2 Consumer Use of Multiple Products and/or Articles in a Relevant Time Frame

Co-exposures to multiple phthalates across products and/or articles are dependent on evidence of co-use and/or co-location. In the context of TSCA, co-uses typically refer to scenarios from which an individual (*e.g.,* consumer) may be exposed to two or more COUs such as when a spray and powdered cleaner are used concurrently to clean a bathtub. Due to the numerous consumer products and articles found in the domestic environment that contain phthalates, it is likely that a consumer may be simultaneously exposed to phthalates from two or more different consumer products or articles. However, for co-exposure to occur, exposure would need to occur in a narrow timeframe (*i.e.,* same day) due to the fast elimination kinetics of phthalates.

As described in EPA's 2023 draft approach (U.S. EPA, 2023b), there is limited information on the co-use and/or co-location of consumer products to serve as evidence for co-exposure to different chemicals present in multiple consumer products. Some studies have investigated co-use patterns for personal care products (Safford et al., 2015; Biesterbos et al., 2013). Thus far, only one co-use study by Han et al. has been identified, which considered multiple TSCA-relevant consumer products in its analysis, including laundry detergents, fabric softeners, air fresheners, dishwashing detergents, and all-purpose cleaners. However, the authors found no strong correlation of co-use between any pair of household and personal care products (Han et al., 2020).

Another approach to determine co-use of products has been to use purchase data or presence of certain consumer products in the home to extrapolate combined exposure and risk (Stanfield et al., 2021; Tornero-Velez et al., 2021). However, the presence of consumer products in the home is insufficient to conclude resultant daily exposure for consumers. This further emphasizes the importance of co-use data that help to describe consumer use patterns (*e.g.,* which combinations of products are used, how often, how much, etc.) for products currently on the market. Currently, available co-use studies indicate that there is lack of evidence of co-use specifically for the TSCA COUs shown in Table_Apx D-4. This may

in part be because many of the TSCA COUs associated with the phthalates are not necessarily common household products regularly studied for concurrent use.

At this time, EPA did not estimate co-exposure of phthalates from multiple consumer products and articles, as there is limited quantitative information on the co-occurrence of exposures to phthalate-containing consumer products and articles within the same day.

3.2.3 Quantitative Cumulative Risk from Exposure to Indoor Dust

As emphasized by the SACC in their review of the draft 2023 approach document, indoor dust is a key pathway for phthalate exposure and represents a sink for mixtures of phthalates from multiple sources, summarized succinctly from their report as follows (U.S. EPA, 2023c):

> "Dust is a very relevant exposure pathway that may vary by community and can reflect many sources – for example outdoor dust and soil can be tracked inside, take home occupation exposures, building materials, furniture and products in the home can all contribute to household dust levels and human exposures to mixtures with phthalates. Household dust exposures will also vary by age, as younger children have faster metabolisms, greater relative surface area, more exposure to the floor, and increased hand to mouth behavior, making them likely to ingest more."

To estimate cumulative risk from phthalate exposure from indoor dust, EPA relied on monitoring data of settled dust for six phthalates (*i.e.,* BBP, DBP, DCHP, DEHP, DIBP and DINP). Using the monitoring studies on settled dust gathered via systematic review, EPA estimated average daily doses for:

- Geometric mean dust ingestion and mean phthalate concentration;
- Geometric mean dust ingestion and 95th percentile phthalate concentration;
- High end dust ingestion and mean phthalate concentration; and
- High end dust ingestion and 95th percentile phthalate concentration.

Settled dust monitoring concentrations were estimated from various monitoring studies across the US (Table 3-1) (Hammel et al., 2019; Bi et al., 2018; Bi et al., 2015; Dodson et al., 2015; Shin et al., 2014; Guo and Kannan, 2011; Wilson et al., 2003; Rudel et al., 2001; Wilson et al., 2001). These studies were selected as they contained original settled dust data, were conducted in the U.S., and reported high quality sampling and analytical methods and measured dust in homes, offices, or other indoor environments representative of the U.S. general population. Studies with unclear sampling descriptions (*e.g.,* unclear number of samples collected, unclear whether suspended dust or settled dust), were excluded from the analysis.

Using monitoring studies listed in Table 3-1, EPA calculated cumulative risk for various age groups (0–1 month, 1–3 months, 3–6 months, 6–12 months, 1–2 years, 2–3 years, 3–6 years, 6–11 years, 11–16 years, 16–21 years, 21–30 years, 30–40 years, 40–50 years, 50–60 years, 60–70 years and over 80 years) using the RPF approach described above in Section 2.

Table 3-2 provides the cumulative phthalate intake estimate for ages 3 to 6 years, and 16 to 50 years from the indoor dust monitoring data. When comparing these dust intake estimates to cumulative risk estimates for NHANES in Table 4-3, the percent contribution of NHANES to the risk cup is always greater than ingestion of settled dust. This is anticipated as NHANES urinary biomonitoring provides an estimate of aggregate exposure (*i.e.,* exposure via all routes and pathways, including dust ingestion) to each phthalate rather than just through ingestion of phthalates in settled dust.

Table 3-1. Confidence in Phthalate Settled Dust Monitoring Studies

Phthalate	Statistic	N[a]	Concentration in Dust (µg/g)	Studies	Study Confidence
BBP	Mean	388	46	(Hammel et al., 2019; Bi et al., 2018; Bi et al., 2015; Guo and Kannan, 2011; Wilson et al., 2001)	Robust
	95th	234	151	(Hammel et al., 2019; Dodson et al., 2015)	
DBP	Mean	329	38.8	(Hammel et al., 2019; Bi et al., 2018; Bi et al., 2015; Dodson et al., 2015; Guo and Kannan, 2011; Rudel et al., 2001; Wilson et al., 2001)	Robust
	95th	234	64.8	(Hammel et al., 2019; Dodson et al., 2015)	
DCHP	Mean	3	1.9	(Rudel et al., 2001)	Slight
	95th	49	7.4	(Dodson et al., 2015)	
DEHP	Mean	346	174	(Hammel et al., 2019; Bi et al., 2018; Bi et al., 2015; Rudel et al., 2001)	Robust
	95th	234	479	(Hammel et al., 2019; Dodson et al., 2015)	
DIBP	Mean	43	16	(Bi et al., 2015)	Moderate
	95th	188	33.9	(Hammel et al., 2019)	
DINP	Mean	188	78.8	(Hammel et al., 2019)	Moderate
	95th	188	787.6	(Hammel et al., 2019)	

[a] EPA did not calculate central tendencies or 95th percentiles for individual studies, rather gathered the central tendencies and 95th percentiles that were reported in the individual studies. This is why the 'n' and number of studies vary between means and 95th percentile estimates as some studies only reported central tendencies while others only reported 95th percentile values.

Table 3-2. Cumulative Phthalate Daily Intake (µg/kg-day) Estimates from Indoor Dust Monitoring Data

Age	Percentile	Phthalate	Aggregate Daily Intake (µg/kg-day) Mean[b]	Aggregate Daily Intake (µg/kg-day) High-End[b]	RPF	Aggregate Daily Intake in DBP Equivalents (µg/kg-day) Mean	Cumulative Daily Intake in DBP Equivalents (µg/kg-day)	Cumulative MOE (POD = 2,100 µg/kg-day)	% Contribution to Risk Cup (Benchmark = 30)[a]
3 – 6 years age	50	BBP	**0.10**	0.66	0.52	0.05	0.34	6,095	0.5%
		DBP	**0.08**	0.47	1	0.08			
		DCHP	**0.00**	0.00	1.66	0.00			
		DEHP	**0.23**	1.45	0.84	0.19			
		DIBP	**0.01**	0.07	0.53	0.01			
		DINP	**0.06**	0.40	0.21	0.01			
	95	BBP	0.07	**0.43**	0.52	0.23	2.39	880	3.4%
		DBP	0.03	**0.17**	1	0.17			
		DCHP	0.00	**0.01**	1.66	0.01			
		DEHP	0.20	**1.26**	0.84	1.06			
		DIBP	0.03	**0.16**	0.53	0.09			
		DINP	0.64	**3.98**	0.21	0.84			
16 – 50 years age[a]	50	BBP	**0.01**	0.08	0.52	0.00	0.02	97,684	0.0%
		DBP	**0.00**	0.06	1	0.00			
		DCHP	**0.00**	0.00	1.66	0.00			
		DEHP	**0.01**	0.18	0.84	0.01			
		DIBP	**0.00**	0.01	0.53	0.00			
		DINP	**0.00**	0.05	0.21	0.00			
	95	BBP	0.00	**0.06**	0.52	0.03	0.31	6,830	0.4%
		DBP	0.00	**0.02**	1	0.02			
		DCHP	0.00	**0.00**	1.66	0.00			
		DEHP	0.01	**0.16**	0.84	0.13			
		DIBP	0.00	**0.02**	0.53	0.01			
		DINP	0.04	**0.51**	0.21	0.11			

[a] Cumulative estimates from the 16–21 years age range were used to represent 16–50 years of age as all of these age groups (16–21 years, 21–30 years, 30–40 years and 40–50 years) had the same % contribution to the risk cup (0.0% and 0.4% for the 50th and 95th percentiles). 16–21 years of age had the lowest MOEs of these age groups (16-21 years, 21–30 years, 30–40 years and 40–50 years).
[b] Bolded values are carried forward to calculate cumulative Daily Intake (DBP Equivalents, µg/kg-day).

3.2.4 Conclusions on Cumulative Consumer and Indoor Dust Phthalate Exposure

For co-exposure to occur, exposure would need to occur in a narrow timeframe (*i.e.*, same day) due to the fast elimination kinetics of phthalates. This could occur from use of a single product containing multiple phthalates but, as discussed above in Sections 3.2.1, EPA has not identified much evidence of multiple phthalates being used in a single consumer product to suggest that this is a substantial pathway of co-exposure to multiple phthalates for consumers.

Due to the numerous consumer products and articles found in the domestic environment that contain phthalates, it is highly plausible that a consumer may be simultaneously exposed to phthalates from two or more different consumer products or articles. EPA identified limited quantitative information on the co-occurrence or co-use of phthalate-containing consumer products and articles within the same day to facilitate a robust and specific cumulative scenario based on specific COUs.

However, as discussed in Section 3.2.3, occurrence of phthalates in house dust is widespread. EPA has estimated cumulative exposure and risk from exposure to phthalates from ingestion of house dust. The highest cumulative phthalate exposure from ingestion of house dust was for children (3–5 years of age) using high-end dust ingestion assumptions and 95th percentile phthalate concentrations in house dust. When comparing these dust intake estimates to cumulative MOEs for NHANES in Table 4-3, the percent contribution of NHANES to the risk cup is always much greater than ingestion of settled dust. This is anticipated as NHANES urinary biomonitoring provides an estimate of aggregate exposure (*i.e.*, exposure via all routes and pathways, including dust ingestion) to each phthalate rather than just through ingestion of phthalates in settled dust.

Therefore, at this time, EPA did not estimate co-exposure of phthalates from the direct use of multiple consumer products (Section 3.2.2) beyond the estimation of non-attributable exposure described further in Section 4. To do so would require additional data, which was not reasonably available, on consumer data to support evidence of co-use and use patterns of products for the development of probabilistic exposure models. Individual exposure scenarios provided estimates of consumer exposure using reasonably available data, but the development of cumulative consumer exposure scenarios that involve combining these deterministic exposure estimates across multiple COUs for multiple phthalates without data to support a coherent exposure profile of a consumer may lead to unrealistic cumulative exposure estimates that may yield both large overestimation and underestimation of exposure scenarios according to the SACC.

3.3 General Population Exposure to Environmental Releases

General population exposures to environmental releases occur when phthalates are released into the environment and the environmental media is then a pathway for exposure. As described in the draft approach, the general population may be exposed to multiple phthalates either from single facilities releasing more than one phthalate or from being in close proximity to co-located facilities. This section provides a brief overview of the chemical properties across the phthalates of interest in Section 3.3.1 and considers the geographic distribution of facilities with phthalate releases in Section 3.3.2.

3.3.1 Comparison of Fate Parameters Across Phthalates

Phthalate releases from facilities are expected to occur to air, water, and land. Based on the fate parameters of the various phthalates, once released into the environment, phthalates are expected to primarily partition to sediment and biosolids. However, despite phthalates being expected primarily in

sediments and biosolid, exposure to the general population would be mostly likely to occur primarily through drinking water and fish ingestion based on the individual phthalate risk evaluation exposure assessments. The physical chemical properties and fate parameters govern environmental fate and transport and are detailed in the technical support documents for each chemical substance: DEHP (U.S. EPA, 2025ab), BBP (U.S. EPA, 2024a), DBP (U.S. EPA, 2025aa), DIBP (U.S. EPA, 2024c), DCHP (U.S. EPA, 2024b), DINP (U.S. EPA, 2025ac). These properties and parameters for the cumulative chemical group are summarized below in Table 3-3 and in this section.

The magnitude of the partitioning coefficients identified for these phthalates suggest that they may exist in surface water in both aqueous form and in suspension, and sorbed to organic carbon fractions in soil, sediment, and air in the environment. The lower Henry's Law constants of these phthalates indicate that they are not expected to volatilize from surface water. DEHP, BBP, DBP, DIBP, DCHP, and DINP have very low to slight solubility in water. DEHP and DIDP have very low water solubility (0.003 mg/L for DEHP; 0.00061 mg/L for DINP; 0.00017 mg/L for DIDP), while BBP, DBP, DIBP, and DCHP are slightly soluble in water (2.3 mg/L for BBP; 11.2 mg/L for DBP; 6.2 mg/L for DIBP; 0.03–1.48 mg/L for DCHP). Sorption to organics present in sediment and suspended and dissolved solids present in water is expected to be a dominant process given the range of identified log K_{OC} values across DEHP, DBP, BBP, DIBP, DCHP, and DINP (Table 3-3). BBP's solubility and range of log K_{OC} values for phthalates in the cumulative chemical group (Table 3-3) suggests that they are unlikely to exhibit mobility in soils, which is also supported by fugacity modeling results. In general, amongst phthalates in the cumulative chemical group, as molecular weight decreases, water solubility and vapor pressure increase, while tendency to partition to organic carbon (sorption to soils and sediments) and environmental half-lives also decrease.

Phthalates in the cumulative chemical group in surface water are subject to two primary competing processes: biodegradation and adsorption to organic matter in suspended solids and sediments. Phthalates in the cumulative chemical group in the freely dissolved phase are expected to show low persistence, with rapid biodegradation under aerobic conditions. The fraction of phthalates in the cumulative chemical group adsorbed to particulates increases with water salinity due to a salting out effect, as indicated by greater log K_{OC} values measured in saltwater as compared to those measured with freshwater. Monitoring data in the U.S. generally show low detection frequencies in surface water. Sampling of U.S. surface water sediments yielded a wide range of concentrations; however, all of these phthalates were generally found in low concentrations where they were detected and often with low detection frequencies. Phthalates in the cumulative chemical group are expected to be removed in conventional drinking water treatment processes by means of aggregation to floccules and subsequent settling and filtration processes, as well as by oxidation by chlorination byproducts in post-treatment and transmission of finished drinking water.

The vapor pressures of the phthalates in the cumulative chemical group indicate that they will preferentially adsorb to particulates in the atmosphere, with adsorbed fractions being resistant to photolysis. This is consistent with measured and estimated octanol:air partition coefficients (Table 3-3). Phthalates in the cumulative chemical group that do occur in the atmosphere will likely degrade via ·OH-mediated indirect photolysis with a half-life of hours to days based on an estimated ·OH reaction rate constants, and assuming a 12-hour day with 1.5×10^{6} ·OH/cm^3 (U.S. EPA, 2017). Phthalates in the cumulative chemical group are generally consistently detected at low concentrations in ambient air; however, given their atmospheric half-lives, they are not expected to be persistent in air or undergo long range transport.

Phthalates in the cumulative chemical group present low bioconcentration potential in fish, are unlikely to biomagnify, and will exhibit trophic dilution in aquatic species. Biomagnification or bioaccumulation of terrestrial and avian species is also not likely.

Table 3-3. Summary of Physical Chemical Properties and Fate Parameters of DCHP, DBP, DIBP, BBP, DEHP, and DINP

Property	DEHP (U.S. EPA, 2025ab)	BBP (U.S. EPA, 2024a)	DBP (U.S. EPA, 2025aa)	DIBP (U.S. EPA, 2024c)	DCHP (U.S. EPA, 2024b)	DINP (U.S. EPA, 2025ac)
Molecular formula	C_{24} H_{38} O_4	$C_{19}H_{20}O_4$	$C_{16}H_{22}O_4$	$C_{16}H_{22}O_4$	$C_{20}H_{26}O_4$	$C_{26}H_{42}O_4$
Molecular Weight (g/mol)	390.56	312.37	278.35	278.35	330.43	418.62
Physical state of the chemical	Colorless, oily liquid	Clear oil, liquid	Colorless to faint yellow, oily liquid	Colorless, clear, viscous liquid	White, granular solid	Clear Liquid
Melting Point (°C)	−55	-35	-35	−64	66	−48
Boiling Point (°C)	384	370	340	296.5	225	>400
Density (g/cm^3)	0.981	1.119	1.0459 to 1.0465	1.049	1.383	0.97578
Vapor Pressure (mmHg)	1.42E-07	8.25E-06	2.01E-05	4.76E-05	8.69E-07	5.40E-07
Water Solubility (ng/L)	3,000	2,690,000	11,200,000	6,200,000	30000 - 1,480,000	610
Log K_{OW}	7.6	4.73	4.5	4.34	4.82	8.8
Log K_{OA} (estimated using EPI Suite™)	10.76	9.2	8.63	9.47	10.23	11.9
Log K_{OC}	3.75-5.48	2.09-2.91	3.16-4.19	2.5-3.14	3.46-4.12	5.5-5.7
Henry's Law Constant (atm-m^3/mol)	1.71E-05	7.61E-07	1.81E-06	1.83E-07	9.446E-08	9.14E-05
Flash Point (°C)	206	199	157.22	185	207	213
Autoflammability (°C)	390	-	402.778	432	No data	400
Viscosity (cP)	57.94	55	20.3	41	Not applicable (solid)	77.6
Overall Environmental Persistence	Low	Low	Low	Low	Low	Low
Bioaccumulation Factor (Log BAF A-G)	3.02	1.60	2.20	1.41	2.14	1.14
Bioconcentration Factor (Log BCF A-G)	2.09	2.88	2.20	1.41	2.13	0.39

3.3.2 Geographic Consideration of Reported Releases of Phthalates

In the draft 2023 approach (U.S. EPA, 2023b), EPA recognized that the general population, those impacted by facility release of phthalates, could be exposed to multiple phthalates from single facilities that release more than one phthalate or be exposed to multiple phthalates due to living in close proximity to co-located facilities. Given the chemical properties described in Section 3.3.1 and the chemical-specific Fate TSDs, the major pathway for any environmental exposure would be sediments and biosolids from continuous or recent concurrent releases. Therefore, EPA analyzed the co-location of all the known phthalate-releasing facilities within common watersheds.

As described above in Section 3.1.2.2, EPA identified DMR, NEI, and TRI data for DEHP, DBP, and BBP, but not for DCHP, DINP, and DIBP. These EPA databases provide information on facilities releasing phthalates to various environmental media and provide latitude and longitude data for releasing facilities. Using the release information, EPA identified 1,461 facilities that report use of a single phthalate, while 461 report use of multiple phthalates (*i.e.*, any combination of DEHP, DBP, or BBP). Using the available location data, EPA mapped the reporting facilities in Figure 3-1 to look for geographic patterns or hotspots. Individual facilities are broadly dispersed around the United States. Of note, no releasing facilities are reported in Alaska, an area of note in the SACC review of the draft 2023 approach (U.S. EPA, 2023c).

EPA also analyzed the locations of the identified facilities by watershed or hydrologic units. A hydrologic unit represents the area of the landscape that drains to a portion of the stream network and is identified by a unique Hydrologic Unit Code (HUC). EPA searched for the HUC12 watershed level, which represents an average size of 36 square miles (The RPS Methodology: Comparing Watersheds, Evaluating Options | US EPA), for each the identified facilities. These are listed in in the *Summary of Facility Release Data for Di(2-ethylhexyl) Phthalate (DEHP), Dibutyl Phthalate (DBP), and Butyl Benzyl Phthalate (BBP)* (U.S. EPA, 2025ah). In the following HUC12 watersheds, four or more releasing facilities are identified:

- 120401040703 in Harris County, TX (11 facilities)
- 180300090701 in Fresno County, CA (9 facilities)
- 120401040706 in Harris County, TX (8 facilities)
- 120402040100 in Harris County and Brazoria County, TX (8 facilities)
- 101900030304 in Denver County, CO (6 facilities)
- 040601020303 in Wexford County, MI (6 facilities)
- 180701050401 in Los Angeles County, CA (5 facilities)
- 180701060701 in Los Angeles County, CA (5 facilities)
- 170900120202 in Multnomah County, OR (5 facilities)
- 180701030202 in Ventura County, CA (5 facilities)
- 030501010804 in Burke and Catawba Counties, NC (5 facilities)
- 030501010701 in Caldwell County, NC (5 facilities)
- 180702030804 in San Bernardino and Riverside Counties, CA (4 facilities)
- 180701060502 in Los Angeles County, CA (4 facilities)
- 180400030205 in San Joaquin County, CA (4 facilities)
- 180701060102 in Los Angeles County, CA (4 facilities)
- 180703041202 in San Diego County, CA (4 facilities)
- 071401010403 in St. Clair County, IL and St. Louis County, MO (4 facilities)
- 020301040205 in Hudson County, NJ and Kings County, NY (4 facilities)

- 020402010407 in Burlington County, NJ and Bucks County, PA (4 facilities)
- 020200041108 in Schenectady County, NY (4 facilities)

Even where co-located facilities within watersheds have been identified, there is difficulty in estimating the cumulative exposures in those locations. First, the programmatic data from DMR, NEI, and TRI are reported per facility for a single reporting year. Although information such as the highest release is reported, there is no information on the timing of release of phthalates into the environment, making it difficult to identify any areas that are impacted by multiple phthalates concurrently.

Additionally, although EPA identified 461 facilities reporting the use of multiple phthalates, the reporting data does not state whether the multiple phthalates are used concurrently within the facility and released simultaneously to the environment. Often, use or production of multiple chemicals such as the phthalates occur in campaigns, where a single phthalate is used for a determined period of time before the facility uses another phthalate for another period of time. In these instances, phthalates would not be released from the facility concurrently and, therefore, may not pose a cumulative exposure to surrounding communities based on the fate parameters of the phthalates. EPA recognizes that the lack of data on the timing of the releases makes it difficult to quantify cumulative exposure from facilities reporting use of multiple phthalates.

In general, EPA recognizes that there may be discrete locations impacted by the release of multiple phthalates either through single facilities releasing multiple phthalates or multiple facilities within the same watershed or releasing to the same wastewater facility. Releases would need to be continuous to lead to ongoing exposure given the relatively low persistence in the environment. In the risk evaluations for the individual phthalates, the general population exposures from pathways such as drinking water, recreational swimming, ambient air, incidental soil ingestion, and fish ingestion for each phthalate are estimated and found to be much lower than exposures for consumer and occupational populations, even when quantified using a screening level assessment using conservative (*e.g.*, low tier, high risk) assumptions.

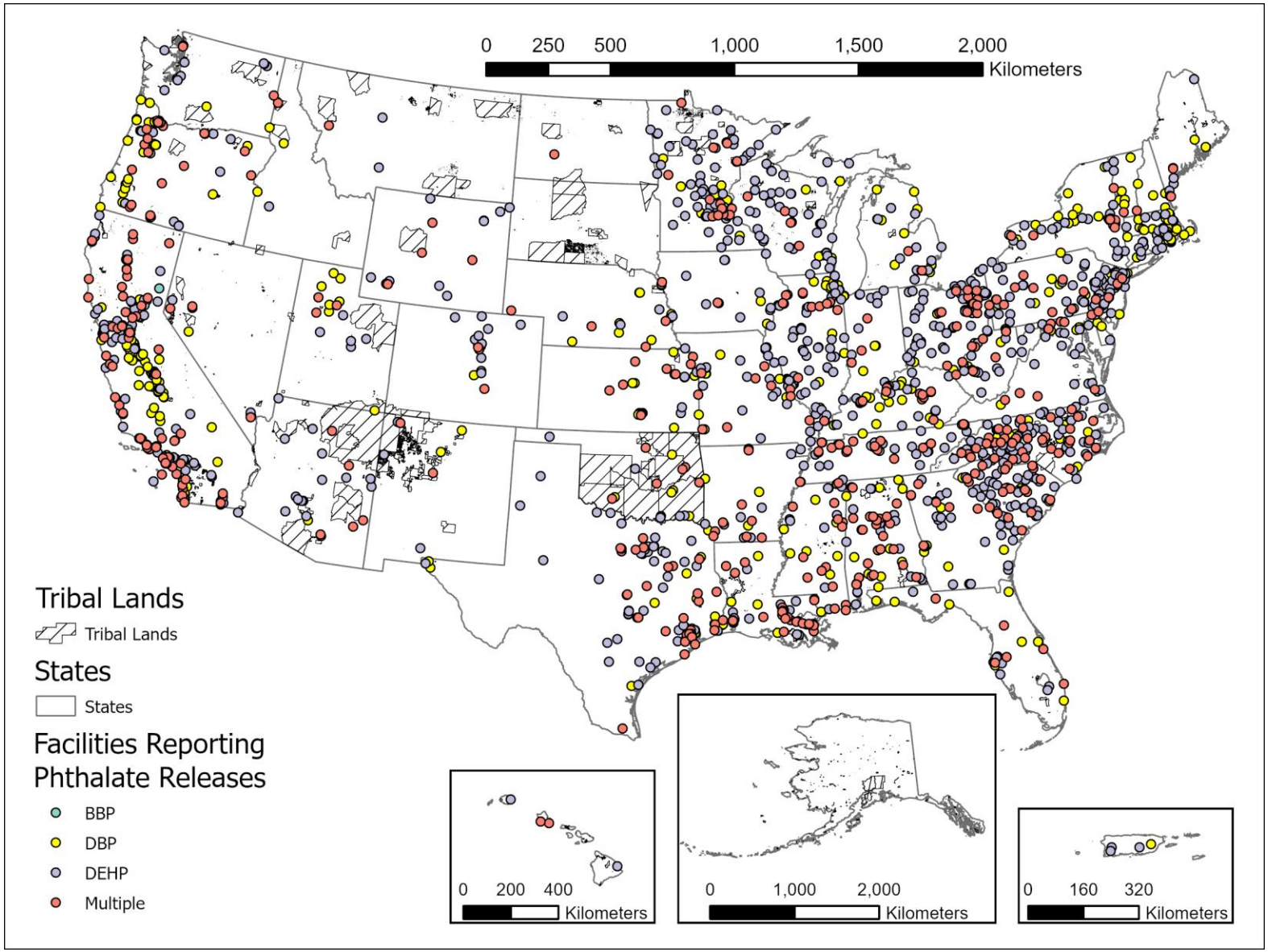


Figure 3-1. Mapping of Facilities with One of Multiple Phthalates

3.3.3 Conclusions on Cumulative General Population Exposure to Environmental Releases of Phthalates

The general population may be exposed to the environmental releases of multiple phthalates from a facility that releases multiple phthalates or from facilities in proximity releasing into the same watershed. As discussed above in Section 3.3.1 and in the individual chemical technical support documents, phthalates are expected to partition primarily to sediments and biosolids with human exposure most likely to occur through drinking water and fish ingestion. However, the phthalates have relatively low persistence, low bioaccumulation potential, and low long-range transport so they are unlikely to build up in the environment, including artic environments. Localized, site specific co-exposures are possible but overall exposures are expected to be marginal compared to total exposure.

Therefore, at this time, EPA did not estimate co-exposure of phthalates from multiple releasing facilities or facilities releasing multiple phthalates. Given the reliance on screening methods for estimating general population exposure to environmental releases, EPA discourages the aggregation of modeled screening estimates without more refined exposure models or monitoring data.

3.4 Non-TSCA Exposures

Non-TSCA exposures to a combination of phthalates may occur through diet which includes the consumption of phthalates from food packaging, as well as through use of personal care products, and other sources. Using a scenario-based approach, U.S. Consumer Product Safety Commission (CPSC) found the majority of women's exposure to DEHP (84–88% of total exposure), DINP (45–95% of total exposure), and DIBP (87–91% of total exposure) was from diet, while the majority of women's exposure to DBP was from nail polish use (59–94% of total exposure) and to a lesser extent diet (4–26% of total exposure)) (DCHP was not included in their analysis) (see Table E1-20 in (CPSC, 2014)). Their estimates were in general agreement (within an order of magnitude) with two other studies estimating phthalate exposure using scenario-based exposure assessment methods with differences attributable to differing approaches for dietary exposure estimation (Clark et al., 2011; Wormuth et al., 2006). U.S. CPSC (2014) estimated dietary exposure using two datasets of phthalate residues in food items (Bradley et al., 2013; Page and Lacroix, 1995). Additional studies were used for food categorization and consumption estimates, including the U.S. EPA National Center for Environmental Assessment's analysis of food intake and diet composition (Clark et al., 2011; U.S. EPA, 2007; Wormuth et al., 2006).

Health Canada concluded that the main sources of exposure to the general Canadian population for medium-chain phthalates were food, indoor air, dust, and breast milk (Health Canada, 2020). For example, Health Canada found that diet accounted for 85 to 96% of total exposure for BBP, 63 to 74 percent of total exposure for DBP, 92 to 98 percent of total exposure of total exposure for DEHP, and 95 to 96 percent of total exposure for adults 20 to 59 years of age. For their estimation of dietary intake of DIBP, BBP, DBP, and DEHP, Health Canada used the 2013 Canadian Total Diet Study (Health Canada, 2020). For other phthalates, they used the 2013 through 2014 and 2014 through 2015 Food Safety Action Plan (Canadian Food Inspection Agency) and/or a dietary exposure study from the United States (Schecter et al., 2013). A United Kingdom total diet study (Bradley et al., 2013) was used to fill in data gaps. The phthalate concentrations were matched to 2004 Canadian Community Health Survey on nutrition (Statistics Canada, 2004) consumption values for each individual food.

In the draft 2023 approach (U.S. EPA, 2023b), EPA proposed using a scenario-based exposure assessment to determine non-attributable and non-TSCA source exposure levels to all phthalates and to

reconstruct an aggregated daily exposure profile for receptors varied by age (women of reproductive age, male infants, toddlers, and children). The approach proposed was to use similar methods to Health Canada (Health Canada, 2020) and U.S. CPSC (2014), which determined that diet comprised a large portion of total daily intake for populations of interest. In its review of the approach, SACC recommended reviewing literature related to estimates of exposure from diet given the highly diverse U.S. population (U.S. EPA, 2023c). EPA conducted a literature search to investigate if there were any large-scale phthalate dietary assessments that would influence a national scale dietary assessment or warrant an update to the previously conducted analyses. However, EPA has concluded that there is limited updated information to substantially change the daily intake estimates previously constructed by the other agencies using scenario-based methods, including for sensitive subpopulations.

Health Canada (Health Canada, 2020) and U.S. CPSC (2014) had both estimated total phthalate daily intake values using reverse dosimetry with human urinary biomonitoring data and scenario-based exposure assessment approaches. Health Canada and U.S. CPSC found that both the reverse dosimetry and scenario-based approaches resulted in daily intake values that were generally similar in magnitude. However, this depended on the recency and quality of data available for use, particularly for data on major exposure pathways like diet. Rather than construct new national estimates of dietary intake, EPA is similarly using reverse dosimetry with national human urinary biomonitoring data, described further in Section 4, which provides total intake for total population and subpopulations by demographic category. National human urinary biomonitoring data are expected to reflect exposure to the major non-TSCA sources of exposure (*e.g.*, diet, personal care products, indoor air, and house dust) identified by U.S. CPSC and Health Canada.

4 PHTHALATE EXPOSURE AND RISK FOR THE U.S. POPULATION USING NHANES URINARY BIOMONITORING DATA

The U.S. Center for Disease Control's (CDC) National Health and Nutrition Examination Survey (NHANES) is an ongoing exposure assessment of the U.S. population's exposure to environmental chemicals using biomonitoring. The NHANES biomonitoring dataset is a national, statistical representation of the general, non-institutionalized, civilian U.S. population. As described in the *Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the Toxic Substances Control Act* (draft 2023 approach) (U.S. EPA, 2023b), a reverse dosimetry approach for exposure and risk analysis relies on CDC's NHANES urinary biomonitoring dataset and a single compartment toxicokinetic model to estimate total exposure to individual phthalates for the U.S. civilian population.

There are several limitations associated with the use of NHANES data. First, exposures measured via NHANES cannot be attributed to specific sources. Given the short half-lives of phthalates, neither can NHANES capture acute, low frequency exposures. Instead, as concluded by the SACC review of the draft 2023 approach, NHANES provides a "snapshot" or estimate of total, non-attributable phthalate exposure for the U.S. population and relevant subpopulations (U.S. EPA, 2023c). These estimates of total non-attributable exposure can supplement assessments of scenario-specific acute risk in individual risk evaluations.

As can be seen from Table 4-1, monoester metabolites of BBP, DBP, DEHP, DIBP, and DINP in human urine are regularly measured as part of the NHANES biomonitoring program and are generally detectable in human urine at a high frequency, including during the most recent NHANES survey period (*i.e.*, 2017 to 2018). For DEHP, four urinary metabolites are regularly monitored as part of NHANES, including mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono(2-ethyl-5-carboxypentyl) phthalate (MECPP), and mono(2-ethyl-5-oxohexyl) phthalate (MEOHP). For DBP and DIBP, two urinary metabolites of each phthalate are regularly monitored, including mono-n-butyl phthalate (MnBP) and mono-3-hydroxybutyl phthalate (MHBP) for DBP and mono-2-methyl-2-hydroxypropyl phthalate (MHiBP) and mono-isobutyl phthalate (MIBP) for DIBP. For DINP, three urinary metabolites are regularly monitored (*i.e.*, mono-isononyl phthalate [MINP], mono-oxoisononyl phthalate [MONP], and mono-(carboxyoctyl) phthalate [MCOP]), while one metabolite is regularly monitored for BBP (*i.e.*, mono-benzyl phthalate [MBzP]). One urinary metabolite of DCHP (*i.e.*, monocyclohexyl phthalate [MCHP]) was included in NHANES from 1999 through 2010, but was excluded from NHANES after 2010 due to low detection levels and a low frequency of detection in human urine (detected in less than 10% of samples in 2009 to 2010 NHANES survey) (CDC, 2013a). Further details regarding the limit of detection, frequency of detection, additional methodological and results for each phthalate can be found in Appendix C, as well as in the environmental media and general population exposure assessments for DEHP (U.S. EPA, 2025j), DBP (U.S. EPA, 2025i), BBP (U.S. EPA, 2025l), DIBP (U.S. EPA, 2025m), DINP (U.S. EPA, 2025k), and DCHP (U.S. EPA, 2025h).

Table 4-1. Urinary Phthalate Metabolites Included in NHANES

Phthalate	NHANES Urinary Metabolite [a]	Associated Parent Compound	NHANES Reporting Years [b]	% Samples Below the LOD in 2017–2018[b] NHANES (All Participants, N=2,762)
DEHP	Mono-2-ethylhexyl phthalate (MEHP)	DEHP	1999–2018	43.77%
	Mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)	DEHP	2001–2018	0.98%
	Mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP)	DEHP	2001–2018	0.83%
	Mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP)	DEHP	2003–2018	0.18%
DBP	Mono-3-hydroxybutyl phthalate (MHBP)	DBP	2013–2018[d]	24.91%
	Mono-n-butyl phthalate (MnBP)	DBP, BBP	1999–2018	0.69%
BBP	Mono-benzyl phthalate (MBzP)	BBP	1999–2018	3.8%
DIBP	Mono-isobutyl phthalate (MIBP)	DIBP	2001–2018	4.89%
	Mono-2-methyl-2-hydroxypropyl Phthalate (MHiBP)	DIBP	2013–2018[d]	2.17%
DCHP	Mono-cyclohexyl phthalate (MCHP)	DCHP	1999–2010	–[c]
DINP	Mono-isononyl phthalate (MiNP)	DINP	1999–2018	12.57%
	Mono-oxoisononyl phthalate (MONP)	DINP	2015–2018	12.85%
	Mono-(carboxyoctyl) phthalate (MCOP)	DINP	2005–2018	0.51%

Abbreviations: LOD = limit of detection
[a] NHANES reports uncorrected and creatinine corrected urine concentrations for each metabolite.
[b] 2017–2018 is the most recently available NHANES dataset.
[c] In the 2009 to 2010 survey year (last survey in which MCHP was monitored), MCHP was above the LOD in 4.3% of samples for all adults 16 years and older, and 7.9% of samples for all children 3 to less than 16 years of age (see Appendix C for further details).
[d] MHBP and MHiBP were measured in the 2013 to 2018 NHANES cycles; however, the data for the 2013 to 2014 NHANES cycle was determined to be inaccurate due to procedural error and only released as surplus data, which are not readily publicly available (https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/2013/DataFiles/SSPHTE_H.htm; accessed December 17, 2025). As a result, the present analysis only includes urinary MHBP data from the 2015 to 2018 NHANES cycles.

EPA analyzed NHANES urinary biomonitoring data from 1999 through 2018 for metabolites of DEHP, DBP, BBP DIBP, DINP, and DCHP for several subpopulations reported within NHANES to determine median and 95th percentile exposure estimates for each urinary metabolite measured in NHANES. EPA also analyzed the available urinary biomonitoring data to understand temporal trends in phthalate exposure for the civilian U.S. population (discussed further in Section 4.1). These analyses were performed for the following populations reported within NHANES, including:

- Male and female children aged 3 to less than 6 years, 6 to 11 years, and 11 to less than 16 years;
- Male and female adults 16 years of age and older; and
- Women of reproductive age (16 to 49 years of age).

Using reverse dosimetry, EPA also estimated non-attributable daily intake values for DEHP, DBP, BBP, DIBP, and DINP using the most recent NHANES urinary biomonitoring data from 2017 to 2018. Reverse dosimetry involves estimating aggregate exposure (expressed as a daily intake value) for each individual phthalate from human urinary biomonitoring data for metabolites unique to each parent phthalate (discussed further in Section 4.2). Reverse dosimetry approaches that incorporate basic

pharmacokinetic information are available for phthalates (Koch et al., 2007; Koch et al., 2003; David, 2000) and have been used in previous human health cumulative risk assessments conducted by U.S. CPSC (2014) and Health Canada (Health Canada, 2020). Consistent with EPA's decision to focus its phthalate CRA on women of reproductive age (16 to 49 years) and male infants, male toddlers, and male children as susceptible subpopulations (Section 1.4) (U.S. EPA, 2023b), EPA used NHANES urinary biomonitoring and reverse dosimetry to estimate daily intake values for:

- Women of reproductive age (16 to 49 years of age);
- Male children 3 to less than 6 years of age (used as a proxy for male infants and toddlers);
- Male children 6 to 11 years of age; and
- Male children 12 to less than 16 years of age.

Daily intake values were calculated for women of reproductive age, because this population most closely aligns with the selected hazard (*i.e.,* reduced fetal testicular testosterone content) and generally too few pregnant women are sampled as part of NHANES to support a statistical analysis in survey years after 2005 to 2006 (CDC, 2013b; Curtin et al., 2012), and other national datasets are not available. Daily intake values were calculated for male children because testosterone plays an important role in male sexual development during fetal and postnatal lifestages. Since NHANES does not include urinary biomonitoring for infants or toddlers, and other national datasets are not available, EPA used biomonitoring data from male children 3 to less than 6 years of age as a proxy for male infants (<1 year) and toddlers (1−2 years).

For women of reproductive age, daily intake values were also calculated based on race as reported in NHANES (*i.e.*, white non-Hispanic, black non-Hispanic, Mexican-American, other) and socioeconomic status (*i.e.*, above or below the poverty line, unknown income) to better understand if these factors influence phthalate exposure and cumulative risk for the U.S. population. A similar analysis by race was not done for male children because the NHANES sample size is smaller for this population.

EPA provides a summary of temporal trends observed for each phthalate metabolite in Section 4.1. Sections 4.2 and 4.3 provide estimates of aggregate and cumulative phthalate daily intake values, respectively, for women of reproductive age and male children reported within NHANES. Section 4.4. provides cumulative MOEs for women of reproductive age and male children within the U.S. population based on daily intake estimates from NHANES. Section 4.5 summarizes EPA weight of scientific evidence conclusions.

4.1 Temporal Trends in Phthalate Exposure Based on NHANES Urinary Biomonitoring Data

EPA evaluated NHANES urinary biomonitoring data from 1999 to 2018 for DEHP, DBP, BBP, DIBP, and DINP to determine any trends in phthalate exposure within the U.S. civilian population over the past two decades. This temporal trends analysis was conducted for the following populations:

- All NHANES participants;
- All adults (16 years and older);
- Female adults (16 years and older);
- Male adults (16 years and older);
- Children 3 to less than 6 years, 6 to less than 11 years, and 11 to less than 16 years (not stratified by sex);
- Male children less than 16 years of age; and

- Female children less than 16 years of age.

Results for this temporal trends analysis are summarized below and in more detail in Appendix C. For convenience, median phthalate urinary metabolite concentrations for the NHANES 'All Participants' group from 1999 through 2018 are provided in Figure 4-1. Overall, several notable trends in phthalate exposure for the U.S. population were observed, including:

- Overall 50th and 95th percentile urinary metabolites of DEHP (MEHP, MEHPP, MEOHP, MEOCP), DBP (MnBP), and BBP (MBzP) have statistically significantly decreased over time (1999−2018) for all populations, indicating declining exposure for these phthalates in the U.S. population (see Appendices C.2.1 − C.2.3 for further details).
- For DIBP, 50th and 95th percentile urinary MIBP concentrations statistically significantly increased over time (1999−2018) for all lifestages, while 50th and 95th percentile MHiBP urinary concentrations statistically significantly decreased over time (2015−2018) for most life stages at the population level (see Appendix C.2.4 for further details). However, urinary MHiBP data are only available from two NHANES survey periods and it is unclear if this trend in declining exposure will persist as additional NHANES data becomes available.
- For DINP, urinary concentrations of MCOP and MINP statistically significantly increased from 2005 through 2014 for all NHANES participants. After 2014, urinary concentrations of MCOP and MINP statistically significantly decreased for all NHANES participants at the population level (see Appendix C.2.5 for further details).

EPA did not conduct a temporal trends analysis for DCHP. The DCHP urinary metabolite, MCHP, was monitored as part of NHANES from 1999 through 2010, but was not included in subsequent survey years because of the low detection levels and low frequency of detection of MCHP in urine. For example, in the 2009 to 2010 NHANES survey, MCHP was detectable in only 4.3 percent of samples for all adults 16 years and older, and 7.9 percent of samples for all children 3 to less than 16 years of age. These results indicate low exposure to DCHP for the U.S. civilian population (Appendix C.1).

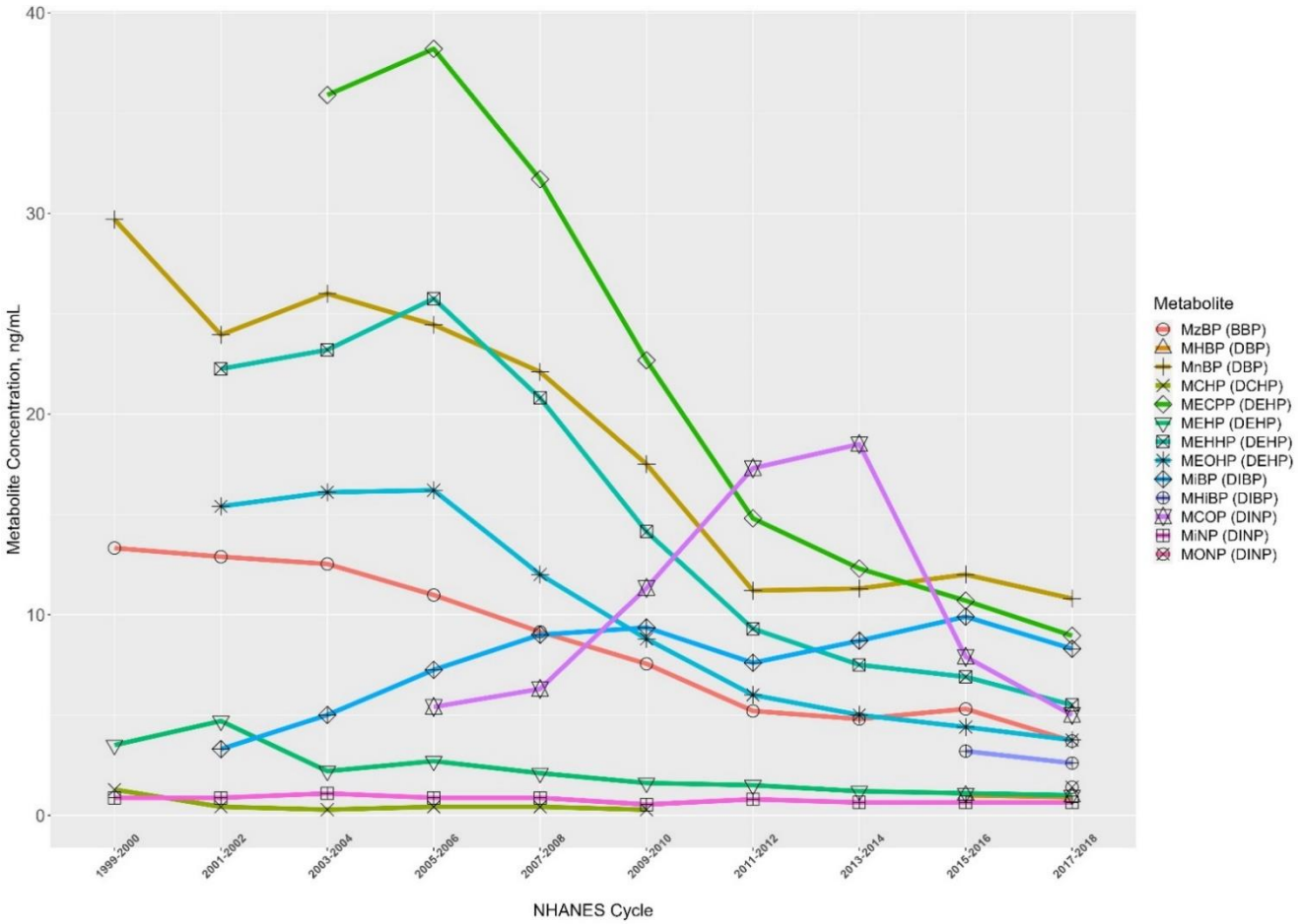


Figure 4-1. Median Phthalate Metabolite Concentrations Over Time for All NHANES Participants From 1999 Through 2018

4.1.1 Trends in National Aggregate Production Volume Data

EPA also considered whether temporal trends in national aggregate production volume data mirror those observed in NHANES urinary biomonitoring data. To do this, EPA extracted national aggregate production volume (PV) data for DEHP, DBP, DIBP, BBP, DCHP, and DINP from the 2016 and 2020 Chemical Data Reporting (CDR) (Appendix D.1). In CDR, national aggregate PV data are reported as a range to protect PV data claimed as confidential business information (CBI). Given the large ranges in reported PV data for each phthalate, EPA was unable to conclude whether there are any trends in PV for any phthalate over this time period.

4.2 Aggregate Phthalate Exposure Based on NHANES Urinary Biomonitoring Data and Reverse Dosimetry

Using DEHP, DBP, BBP, DIBP, and DINP urinary metabolite concentrations measured in the most recently available NHANES survey from 2017 to 2018, EPA estimated the daily intake of each phthalate through reverse dosimetry. NHANES provides an estimate of aggregate exposure for each individual phthalate. EPA defines *aggregate exposure* as the "combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways" (40 CFR § 702.33). Reverse dosimetry approaches that incorporate basic pharmacokinetic information are available for phthalates

(Koch et al., 2007; Koch et al., 2003; David, 2000) and have been used in previous phthalate risk assessments conducted by U.S. CPSC (2014) and Health Canada (Health Canada, 2020) to estimate daily intake values for exposure assessment. For phthalates, reverse dosimetry can be used to estimate a daily intake value for a parent phthalate diester based on phthalate monoester metabolites measured in human urine. Further details regarding the reverse dosimetry method used by EPA to estimate daily intake values, as well as a discussion of limitations and uncertainties associated with the reverse dosimetry method, are provided in Appendices C.3 and C.5, respectively.

Table 4-2 shows the 50th and 95th percentile aggregate daily intake values for DBP, DEHP, BBP, DIBP, and DINP for women of reproductive age (16 to 49 years) and male children (ages 3 to 5, 6 to 11, and 12 to 15 years), while Table 4-3 shows the aggregate 50th and 95th percentile daily intake values for women of reproductive age stratified by race and socioeconomic status. For women of reproductive age (Table 4-2), aggregate daily intake values were highest for DEHP and DINP, with 50th and 95th percentile aggregate daily intake values of 0.53 and 1.48 µg/kg-day, respectively, for DEHP and 0.7 and 5.6 µg/kg-day, respectively, for DINP. Comparatively, aggregate daily intake values for women of reproductive age were lower for DBP (50th and 95th percentile daily intake values: 0.21 and 0.61 µg/kg-day, respectively), BBP (50th and 95th percentile daily intake values: 0.08 and 0.42 µg/kg-day, respectively), and DIBP (50th and 95th percentile daily intake values: 0.2 and 0.57 µg/kg-day, respectively) (Table 4-2).

As can be seen from Table 4-2, for male children, aggregate exposure to each individual phthalate was generally the highest for male children 3 to 5 years old, and declined with age such that male children 11 to 15 years old generally had the lowest aggregate exposure estimates. Similar to women of reproductive age, aggregate daily intake values were highest for DEHP and DINP for all age groups for male children, followed by DBP, DIBP, and BBP (Table 4-2). Aggregate daily intake values ranged from 0.66 to 2.11 µg/kg-day and 2.51 to 6.44 µg/kg-day at the 50th and 95th percentiles, respectively, for DEHP (depending on age group), and ranged from 0.6 to 1.4 µg/kg-day and 3.4 to 4.8 µg/kg-day at the 50th and 95th percentiles, respectively, for DINP (depending on age group) (Table 4-2). Comparatively, aggregate daily intake values for male children were lower for DBP (ranging from 0.33 to 0.56 µg/kg-day and 0.62 to 2.02 µg/kg-day day at the 50th and 95th percentiles, respectively, depending on age group); BBP (ranging from 0.14 to 0.22 µg/kg-day and 0.64 to 2.46 µg/kg-day day at the 50th and 95th percentiles, respectively, depending on age group); and DIBP (ranging from 0.21 to 0.57 µg/kg-day and 0.59 to 2.12 µg/kg-day day at the 50th and 95th percentiles, respectively, depending on age group) (Table 4-2).

A public commentor on the draft risk evaluations for DIDP and DINP (EPA-HQ-OPPT-2024-0073-0081) indicated that EPA may be overestimating phthalate daily intake values using reverse dosimetry compared to a more recent Bayesian approach developed by scientists in EPA's Office of Research and Development (Stanfield et al., 2024). EPA considered the Bayesian approach for estimating phthalate daily intake values reported by Stanfield et al. However, an important limitation of the Bayesian approach published by Stanfield et al. is that it does not incorporate phthalate-specific information, such as fractional urinary excretion values, which will lead to an underestimation of daily intake values for phthalates. For example, Stanfield et al. report a median daily intake value of 0.41 µg/kg-day DEHP for all NHANES participants in the 2015 to 2016 NHANES cycle using the Bayesian approach (see Table S8 of Stanfield et al.), while EPA estimated a daily intake of 1.07 µg/kg-day for the same population in the 2017 to 2018 NHANES cycle (Note: an exact comparison was not possible because Stanfield et al. did not evaluate 2017-2018 NHANES data, while EPA only estimated daily intake values for 2017-2018 data). For DEHP, the sum fractional urinary excretion of urinary metabolites (MEHP, MEHHP,

MEOHP, MECPP) is 0.453, and normalizing the Bayesian daily intake estimates for fractional urinary excretion provides a very similar daily intake estimate as that obtained using the reverse dosimetry approach (*i.e.*, 0.41 µg/kg-day ÷ 0.453 = 0.91 µg/kg-day). Therefore, EPA expects that if the Bayesian approach were to account for fractional urinary excretion values, daily intake estimates using the Bayesian approach would be similar to the reverse dosimetry daily intake estimates.

4.3 Cumulative Phthalate Exposure Estimates Based on NHANES Urinary Biomonitoring

In contrast to aggregate exposure, which refers to exposure to a single chemical substance, cumulative exposure refers to aggregate exposure to multiple chemical substances. To estimate cumulative phthalate exposure, EPA scaled the individual aggregate phthalate daily intake estimates for each population by relative potency using the RPFs shown in Table 2-4. Phthalate daily intake values, expressed in terms of index chemical equivalents (*i.e.,* DBP equivalents in µg/kg-day), were then summed to estimate cumulative phthalate daily intake values for each population. Table 4-2 shows the 50th and 95th percentile cumulative daily intake values for DBP, DEHP, BBP, DIBP, and DINP for women of reproductive age (16 to 49 years old) and male children (ages 3 to 5, 6 to 11, and 12 to 15), while Table 4-3 shows 50th and 95th percentile cumulative daily intake values for women of reproductive age stratified by race and socioeconomic status.

For women of reproductive age, 50th and 95th percentile cumulative daily intake estimates were 0.95 and 3.55 µg DBP-equivalents/kg-day (Table 4-2). When stratified by race and socioeconomic status, there was some evidence for higher cumulative exposure for black non-Hispanic women of reproductive age at the 95th percentile. For this population 50th and 95th percentile cumulative daily intake estimates were 0.67 and 5.16 µg DBP-equivalents/kg-day (Table 4-3). However, differences in cumulative exposure between races and socioeconomic status for women of reproductive age at the 50th or 95th percentiles were statistically non-significant (Appendix C.4). As can be seen from Figure 4-2 and Figure 4-3, DEHP was the largest contributor to 50th percentile cumulative exposure estimates (contributing 36 to 52%, depending on race and socioeconomic status), followed by DBP (15 to 28%), DINP (12 to 22%), DIBP (7 to 12%), and BBP (3 to 5%). For 95th percentile cumulative exposure estimates, DEHP (contributing 28 to 70%, depending on race and socioeconomic status) and DINP (14 to 47%) were the largest contributors to cumulative exposure, followed by DBP (9 to 25%), DIBP (4 to 12%), and BBP (3 to 8%).

For male children ages 3 to 5 year, 6 to 11 years, and 12 to 15 years, 50th and 95th percentile cumulative daily intake estimates decreased with age at the population level, with the highest cumulative exposure being estimated for male children ages 3 to 5 years (50th and 95th percentile: 3.04 and 10.8 µg DBP-equivalents/kg-day), followed by 6 to 11 year olds (50th and 95th percentile: 1.89 and 7.35 µg DBP-equivalents/kg-day), and then 12 to 15 year olds (50th and 95th percentile: 1.19 and 4.36 µg DBP-equivalents/kg-day) (Table 4-2). However, the differences between age groups were not statistically significantly different at either the 50th or 95th percentiles (Appendix C.4). As can be seen from Figure 4-4, DEHP was the largest contributor to both 50th and 95th percentile cumulative exposure for all age groups (contributing 48 to 58% depending on age group), followed by DBP (14 to 23%), DINP (9 to 23%), DIBP (7 to 12%), and BBP (4 to 12%).

4.4 Cumulative Phthalate Risk Based on NHANES Urinary Biomonitoring

To calculate cumulative risk based on phthalate exposure for the U.S. civilian population from NHANES, cumulative margins of exposure (MOEs) were calculated for each population by dividing the index chemical POD (*i.e.,* 2,100 µg/kg-day for DBP) by the cumulative daily intake estimate (in DBP equivalents) for each population. As can be seen from Table 4-2 and Table 4-3, for women of reproductive age, cumulative MOEs ranged from 407 for black non-Hispanic women of reproductive age at the 95th percentile to 3,151 for black non-Hispanic women of reproductive age at the 50th percentile. These MOEs are above the benchmark of 30, therefore representing less risk than the benchmark. Specifically, in terms of a risk cup, these MOEs indicate that the risk cup is 1.0 to 7.4 percent full at a benchmark MOE of 30. Of note, the 95th percentile for black non-Hispanic women represents a value at which approximately one million individuals would be expected to have higher exposures, assuming a subpopulation size near 20 million**.** *These results indicate that cumulative exposure to DEHP, DBP, DIBP, BBP, and DINP, based on the most recent NHANES survey data (2017 to 2018), does not currently pose a risk to most women of reproductive age within the U.S. civilian population.*

As can be seen from Table 4-2, cumulative MOEs ranged from 194 for male children 3 to 5 years of age at the 95th percentile to 1,758 for male children 12 to 15 years of age at the 50th percentile. These MOEs indicate that the risk cup is 1.7 to 15.5 percent full at a benchmark MOE of 30. *These results indicate that cumulative exposure to DEHP, DBP, DIBP, BBP, and DINP, based on the most recent NHANES survey data (2017 to 2018), does not currently pose a risk to most male children within the U.S. civilian population.*

4.5 Conclusions from NHANES Analysis

Herein, EPA used NHANES urinary biomonitoring data for DEHP, BBP, DBP, DIBP, and DINP to evaluate temporal trends in phthalate exposure for the U.S. population, to estimate aggregate and cumulative phthalate exposure via reverse dosimetry, and to estimate cumulative risk exposure to DEHP, BBP, DBP, DIBP, and DINP for all populations, including women of reproductive age and male children. Based on this analysis, EPA concludes the following:

- Temporal trends analysis of NHANES urinary biomonitoring data from 1999 to 2018 indicates declining exposure to DEHP, DBP, and BBP for the U.S. population. In contrast, exposure to DIBP for the U.S. population has increased from 1999 to 2018, while exposure to DINP has fluctuated (*i.e.,* increased from 2005 to 2014, then declined back to approximately 2005 levels in 2018) (Section 4.1).
- Aggregate phthalate exposure for all subpopulations in the U.S. was highest for DEHP and DINP based on the most recent NHANES survey data (2017 to 2018) (Section 4.2).
- DEHP was the largest contributor to cumulative phthalate exposure for all subpopulations in the U.S., followed by DINP or DBP, and then BBP and DIBP (Section 4.3).
- Based on the most recent NHANES survey data (2017 to 2018), cumulative exposure to non-attributable sources of DEHP, DBP, DIBP, BBP, and DINP does not currently pose a risk to most of the U.S. population, including most women of reproductive age or male children within the U.S. population (Section 4.4). Cumulative MOEs for all populations were above the benchmark of 30 and ranged from 194 to 636 based on 95th percentile exposure estimates. However, these data do not account for acute or low-frequency exposures assessed in individual

chemical risk evaluations, such as those that may occur as a result of use of certain consumer products or occupational exposures.

Ultimately the NHANES reverse dosimetry combined with the relative potency factors provides a common understanding of regular exposures and risks to the U.S. population, including the susceptible subpopulations of women of reproductive age or male children. However, as national biomonitoring data does not oversample highly exposed subpopulations, this conclusion cannot be extrapolated to low-frequency, high-exposure scenarios. Consistent with this, during the August 2025 phthalate peer-review meeting, SACC stated: "[w]ith only 5,000 total participants per year to monitor the nation's general health and nutritional status, this survey, although exceedingly valuable, cannot be viewed—and was never intended to be viewed—as a monitoring system for any given group who may be highly exposed to a chemical, may live or work in a particular industry or environment, or for any other particular outlier scenario…And although it is possible that one or more persons exist in the NHANES survey who did experience high exposure scenarios, it is not statistically possible to claim that NHANES survey results represent PESS or workers or to claim that the phthalate measurements infer that no US subpopulations experience high exposure scenarios." Therefore, NHANES reverse dosimetry provides a basis for estimating total exposure that can augment specific acute scenarios in individual risk evaluations, as described further in Section 5.

Table 4-2. Cumulative Phthalate Daily Intake (µg/kg-day) Estimates for Women of Reproductive Age and Male Children from the 2017−2018 NHANES Cycle

Population	Percentile	Phthalate	Aggregate Daily Intake (µg/kg-day)	RPF	Aggregate Daily Intake in DBP Equivalents (µg/kg-day)	% Contribution to Cumulative Exposure	Cumulative Daily Intake (DBP Equivalents, µg/kg-day)	Cumulative MOE (POD = 2,100 µg/kg-day)	% Contribution to Risk Cup (Benchmark = 30)[a]
Females (16–49 years old; N = 1,620)	50	DBP	0.21	1	0.210	22.1	0.950	2,211	1.4%
		DEHP	0.53	0.84	0.445	46.9			
		BBP	0.08	0.52	0.042	4.38			
		DIBP	0.2	0.53	0.106	11.2			
		DINP	0.7	0.21	0.147	15.5			
	95	DBP	0.61	1	0.610	17.2	3.55	592	5.1%
		DEHP	1.48	0.84	1.24	35.0			
		BBP	0.42	0.52	0.218	6.15			
		DIBP	0.57	0.53	0.302	8.51			
		DINP	5.6	0.21	1.18	33.1			
Males (3–5 years old; N = 267)	50	DBP	0.56	1	0.560	18.4	3.04	690	4.3%
		DEHP	2.11	0.84	1.77	58.2			
		BBP	0.22	0.52	0.114	3.76			
		DIBP	0.57	0.53	0.302	9.93			
		DINP	1.4	0.21	0.294	9.66			
	95	DBP	2.02	1	2.02	18.6	10.8	194	15.5%
		DEHP	6.44	0.84	5.41	49.9			
		BBP	2.46	0.52	1.28	11.8			
		DIBP	2.12	0.53	1.12	10.4			
		DINP	4.8	0.21	1.01	9.30			
Males (6–11 years old; N = 553)	50	DBP	0.38	1	0.380	20.1	1.89	1,111	2.7%
		DEHP	1.24	0.84	1.04	55.1			
		BBP	0.16	0.52	0.083	4.40			
		DIBP	0.33	0.53	0.175	9.26			

Population	Percentile	Phthalate	Aggregate Daily Intake (µg/kg-day)	RPF	Aggregate Daily Intake in DBP Equivalents (µg/kg-day)	% Contribution to Cumulative Exposure	Cumulative Daily Intake (DBP Equivalents, µg/kg-day)	Cumulative MOE (POD = 2,100 µg/kg-day)	% Contribution to Risk Cup (Benchmark = 30)[a]
Males (6–11 years old; N = 553)		DINP	1	0.21	0.210	11.1			
	95	DBP	1.41	1	1.41	19.2	7.35	286	10.5%
		DEHP	4.68	0.84	3.93	53.5			
		BBP	0.84	0.52	0.437	5.94			
		DIBP	1.62	0.53	0.859	11.7			
		DINP	3.4	0.21	0.714	9.71			
Males (12–15 years old; N =308)	50	DBP	0.33	1	0.330	27.6	1.19	1,758	1.7%
		DEHP	0.66	0.84	0.554	46.4			
		BBP	0.14	0.52	0.073	6.09			
		DIBP	0.21	0.53	0.111	9.32			
		DINP	0.6	0.21	0.126	10.5			
	95	DBP	0.62	1	0.620	14.2	4.36	482	6.2%
		DEHP	2.51	0.84	2.11	48.3			
		BBP	0.64	0.52	0.333	7.63			
		DIBP	0.59	0.53	0.313	7.17			
		DINP	4.7	0.21	0.987	22.6			

[a] Cumulative exposure of 70 µg DBP equivalents/kg-day would result in a cumulative MOE of 30 (*i.e.*, 2,100 µg DBP-equivalents/kg-day ÷ 70 µg DBP equivalents/kg-day = 30), which is equivalent to the benchmark of 30, indicating that the exposure is at the threshold for risk. Therefore, to estimate the percent contribution to the risk cup, the cumulative exposure expressed in DBP equivalents is divided by 70 µg DBP equivalents/kg-day to estimate percent contribution to the risk cup.

Table 4-3. Cumulative Phthalate Daily Intake (µg/kg-day) Estimates for Women of Reproductive Age (16 to 49 years old) by Race and Socioeconomic Status from the 2017−2018 NHANES Cycle

Race/ Socioeconomic Status (SES)	Percentile	Phthalate	Aggregate Daily Intake (µg/kg-day)	RPF	Aggregate Daily Intake in DBP Equivalents (µg/kg-day)	% Contribution to Cumulative Exposure	Cumulative Daily Intake (DBP Equivalents, µg/kg-day)	Cumulative MOE (POD = 2,100 µg/kg-day)	% Contribution to Risk Cup (Benchmark = 30) [a]
Race: White Non-Hispanic (N = 494)	50	DBP	0.22	1	0.22	21.6	1.02	2,058	1.5%
		DEHP	0.59	0.84	0.50	48.6			
		BBP	0.10	0.52	0.05	5.1			
		DIBP	0.20	0.53	0.11	10.4			
		DINP	0.70	0.21	0.15	14.4			
	95	DBP	0.58	1	0.58	17.6	3.30	636	4.7%
		DEHP	1.44	0.84	1.21	36.6			
		BBP	0.29	0.52	0.15	4.6			
		DIBP	0.55	0.53	0.29	8.8			
		DINP	5.10	0.21	1.07	32.4			
Race: Black Non-Hispanic (N = 371)	50	DBP	0.10	1	0.10	15.0	0.667	3,151	1.0%
		DEHP	0.38	0.84	0.32	47.9			
		BBP	0.04	0.52	0.02	3.1			
		DIBP	0.15	0.53	0.08	11.9			
		DINP	0.70	0.21	0.15	22.1			
	95	DBP	0.48	1	0.48	9.3	5.16	407	7.4%
		DEHP	4.28	0.84	3.60	69.7			
		BBP	0.30	0.52	0.16	3.0			
		DIBP	0.40	0.53	0.21	4.1			
		DINP	3.40	0.21	0.71	13.8			
Race: Mexican American (N = 259)	50	DBP	0.19	1	0.19	22.4	0.849	2,474	1.2%
		DEHP	0.49	0.84	0.41	48.5			
		BBP	0.06	0.52	0.03	3.7			
		DIBP	0.17	0.53	0.09	10.6			

Race/ Socioeconomic Status (SES)	Percentile	Phthalate	Aggregate Daily Intake (µg/kg-day)	RPF	Aggregate Daily Intake in DBP Equivalents (µg/kg-day)	% Contribution to Cumulative Exposure	Cumulative Daily Intake (DBP Equivalents, µg/kg-day)	Cumulative MOE (POD = 2,100 µg/kg-day)	% Contribution to Risk Cup (Benchmark = 30) [a]
Race: Mexican American (N = 259)		DINP	0.60	0.21	0.13	14.8			
	95	DBP	0.42	1	0.42	11.6	3.61	582	5.2%
		DEHP	1.24	0.84	1.04	28.9			
		BBP	0.39	0.52	0.20	5.6			
		DIBP	0.46	0.53	0.24	6.8			
		DINP	8.10	0.21	1.70	47.1			
Race: Other (N = 496)	50	DBP	0.26	1	0.26	25.3	1.03	2041	1.5%
		DEHP	0.64	0.84	0.54	52.2			
		BBP	0.07	0.52	0.04	3.5			
		DIBP	0.15	0.46	0.07	6.7			
		DINP	0.60	0.21	0.13	12.2			
	95	DBP	0.84	1	0.84	20.7	4.06	517	5.8%
		DEHP	1.37	0.84	1.15	28.3			
		BBP	0.41	0.52	0.21	5.2			
		DIBP	0.46	0.53	0.24	6.0			
		DINP	7.70	0.21	1.62	39.8			
SES: Below Poverty Level (N = 1,056)	50	DBP	0.21	1	0.21	22.0	0.955	2,199	1.4%
		DEHP	0.53	0.84	0.45	46.6			
		BBP	0.09	0.52	0.05	4.9			
		DIBP	0.20	0.53	0.11	11.1			
		DINP	0.70	0.21	0.15	15.4			
	95	DBP	0.82	1	0.82	18.2	4.50	467	6.4%
		DEHP	1.75	0.84	1.47	32.7			
		BBP	0.34	0.52	0.18	3.9			
		DIBP	0.51	0.53	0.27	6.0			
		DINP	8.40	0.21	1.76	39.2			

Race/ Socioeconomic Status (SES)	Percentile	Phthalate	Aggregate Daily Intake (µg/kg-day)	RPF	Aggregate Daily Intake in DBP Equivalents (µg/kg-day)	% Contribution to Cumulative Exposure	Cumulative Daily Intake (DBP Equivalents, µg/kg-day)	Cumulative MOE (POD = 2,100 µg/kg-day)	% Contribution to Risk Cup (Benchmark = 30) [a]
SES: At or Above Poverty Level (N = 354)	50	DBP	0.20	1.00	0.20	27.9	0.718	2,924	1.0%
		DEHP	0.31	0.84	0.26	36.3			
		BBP	0.06	0.52	0.03	4.3			
		DIBP	0.15	0.53	0.08	11.1			
		DINP	0.70	0.21	0.15	20.5			
	95	DBP	0.48	1.00	0.48	16.3	2.94	713	4.2%
		DEHP	1.07	0.84	0.90	30.5			
		BBP	0.45	0.52	0.23	7.9			
		DIBP	0.65	0.53	0.34	11.7			
		DINP	4.70	0.21	0.99	33.5			
SES: Unknown (N = 210)	50	DBP	0.26	1.00	0.26	23.2	1.12	1,870	1.6%
		DEHP	0.67	0.84	0.56	50.1			
		BBP	0.06	0.52	0.03	2.8			
		DIBP	0.23	0.53	0.12	10.9			
		DINP	0.70	0.21	0.15	13.1			
	95	DBP	0.60	1.00	0.60	25.5	2.35	893	3.4%
		DEHP	0.86	0.84	0.72	30.7			
		BBP	0.21	0.52	0.11	4.6			
		DIBP	0.35	0.53	0.19	7.9			
		DINP	3.50	0.21	0.74	31.2			

[a] Cumulative exposure of 70 µg DBP equivalents/kg-day would result in a cumulative MOE of 30 (*i.e.*, 2,100 µg DBP-equivalents/kg-day ÷ 70 µg DBP equivalents/kg-day = 30), which is equivalent to the benchmark of 30, indicating that the exposure is at the threshold for risk. Therefore, to estimate the percent contribution to the risk cup, the cumulative exposure expressed in DBP equivalents is divided by 70 µg DBP equivalents/kg-day to estimate percent contribution to the risk cup.

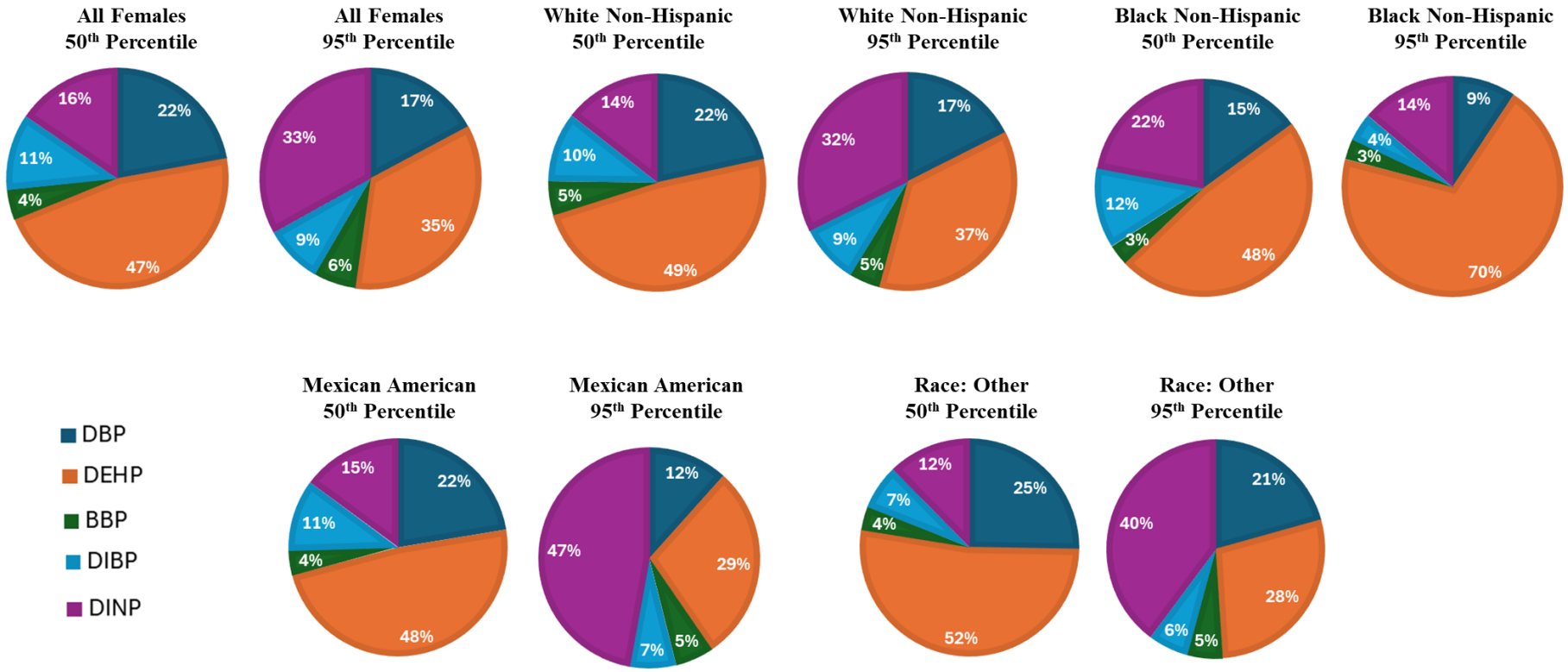


Figure 4-2. Percent Contribution to Cumulative Exposure for DEHP, DBP, BBP, DIBP, and DINP for Women of Reproductive Age (16 to 49 years) in 2017−2018 NHANES, Stratified by Race

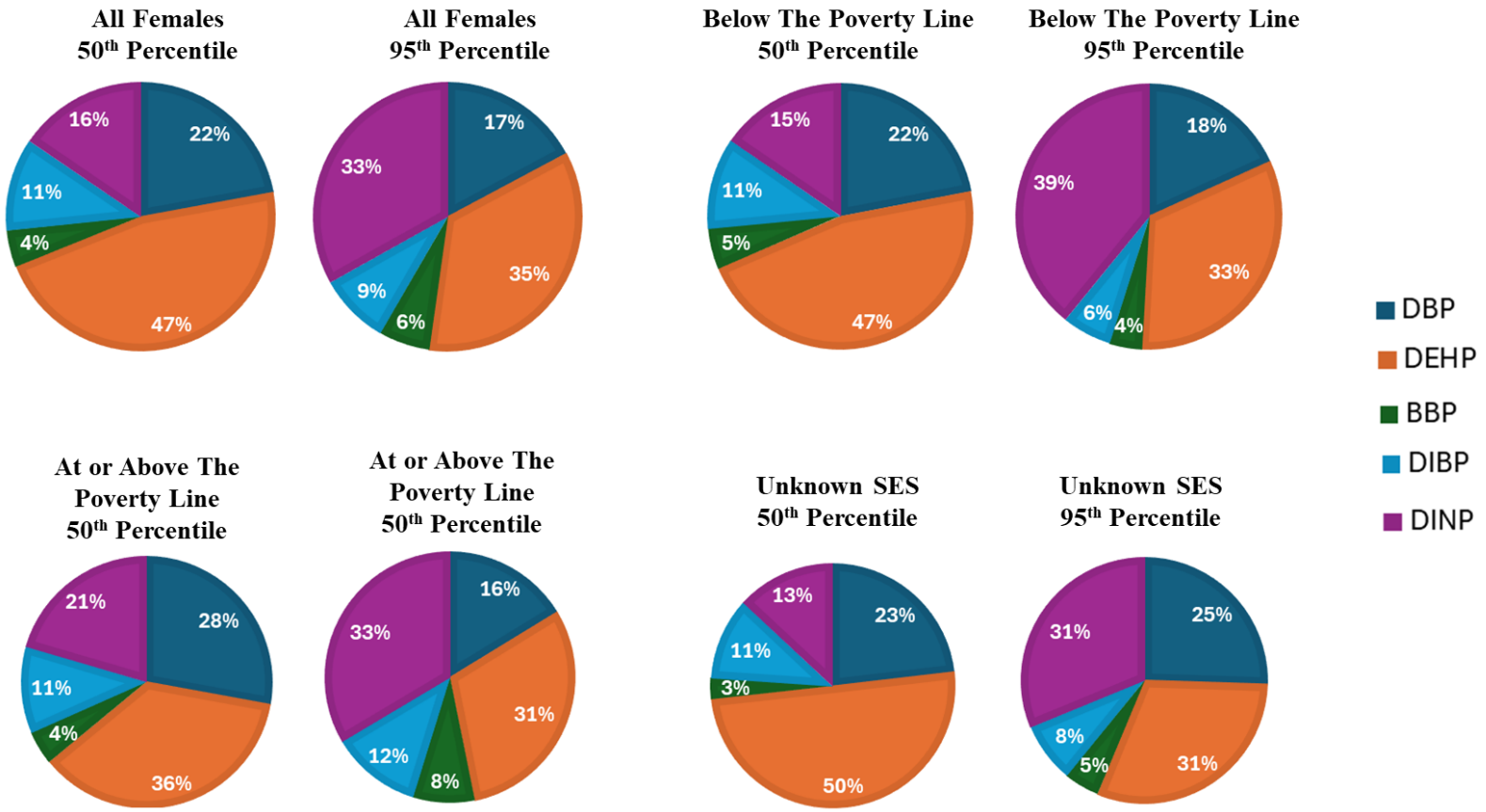


Figure 4-3. Percent Contribution to Cumulative Exposure for DEHP, DBP, BBP, DIBP, and DINP for Women of Reproductive Age (16 to 49 years) in 2017−2018 NHANES, Stratified by Socioeconomic Status

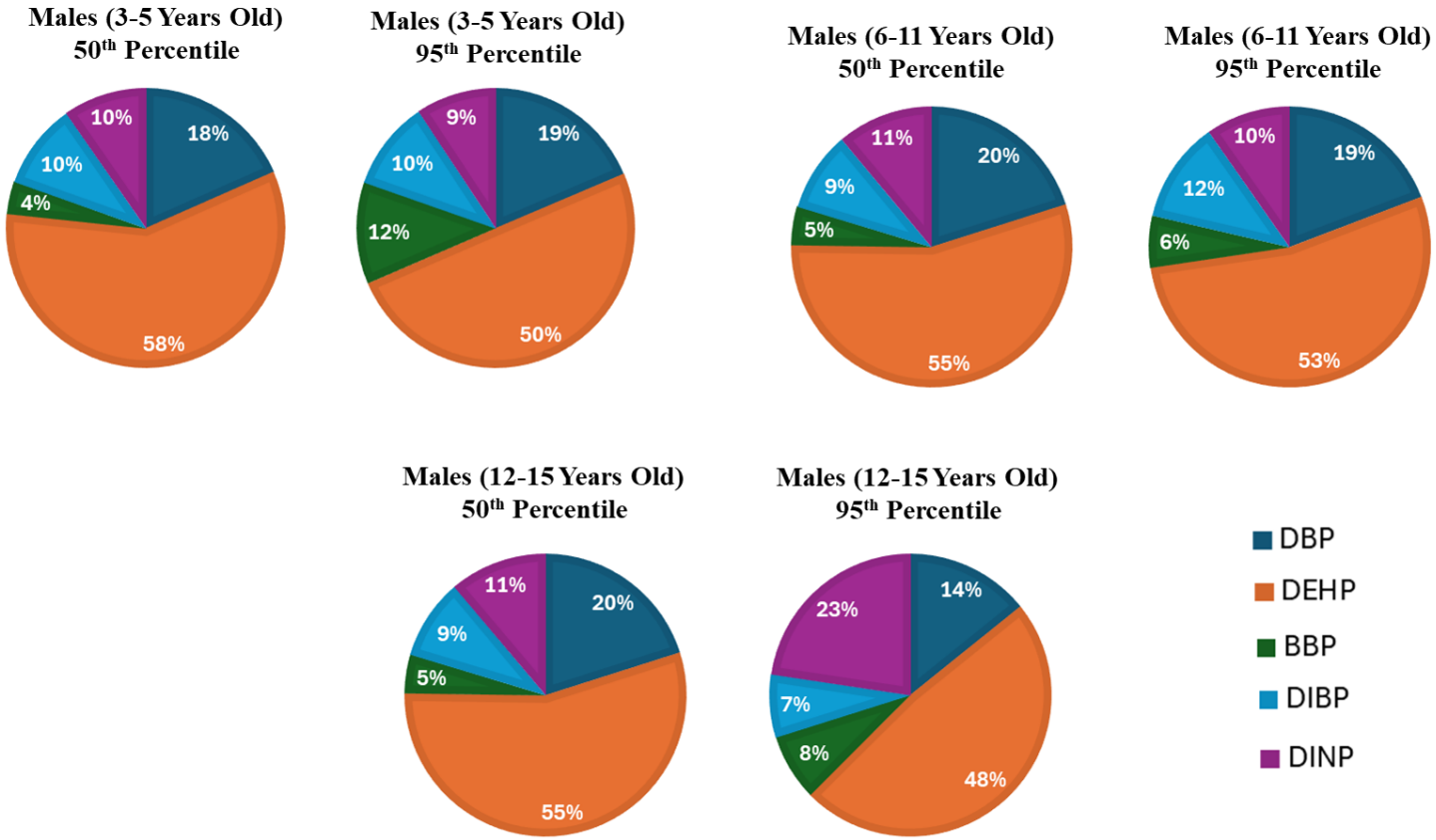


Figure 4-4. Percent Contribution to Cumulative Exposure for DEHP, DBP, BBP, DIBP, and DINP for Male Children Ages 3 to 5, 6 to 11, and 12 to 15 years in 2017–2018 NHANES

5 APPROACHES FOR CHARACTERIZING CUMULATIVE RISK

EPA's draft 2023 approach (U.S. EPA, 2023b) laid out a multi-step method and conceptual model for assessing cumulative risk, with the final two steps in EPA's draft conceptual model as follows:

- Estimate cumulative exposure by combining exposures from TSCA COUs from individual phthalates (scaled by relative potency and expressed in index chemical (DBP) equivalents) with the relevant non-attributable cumulative exposures to estimate cumulative exposure in a reasonable manner for consumers and workers.
- Estimate cumulative risk for each specific exposure scenario by calculating a cumulative MOE that can in turn be compared to the benchmark MOE.

As described in Section 1.6, the SACC specifically expressed concern about combining estimates from individual assessments that represent a mix of deterministic and probabilistic methods as well as differing tiers of analyses (*i.e.* screening through more refined approaches) (U.S. EPA, 2023b). In Section 3.1, EPA explored the potential for co-exposures in occupational settings but concluded it would not be feasible to provide a robust multichemical quantitative assessment due to the wide range of plausible exposure scenarios and instead calculated an option for deriving an OEV based on cumulative exposure and relative potency assumptions (Appendix E). EPA calculated the anticipated contribution to the risk cup from monitored concentrations of phthalates in dust, a key pathway for consumer exposure, in Section 3.2 and found the contribution to be a fraction of total exposure.

Therefore, EPA has authored this technical support document to support a cumulative risk analysis for each chemical substance by adding non-attributable cumulative phthalate exposure (from NHANES) to the relevant exposure scenarios for individual TSCA COUs. These cumulative MOEs are estimated using the RPFs for phthalate syndrome based on the shared endpoint and pooled dataset for assessing fetal testicular testosterone health endpoint, as laid out in Section 2.

Sections 5.1 and 5.2 describe two approaches for how to apply this quantitative approach for evaluating cumulative risk resulting from aggregate exposure to a single phthalate from an exposure scenario or COU plus non-attributable cumulative risk from NHANES. A comparison of the similarities and differences between both approaches is provided in Table 5-1. The first approach presented in Section 5.1 estimates cumulative risk by first scaling each individual phthalate exposure for a consumer or occupational COU by relative potency before combining with non-attributable cumulative exposure estimated using NHANES. In the second approach presented in Section 5.2, individual phthalate exposures for consumer and occupational COUs are not scaled by RPFs but use the individual phthalate hazard values and are still combined with non-attributable cumulative exposures estimated using NHANES. Empirical examples of estimating cumulative risk for DCHP and DEHP using both approaches are presented in Sections 5.1 and 5.2. Examples for DCHP and DEHP were chosen to demonstrate the varying impact of approach 1 across different phthalates. Estimating cumulative risk using approach 1 will have a large impact for DCHP, but no impact for DEHP because the individual DEHP POD of 1.1 mg/kg-day is lower (*i.e.*, more sensitive) than the index chemical (DBP) POD of 2.1 mg/kg-day. Approach 2 will have the same impact on cumulative MOEs for every phthalates, resulting in cumulative MOEs that are approximately 1.1–1.2× lower than aggregate MOEs from the individual phthalate assessment (*i.e.*, more sensitive) for both DCHP and DEHP as shown in Section 5.2.

Table 5-1. Comparison of CRA Approaches 1 and 2

Step for Calculating the Cumulative Risk	Approach 1	Approach 2
Step 1: Exposure estimates for the individual phthalates individual TSCA COUs	Individual exposures scaled by relative potency and expressed in index chemical (DBP) equivalents	Individual exposures not scaled by relative potency
Step 2: Estimate non-attributable cumulative exposure	No differences between approaches	
Step 3: Calculate the MOEs for each exposure to the individual phthalate	Individual MOEs calculated using the index chemical (DBP) POD	Individual MOEs calculated using the individual phthalate POD
Step 4: Calculate the cumulative MOE	No differences between approaches	

Both approaches were subject to public comment and peer-reviewed by SACC during the August 2025 phthalate peer-review meeting (U.S. EPA, 2025ag). Overall, SACC concluded that both approaches have strengths and uncertainties, but that the two approaches can complement one another with Approach 1 being grounded on the CRA principle of shared toxicological characteristic with strong scientific evidence for assessing via the fetal testicular testosterone endpoint while Approach 2, which rely on phthalate-specific endpoints, leverages more data available for the individual phthalates. Therefore, SACC recommended that EPA should present both approaches in the individual risk evaluations for each phthalate and select the most scientifically defensible approach for the final individual risk characterization and decision making process for each phthalate (U.S. EPA, 2025ag). Based on SACC recommendations, EPA has considered both cumulative risk characterization approaches in each individual phthlate risk evaluation. Readers are directed to EPA's response to public comments summary document and EPA's response to the 2025 phthalates SACC meeting report for further details regarding SACC recommendations and public comments and how they were addressed by EPA.

Section 5.3 discusses the impacts that the two approaches will have for each of the phthalates being evaluated under TSCA. Section 5.4 provides a comparison of the strengths, limitations, and uncertainties of the two approaches for each of the phthalates being evaluated under TSCA, as well as the selected approach for use in each individual phthalate risk evaluation.

5.1 Estimation of Cumulative Risk – Approach 1

As described above, EPA is focusing its exposure assessment for the cumulative risk analysis on evaluation of exposures through individual TSCA consumer and occupational COUs for each phthalate and non-attributable cumulative exposure to DEHP, DBP, BBP, DIBP, and DINP using NHANES urinary biomonitoring data and reverse dosimetry. To estimate cumulative risk, EPA first scaled each individual phthalate exposure by relative potency using the RPFs presented in Table 2-4 to express phthalate exposure in terms of index chemical (DBP) equivalents. Exposures from individual consumer or worker COUs/OES (occupational exposure scenario) were then combined with non-attributable exposures estimated from NHANES biomonitoring data to estimate cumulative risk. Cumulative risk was estimated using the four-step process outlined below, along with two empirical examples of how

EPA calculated cumulative risk for one occupational OES for DCHP (*i.e.,* Application of Paints and Coatings (Solids)) and one occupational OES for DEHP (*i.e.,* Recycling). Empirical Examples for DCHP and DEHP are also shown in Table 5-2 and Table 5-3, respectively, where they are compared against approach 2. Figure 5-1 and Figure 5-2 provide visual representations of the risk cup associated with the example calculations.

Step 1: Convert Exposure Estimates for the Individual Phthalate from Each Individual Consumer and Occupational COU to Index Chemical Equivalents

In this step, acute duration exposure estimates for an individual phthalate from each consumer and occupational COU/OES are scaled by relative potency and expressed in terms of index chemical (DBP) equivalents using Equation 5-1. This step is repeated for all individual exposure estimates for each route of exposure being assessed for each COU (*i.e.,* inhalation, dermal, and aggregate exposures for occupational COUs; inhalation, ingestion, dermal, and aggregate exposure for consumer COUs).

Equation 5-1. Scaling Phthalate Exposures by Relative Potency

$$Phthalate\ Exposure\ (in\ DBP\ equivalents) = AD_{Route\ 1} x\ RPF_{Phthalate}$$

Where:

- Phthalate exposure is the acute exposure for a given route of exposure for an individual phthalate from a single occupational or consumer COU expressed in terms of µg/kg index chemical (DBP) equivalents.
- $AD_{Route\ 1}$ is the acute dose in µg/kg from a given route of exposure from a single occupational or consumer COU/OES.
- $RPF_{Phthalate}$ is the relative potency factor (unitless) for each respective phthalate (Table 2-4).

Example (DCHP): 50th percentile inhalation and dermal DCHP exposures for female workers of reproductive age are 38.7 and 2.07 µg/kg for the Application of Paints and Coatings (Solids) OES (U.S. EPA, 2025ad). Using Equation 5-1, inhalation, dermal, and aggregate DCHP exposures for this OES can be scaled by relative potency to 64.24, 3.44, and 67.68 µg/kg DBP equivalents, respectively (Table 5-2).

$$DCHP_{Inhalation-COU} = 64.24\ \mu g/kg\ DBP\ equivalents = 38.7\ \mu g/kg\ DCHP\ x\ 1.66$$

$$DCHP_{Dermal-COU} = 3.44\ \mu g/kg\ DBP\ equivalents = 2.07\ \mu g/kg\ DCHP\ x\ 1.66$$

$$DCHP_{Aggregate-COU} = 67.68\ \mu g/kg\ DBP\ equivalents = (2.07\ \mu g/kg\ DCHP + 38.7\ \mu g/kg\ DCHP)\ x\ 1.66$$

Example (DEHP): 50th percentile inhalation and dermal DEHP exposures for female workers of reproductive age are 46.9 and 2.36 µg/kg for the Recycling OES (U.S. EPA, 2025q). Using Equation 5-1, inhalation, dermal, and aggregate DEHP exposures for this OES can be scaled by relative potency to 39.0, 1.96, and 40.9 µg/kg DBP equivalents, respectively (Table 5-3).

$$DEHP_{Inhalation-COU} = 39.0\ \mu g/kg\ DBP\ equivalents = 46.9\ \mu g/kg\ DEHP\ x\ 0.84$$

$$DEHP_{Dermal-COU} = 1.96\ \mu g/kg\ DBP\ equivalents = 2.36\ \mu g/kg\ DEHP\ x\ 0.84$$

$$DEHP_{Aggregate-COU} = 40.9\ \mu g/kg\ DBP\ equivalents$$
$$= (46.9\ \mu g/kg\ DEHP + 2.36\ \mu g/kg\ DEHP)\ x\ 0.84$$

Step 2: Estimate Non-attributable Cumulative Exposure to DEHP, DBP, BBP, DIBP, and DINP Using NHANES Urinary Biomonitoring Data and Reverse Dosimetry (see Section 4 for further details)

Non-attributable exposure for a national population to DEHP, DBP, BBP, DIBP, and DINP was estimated using Equation 5-2, where individual phthalate daily intake values estimated from NHANES biomonitoring data and reverse dosimetry were scaled by relative potency, expressed in terms of index chemical (DBP) equivalents, and summed to estimate non-attributable cumulative exposure in terms of DBP equivalents. Equation 5-2 was used to calculate the cumulative exposure estimates provided in Table 4-2 and Table 4-3.

Equation 5-2. Estimating Non-attributable Cumulative Exposure to DEHP, DBP, BBP, DIBP, and DINP

$$Cumulative\ Exposure\ (Non-attributable)$$
$$= (DI_{DEHP}\ x\ RPF_{DEHP}) + (DI_{DBP}\ x\ RPF_{DBP}) + (DI_{BBP}\ x\ RPF_{BBP})$$
$$+ (DI_{DIBP}\ x\ RPF_{DIBP}) + (DI_{DINP}\ x\ RPF_{DINP})$$

Where:

- Cumulative exposure (non-attributable) is expressed in index chemical (DBP) equivalents (µg/kg-day).
- DI is the daily intake value (µg/kg-day) for each phthalate that was calculated using NHANES urinary biomonitoring data and reverse dosimetry (DI values for each phthalate for each assessed population are provided in Table 4-2 and Table 4-3).
- RPF is the relative potency factor (unitless) for each phthalate from Table 2-4.

Example: The 95th percentile cumulative exposure estimate of 5.16 µg/kg-day DBP equivalents for black, non-Hispanic women of reproductive age (Table 4-3) is calculated using Equation 5-2 as follows:

$$5.16\ \mu g/kg\ DBP\ equivalents$$
$$= (4.28\ \mu g/kg\ DEHP\ x\ 0.84) + (0.48\ \mu g/kg\ DBP\ x\ 1) + (0.30\ \mu g/kg\ BBP\ x\ 0.52)$$
$$+ (0.40\ \mu g/kg\ DIBP\ x\ 0.53) + (3.40\ \mu g/kg\ DINP\ x\ 0.21)$$

Step 3: Calculate MOEs for Each Exposure to the Individual Phthalate and for the Non-attributable Cumulative Exposure

Next, MOEs are calculated for each exposure of interest that is included in the cumulative scenario using Equation 5-3. For example, this step involves calculating MOEs for inhalation and dermal phthalate exposures expressed in index chemical equivalents for each individual COU/OES in step 1 and an MOE for non-attributable cumulative phthalate exposure from step 2 above.

Equation 5-3. Calculating MOEs for Exposures of Interest for use in the RPF and Cumulative Approaches

$$MOE_1 = \frac{Index\ Chemical\ (DBP)\ POD}{Exposure_1\ in\ DBP\ Equivalents}$$

Where:

- MOE_1 (unitless) is the MOE calculated for each exposure of interest included in the cumulative scenario.
- Index chemical (DBP) POD is the POD selected for the index chemical, DBP. The index chemical POD is 2,100 µg/kg.
- $Exposure_1$ is the exposure estimate in DBP equivalents for the pathway of interest (*i.e.,* from step 1 or 2 above).

Example (DCHP): Using Equation 5-3, the MOEs for inhalation and dermal DCHP exposure estimates for the Application of Paints and Coatings (Solids) OES in DBP equivalents from step 1 and the MOE for the non-attributable cumulative exposure estimate in DBP equivalents from step 2, are 33, 610, and 407, respectively (Table 5-2).

$$MOE_{Cumulative\ Non-attributable} = 407 = \frac{2{,}100\ \mu g/kg}{5.16\ \mu g/kg}$$

$$MOE_{COU-Inhalation} = 32.7 = \frac{2{,}100\ \mu g/kg}{64.2\ \mu g/kg}$$

$$MOE_{COU-Dermal} = 610 = \frac{2{,}100\ \mu g/kg}{3.44\ \mu g/kg}$$

Example (DEHP): Using Equation 5-3, the MOEs for inhalation and dermal DEHP exposure estimates for the Recycling OES in DBP equivalents from step 1 and the MOE for the non-attributable cumulative exposure estimate in DBP equivalents from step 2, are 54, 1,072, and 407, respectively (Table 5-3).

$$MOE_{Cumulative\ Non-attributable} = 407 = \frac{2{,}100\ \mu g/kg}{5.16\ \mu g/kg}$$

$$MOE_{COU-Inhalation} = 54 = \frac{2{,}100\ \mu g/kg}{39.0\ \mu g/kg}$$

$$MOE_{COU-Dermal} = 1{,}072 = \frac{2{,}100\ \mu g/kg}{1.96\ \mu g/kg}$$

Step 4: Calculate the Cumulative MOE

For the cumulative MOE approach, MOEs for each exposure of interest in the cumulative scenario are first calculated (Step 3). The cumulative MOE for the cumulative scenario can then be calculated using Equation 5-4. Equation 5-4 shows the addition of MOEs for the inhalation and dermal exposures routes from an individual COU, as well as the MOE for non-attributable cumulative exposure to phthalates

from NHANES urinary biomonitoring and reverse dosimetry. Additional MOEs can be added to the equation as necessary (*e.g.,* for the ingestion route for consumer scenarios).

Equation 5-4. Cumulative Margin of Exposure Calculation

$$Cumulative\ MOE = \frac{1}{\frac{1}{MOE_{COU-Inhalation}} + \frac{1}{MOE_{COU-Dermal}} + \frac{1}{MOE_{Cumulative-Non-attributable}} \ldots}$$

Example (DCHP): The cumulative MOE for the Application of Paints and Coatings (Solids) OES is 28.9 and is calculated by summing the MOEs for each exposure of interest from step 3 as follows (Table 5-2):

$$Cumulative\ MOE = 28.9 = \frac{1}{\frac{1}{32.7} + \frac{1}{610} + \frac{1}{407}}$$

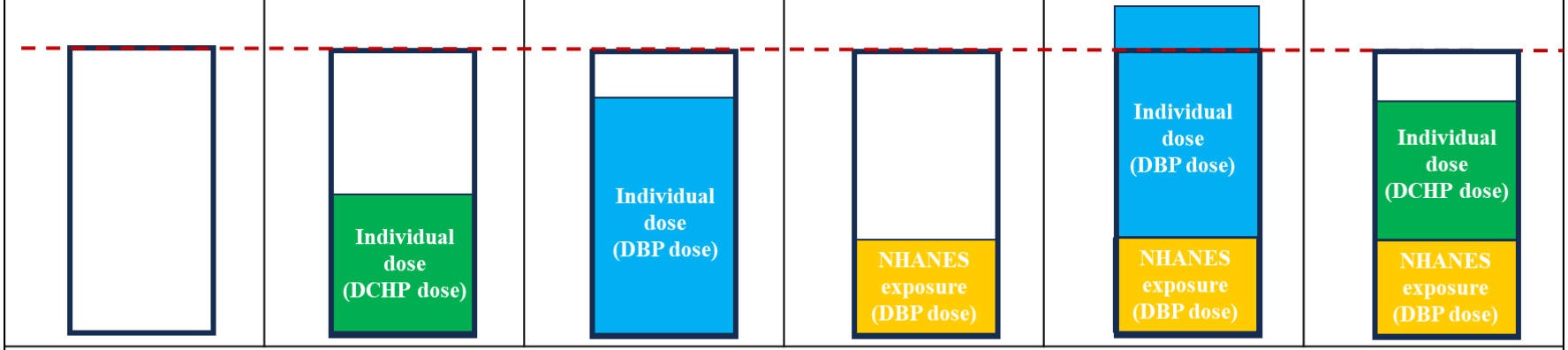
Example (DEHP): The cumulative MOE for the Recycling OES is 46 and is calculated by summing the MOEs for each exposure of interest from step 3 as follows (Table 5-3):

$$Cumulative\ MOE = 46 = \frac{1}{\frac{1}{54} + \frac{1}{1072} + \frac{1}{407}}$$

Table 5-2. DCHP Risk Calculation Example for Female Workers of Reproductive Age

OES	Exposure Level	**Acute MOEs From Individual DCHP Risk Evaluation** (MOEs calculated by dividing the DCHP POD in µg/kg by DCHP exposure in µg/kg)[a] (Benchmark = 30)			**Acute MOEs From Individual DCHP Risk Evaluation Scaled by Relative Potency** (MOEs calculated by dividing the index chemical (DBP) POD in µg/kg by the DCHP exposure scaled by relative potency (RPF = 1.66) and expressed in µg/kg index chemical equivalents)[a] (Benchmark = 30)			**Cumulative Non-Attributable MOE (NHANES)** (MOEs calculated by dividing the index chemical (DBP) POD in µg/kg by the non-attributable cumulative exposure expressed in µg/kg index chemical equivalents) (Benchmark = 30)	**Approach 1: Cumulative MOE (Aggregate MOE + Cumulative Non-attributable MOE)** (Benchmark = 30)	**Approach 2: Cumulative MOE (Aggregate MOE + Cumulative Non-attributable MOE)** (Benchmark = 30)
		Inhalation MOE	**Dermal MOE**	**Aggregate MOE**	**Inhalation MOE (DCHP COU)**	**Dermal MOE (DCHP COU)**	**Aggregate MOE (DCHP COU)**			
Application of Paints and Coatings (Solids)	CT	62 (2,400/38.7)	1,157 (2,400/2.07)	59 (2,400/40.7)	33 (2,100/64.2)	610 (2,100/3.44)	31 (2,100/67.6)	407 (2,100/5.16)	29	51
	HE	3.5 (2,400/677)	579 (2,400/4.15)	3.5 (2,400/681)	1.9 (2,100/1,120)	305 (2,100/6.89)	1.9 (2,100/1,130)	407 (2,100/5.16)	1.8	3.5

[a] Doses shown to three significant figures.

Empty Risk Cup Benchmark MOE = 30 (Represented by dotted red line)	Risk Cup[a] Associated with Acute MOEs (Aggregate MOE) From Individual DCHP Risk Evaluation Aggregate MOE	Risk Cup[a] Associated with Acute MOEs Scaled by Relative Potency (Aggregate MOE)	Risk Cup[a] Associated with Cumulative Non-Attributable MOE	Risk Cup[a] Associated with Approach 1: Cumulative MOE (Aggregate MOE + Cumulative Non-Attributable MOE)	Risk Cup[a] Associated with Approach 2: Cumulative MOE (Aggregate MOE + Cumulative Non-Attributable MOE)
					

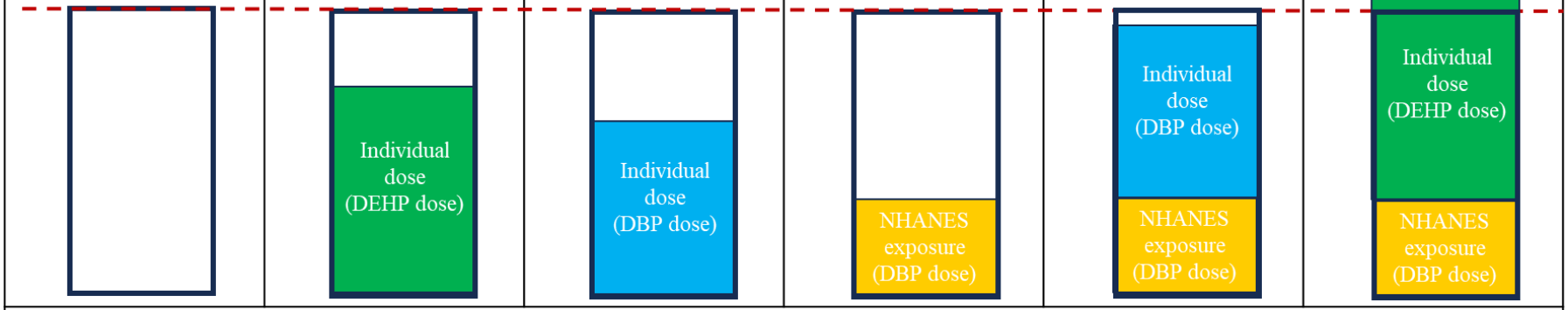
[a]Risk cup visualized here is just an example showing the contributions of various exposures to the risk cup and is for illustrative purposes only. The MOE has an inverse relationship with the exposure dose so adding exposure to the risk cup yield a lower MOE.

Figure 5-1. DCHP Risk Calculation Generic Example (Not to Scale) for Female Workers of Reproductive Age

Table 5-3. DEHP Risk Calculation Example for Female Workers of Reproductive Age

OES	Exposure Level	**Acute MOEs From Individual DEHP Risk Evaluation** (MOEs calculated by dividing the DEHP POD in µg/kg by DEHP exposure in µg/kg)[a] (Benchmark = 30)			**Acute MOEs From Individual DEHP Risk Evaluation Scaled by Relative Potency** (MOEs calculated by dividing the index chemical (DBP) POD in µg/kg by the DEHP exposure scaled by relative potency (RPF = 0.84) and expressed in µg/kg index chemical equivalents)[a] (Benchmark = 30)			**Cumulative Non-Attributable MOE (NHANES)** (MOEs calculated by dividing the index chemical (DBP) POD in µg/kg by the non-attributable cumulative exposure expressed in µg/kg index chemical equivalents) (Benchmark = 30)	**Approach 1: Cumulative MOE (Aggregate MOE + Cumulative Non-attributable MOE)** (Benchmark = 30)	**Approach 2: Cumulative MOE (Aggregate MOE + Cumulative Non-attributable MOE)** (Benchmark = 30)
		Inhalation MOE	**Dermal MOE**	**Aggregate MOE**	**Inhalation MOE (DCHP COU)**	**Dermal MOE (DCHP COU)**	**Aggregate MOE (DCHP COU)**			
Recycling	CT	23 (1,100/46.9)	466 (1,100/2.36)	22 (1,100/49.3)	54 (2,100/39.0)	1,072 (2,100/1.96)	51 (2,100/40.9)	407 (2,100/5.16)	46	21
	HE	15 (1,100/73.2)	233 (1,100/4.72)	14 (1,100/77.9)	35 (2,100/60.7)	536 (2,100/3.92)	32 (2,100/64.7)	407 (2,100/5.16)	30	14

[a] Doses shown to three significant figures.

Empty Risk Cup Benchmark MOE = 30 (Represented by dotted red line)	Risk Cup[a] Associated with Acute MOEs (Aggregate MOE) From Individual DEHP Risk Evaluation Aggregate MOE	Risk Cup[a] Associated with Acute MOEs Scaled by Relative Potency (Aggregate MOE)	Risk Cup[a] Associated with Cumulative Non-Attributable MOE	Risk Cup[a] Associated with Approach 1: Cumulative MOE (Aggregate MOE + Cumulative Non-Attributable MOE)	Risk Cup[a] Associated with Approach 2: Cumulative MOE (Aggregate MOE + Cumulative Non-Attributable MOE)
					

[a]Risk cup visualized here is just an example showing the contributions of various exposures to the risk cup and is for illustrative purposes only. The MOE has an inverse relationship with the exposure dose so adding exposure to the risk cup yield a lower MOE.

Figure 5-2. DEHP Risk Calculation Generic Example (Not to Scale) for Female Workers of Reproductive Age

5.2 Estimation of Cumulative Risk – Approach 2

As described above, EPA is focusing its exposure assessment for the cumulative risk analysis on evaluation of exposures through individual TSCA consumer and occupational COUs for each phthalate and non-attributable cumulative exposure to DEHP, DBP, BBP, DIBP, and DINP using NHANES urinary biomonitoring data and reverse dosimetry. In Section 5.1, EPA presented an approach for estimating cumulative risk by first scaling each individual phthalate exposure by relative potency using the RPFs presented in Table 2-4 to express phthalate exposure in terms of index chemical (DBP) equivalents. Exposures from individual consumer or worker COUs/OES (occupational exposure scenario) were then combined with non-attributable cumulative exposures estimated using NHANES to estimate cumulative risk under TSCA. In this second approach, individual phthalate exposures for consumer and occupational COUs are not scaled by RPFs but use the individual phthalate hazard values and are still combined with non-attributable cumulative exposures estimated using NHANES.

The four-step process for Approach 2 is outlined below, along with two empirical examples of how EPA calculated cumulative risk for one occupational OES for DCHP (*i.e.*, Application of Paints and Coatings (Solids)) and one occupational OES for DEHP (*i.e.*, Recycling). Empirical examples for DCHP and DEHP are also shown in Table 5-2 and Table 5-3, respectively, where they are compared against Approach 1. Figure 5-1 and Figure 5-2 provide visual representations of the risk cup associated with the example calculations. Section 5.4 compares the differences in the cumulative MOEs between the two approaches.

Step 1: Identify Exposure Estimates for the Individual Phthalate from Each Individual Consumer and Occupational COU to be used for the Cumulative Risk Estimate

In this step, acute duration exposure estimates for an individual phthalate from each consumer and occupational COU/OES are identified for use in the cumulative risk estimate, including exposure estimates for each route of exposure being assessed for each COU (*i.e.*, inhalation, dermal, and aggregate exposures for occupational COUs; inhalation, ingestion, dermal, and aggregate exposure for consumer COUs). Unlike in Approach 1, however, these estimates are not scaled by relative potency and instead remain in dose units of the individual phthalate.

Example (DCHP): 50th percentile inhalation and dermal DCHP exposures for female workers of reproductive age are 38.7 and 2.07 µg/kg for the Application of Paints and Coatings (Solids) OES (U.S. EPA, 2025ad) and the aggregate exposure combining inhalation and dermal exposure is 40.7 µg/kg (Table 5-2).

Example (DEHP): 50th percentile inhalation and dermal DEHP exposures for female workers of reproductive age are 46.9 and 2.36 µg/kg for the Recycling OES (U.S. EPA, 2025q) and the aggregate exposure combining inhalation and dermal exposure is 49.3 µg/kg (Table 5-3).

Step 2: Estimate Non-attributable Cumulative Exposure to DEHP, DBP, BBP, DIBP, and DINP Using NHANES Urinary Biomonitoring Data and Reverse Dosimetry (see Section 4 for further details)

The step is identical to Step 2 shown for Approach 1 in Section 5.1, where non-attributable exposure for a national population to DEHP, DBP, BBP, DIBP, and DINP was estimated using Equation 5-2, where individual phthalate daily intake values estimated from NHANES biomonitoring data and reverse dosimetry were scaled by relative potency, expressed in terms of index chemical (DBP) equivalents, and summed to estimate non-attributable cumulative exposure in terms of DBP equivalents. As shown in the example in Step 2 in Section 5.1, the 95th percentile cumulative exposure estimate of 5.16 µg/kg-day DBP equivalents for black, non-Hispanic women of reproductive age (Table 4-3) is calculated using Equation 5-2.

Step 3: Calculate MOEs for Each Exposure to the Individual Phthalate and for the Non-attributable Cumulative Exposure

Next, MOEs are calculated for each exposure of interest that is included in the cumulative scenario using Equation 5-5 and Equation 5-6. In Approach 2, inhalation and dermal phthalate exposures for individual COU/OES are not scaled by the RPF so MOEs for individual phthalates are calculated using the individual phthalate PODs as shown in Equation 5-5.

For example, this step involves calculating MOEs for inhalation and dermal phthalate exposures for each individual COU/OES in step 1 using PODs for the given phthalates and an MOE for non-attributable cumulative phthalate exposure expressed in DBP equivalents from step 2 above using the DBP POD.

Equation 5-5. Calculating MOEs for Exposures of Interest for Approach 2

$$MOE_1 = \frac{Individual\ Chemical\ POD}{Inidividual\ Chemical\ Exposure}$$

Where:

- MOE_1 (unitless) is the MOE calculated for each exposure of interest included in the cumulative scenario.
- Individual chemical POD is the POD selected for the individual phthalate. The PODs for DCHP and DEHP are 2,400 and 1,100 µg/kg, respectively.
- Individual chemical exposure is the exposure estimate from the COU/OES in units µg/kg for the individual chemical (not converted to index chemical equivalents).

Equation 5-6. Calculating MOE for Non-Attributable Exposure from NHANES

$$MOE_{NHANES} = \frac{Index\ Chemical\ (DBP)\ POD}{Exposures_{NHANES}\ in\ DBP\ Equivalents}$$

Where:

- MOE_{NHANES} (unitless) is the MOE calculated for the exposure estimate in DBP equivalents for the non-attributable exposure estimated from NHANES.
- Index chemical (DBP) POD is the POD selected for the index chemical, DBP. The index chemical POD is 2,100 µg/kg.
- $Exposure_{NHANES}$ is the exposure estimate in DBP equivalents for the non-attributable exposure estimated from NHANES (*i.e.,* from step 2 above).

Example (DCHP): Using Equation 5-5, the 50th percentile MOEs for inhalation, dermal, and aggregate DCHP exposure estimates for the Application of Paints and Coatings (Solids) OES are 62, 1157, and 59, respectively Table 5-2.

Using Equation 5-6, the MOE for the non-attributable cumulative exposure estimate in DBP equivalents is 407.

$$MOE_{Cumulative\ Non-attributable} = 407 = \frac{2{,}100\ \mu g/kg}{5.16\ \mu g/kg}$$

$$MOE_{COU-Inhalation} = 62 = \frac{2{,}400\ \mu g/kg}{38.7\ \mu g/kg}$$

$$MOE_{COU-Dermal} = 1{,}157 = \frac{2{,}400\ \mu g/kg}{2.07\ \mu g/kg}$$

$$MOE_{COU-Aggregate} = 59 = \frac{2{,}400\ \mu g/kg}{40.7\ \mu g/kg}$$

Example (DEHP): Using Equation 5-5, the 50th percentile MOEs for inhalation, dermal, and aggregate DEHP exposure estimates for the Recycling OES are 23, 466, and 22, respectively Table 5-3.

Using Equation 5-6, the MOE for the non-attributable cumulative exposure estimate in DBP equivalents is 407.

$$MOE_{Cumulative\ Non-attributable} = 407 = \frac{2{,}100\ \mu g/kg}{5.16\ \mu g/kg}$$

$$MOE_{COU-Inhalation} = 23 = \frac{1{,}100\ \mu g/kg}{46.9\ \mu g/kg}$$

$$MOE_{COU-Dermal} = 466 = \frac{1{,}100\ \mu g/kg}{2.36\ \mu g/kg}$$

$$MOE_{COU-Aggregate} = 22 = \frac{1{,}100\ \mu g/kg}{49.3\ \mu g/kg}$$

Step 4: Calculate the Cumulative MOE

For the cumulative MOE approach, MOEs for each exposure of interest in the cumulative scenario are first calculated (Step 3). The cumulative MOE for the cumulative scenario can then be calculated using Equation 5-7. Equation 5-7 shows the addition of MOEs for the inhalation and dermal exposures routes from an individual COU, as well as the MOE for non-attributable cumulative exposure to phthalates from NHANES urinary biomonitoring and reverse dosimetry. Additional MOEs can be added to the equation as necessary (*e.g.*, for the ingestion route for consumer scenarios).

Equation 5-7. Cumulative Margin of Exposure Calculation

$$Cumulative\ MOE = \frac{1}{\frac{1}{MOE_{COU-Inhalation}} + \frac{1}{MOE_{COU-Dermal}} + \frac{1}{MOE_{Cumulative-Non-attributable}} \ldots}$$

Example (DCHP): The cumulative MOE for the Application of Paints and Coatings (Solids) OES is 51 and is calculated by summing the MOEs for each exposure of interest from step 3 as follows (Table 5-2):

$$Cumulative\ MOE = 51 = \frac{1}{\frac{1}{62} + \frac{1}{1{,}157} + \frac{1}{407}}$$

Example (DEHP): The cumulative MOE for the Recycling OES is 21 and is calculated by summing the MOEs for each exposure of interest from step 3 as follows (Table 5-3):

$$Cumulative\ MOE = 21 = \frac{1}{\frac{1}{23} + \frac{1}{466} + \frac{1}{407}}$$

5.3 Impact of the Cumulative Analysis on Phthalates being Evaluated Under TSCA Under Approach 1 and Approach 2

5.3.1 Impact of the Cumulative Analysis on Phthalates being Evaluated Under TSCA Using Approach 1

The cumulative analysis approach outlined in Section 5.1 is being used by EPA to supplement the individual phthalate risk evaluations. The cumulative analysis using Approach 1 will have varying impacts on each of the individual phthalate risk evaluations and will be influenced by three key factors. This includes: (1) scaling individual phthalate acute exposure estimates for each COU/OES by relative potency; (2) calculation of the cumulative MOE using the index chemical POD; and (3) addition of non-attributable cumulative exposure from NHANES. The overall effect of these three factors for each phthalate being evaluated under TSCA is summarized in Table 5-5 and is discussed further in Section 5.3.1.1 through Section 5.3.1.6.

5.3.1.1 Dibutyl Phthalate (DBP)

Application of the cumulative analysis outlined in Section 5.1 will have a small overall effect for DBP. Cumulative risk estimates will be approximately 1.1 to 1.2× more sensitive than in the individual DBP risk evaluation (Table 5-5). This conclusion is based on the following considerations:

- ***Scaling by Relative Potency:*** DBP is the index chemical and the RPF for DBP is 1 (Table 2-4). Scaling by relative potency will have no effect on scaled exposure estimates.
- ***Index Chemical POD:*** EPA selected the same POD of 2.1 mg/kg-day based on the $BMDL_5$ for reduced fetal testicular testosterone as the acute POD for the individual DBP risk evaluation

(U.S. EPA, 2025u) and as the index chemical POD for use in the CRA, so this also will have no effect.

- ***Addition of Non-Attributable Cumulative Exposure:*** This will add 6.2 to 15.5 percent to the risk cup, depending on the population and lifestage being assessed (Table 5-4). This is the only factor that will contribute to the slightly more sensitive cumulative risk estimates for DBP.

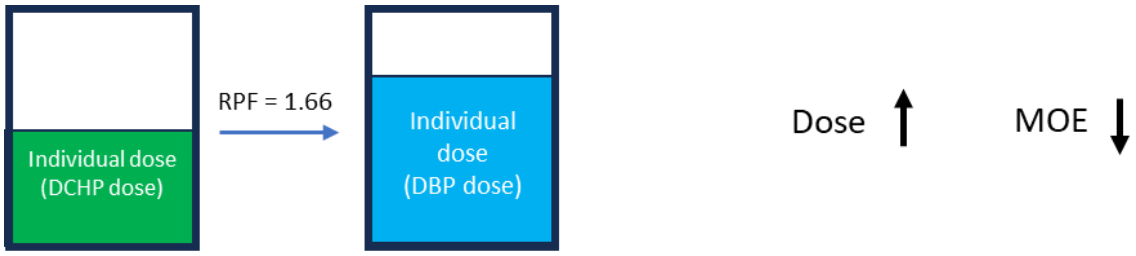
Table 5-4. Summary of Non-Attributable Cumulative Exposure from NHANES Being Combined for Each Assessed Population

Population	Lifestage	Non-Attributable Cumulative Exposure from NHANES (DBP Equivalents, µg/kg-day)	NHANES Population	% Contribution to Risk Cup
Worker	Women of reproductive age (16-49 years)	5.16	Black, non-Hispanic women of reproductive age (16-49 years)	7.4%
Consumer	Adult (≥21 years)			
	Teenager (16-20 years)			
	Young Teen (11-15 years)	4.36	Males (12-15 years)	6.2%
	Child (6-10 years)	7.35	Males (6-11 years)	10.5%
	Preschooler (3-5 years)	10.8	Males (3-5 years)	15.5%
	Toddler (1-2 years)			
	Infant (<1 year)			

5.3.1.2 Dicyclohexyl Phthalate (DCHP)

Application of the cumulative analysis outlined in Section 5.1 will lead to risk estimates that are approximately 2× to 2.2× more sensitive than in the individual DCHP risk evaluation (Table 5-5). This conclusion is based on the following considerations:

- ***Scaling by Relative Potency:*** The RPF for DCHP is 1.66 (Table 2-4). This means acute DCHP exposures when multiplied by the RPF and expressed in terms of index chemical (DBP) equivalents will increase by 66 percent, which will be the primary factor contributing to the more sensitive risk estimates.



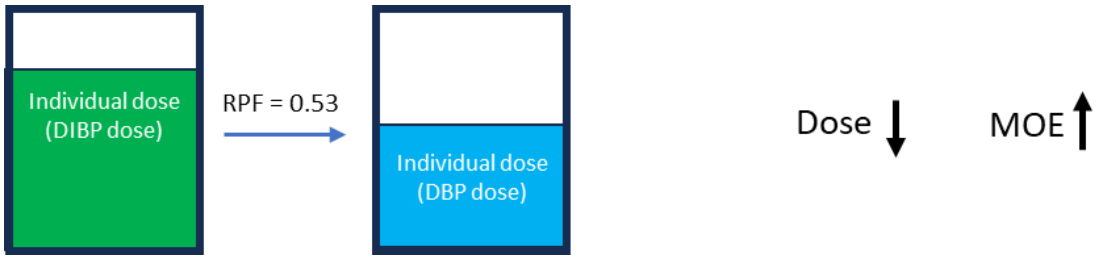
- ***Index Chemical POD:*** The POD for the index chemical (DBP) used to calculate cumulative risk is 2.1 mg/kg (derived from a $BMDL_5$ of 9 mg/kg-day for reduced fetal testicular testosterone from the meta-analysis of data from 8 studies), while the POD for DCHP used to calculate MOEs in the individual DCHP risk evaluation is 2.4 mg/kg (derived from a NOAEL of 10 mg/kg-day based on a spectrum of effects on the developing male reproductive system consistent with phthalate syndrome). The index chemical (DBP) POD is slightly (12.5%) lower (*i.e.*, more sensitive) than the individual DCHP POD, which will contribute to the more sensitive risk estimates.

- ***Addition of Non-Attributable Cumulative Exposure:*** This will add 6.2 to 15.5 percent to the risk cup, depending on the population and lifestage being assessed (Table 5-4) and will contribute to the more sensitive risk estimates.

5.3.1.3 Diisobutyl Phthalate (DIBP)

Application of the cumulative analysis outlined in Section 5.1 will lead to risk estimates that are approximately 1.5× to 1.7× more sensitive (Table 5-5). This conclusion is based on the following considerations:

- ***Scaling by Relative Potency:*** The RPF for DIBP is 0.53 (Table 2-4). This means acute DIBP exposures when multiplied by the RPF and expressed in terms of index chemical (DBP) equivalents will decrease by a factor of approximately 2.



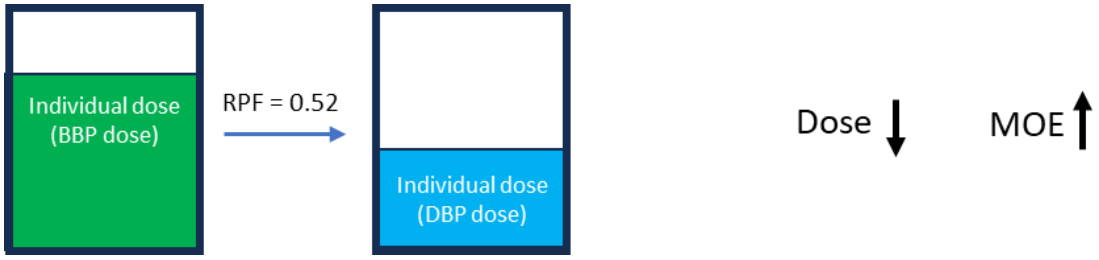
- ***Index Chemical POD:*** The POD for the index chemical (DBP) used to calculate cumulative risk is 2.1 mg/kg (derived from a $BMDL_5$ of 9 mg/kg-day for reduced fetal testicular testosterone from the meta-analysis of data from 8 studies), while the POD for DIBP used to calculate MOEs in the individual DIBP risk evaluation is 5.7 mg/kg (derived from a $BMDL_5$ of 24 mg/kg-day for reduced fetal testicular testosterone from one study) (U.S. EPA, 2025y). The index chemical (DBP) POD is 2.7 times lower (*i.e.*, more sensitive) than the DIBP POD, which will contribute to lower cumulative MOEs.

- ***Addition of Non-Attributable Cumulative Exposure:*** This will add 6.2 to 15.5 percent to the risk cup, depending on the population and lifestage being assessed (Table 5-4) and will contribute to the more sensitive risk estimates.

5.3.1.4 Butyl Benzyl Phthalate (BBP)

Application of the cumulative analysis outlined in Section 5.1 will lead to risk estimates that are approximately 3.2× to 3.5× more sensitive (Table 5-5). This conclusion is based on the following considerations:

- ***Scaling by Relative Potency:*** The RPF for BBP is 0.52 (Table 2-4). This means acute BBP exposures when multiplied by the RPF and expressed in terms of index chemical (DBP) equivalents will decrease by a factor of approximately 2.



- ***Index Chemical POD:*** The POD for the index chemical (DBP) used to calculate cumulative risk is 2.1 mg/kg (derived from a $BMDL_5$ of 9 mg/kg-day for reduced fetal testicular testosterone from the meta-analysis of data from 8 studies), while the POD for BBP used to calculate MOEs in the individual BBP risk evaluation is 12 mg/kg (derived from a NOAEL of 50 mg/kg-day based on a spectrum of effects on the developing male reproductive system consistent with phthalate syndrome). The index chemical (DBP) POD is 5.7 times lower (*i.e.*, more sensitive) than the BBP POD, which will contribute to lower cumulative MOEs.

- ***Addition of Non-Attributable Cumulative Exposure:*** This will add 6.2 to 15.5 percent to the risk cup, depending on the population and lifestage being assessed (Table 5-4) and will contribute to the more sensitive risk estimates.

5.3.1.5 Diisononyl Phthalate (DINP)

Application of the cumulative analysis outlined in Section 5.1 will lead to risk estimates that are approximately 1.3× to 1.4× more sensitive (Table 5-5). This conclusion is based on the following considerations:

- ***Scaling by Relative Potency:*** The RPF for DINP is 0.21 (Table 2-4). This means acute DINP exposures when multiplied by the RPF and expressed in terms of index chemical (DBP) equivalents will decrease by a factor of approximately 5.

- ***Index Chemical POD:*** The POD for the index chemical (DBP) used to calculate cumulative risk is 2.1 mg/kg (derived from a $BMDL_5$ of 9 mg/kg-day for reduced fetal testicular testosterone from the meta-analysis of data from 8 studies), while the POD for DINP used to calculate MOEs in the individual DINP risk evaluation is 12 mg/kg (derived from a $BMDL_5$ of 49 mg/kg-day for reduced fetal testicular testosterone from the meta-analysis of data from 4 studies). The index chemical (DBP) POD is 5.7 times lower (*i.e.*, more sensitive) than the DINP POD, which will contribute to lower cumulative MOEs.

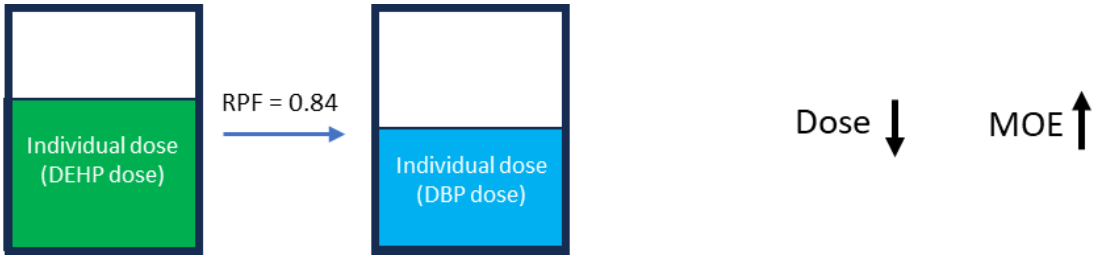
POD ↓ MOE ↓

- ***Addition of Non-Attributable Cumulative Exposure:*** This will add 6.2 to 15.5 percent to the risk cup, depending on the population and lifestage being assessed (Table 5-4) and will contribute to the more sensitive risk estimates.

5.3.1.6 Diethylhexyl Phthalate (DEHP)

Application of the cumulative analysis outlined in Section 5.1 will lead to risk estimates that are less sensitive than in the individual DEHP risk evaluation (Table 5-2). This is because DEHP is data-rich and the POD used for the individual chemical assessment based on male reproductive tract malformations is more sensitive than the index chemical POD, which washes out the addition of the non-attributable cumulative exposure. This conclusion is based on the following considerations:

- ***Scaling by Relative Potency:*** The RPF for DEHP is 0.84 (Table 2-4). This means acute DEHP exposures when multiplied by the RPF and expressed in terms of index chemical (DBP) equivalents will decrease by 16 percent.



- ***Index Chemical POD:*** The POD for the index chemical (DBP) used to calculate cumulative risk is 2.1 mg/kg (derived from a $BMDL_5$ of 9 mg/kg-day for reduced fetal testicular testosterone from the meta-analysis of data from 8 studies), while the acute POD for DEHP used to calculate MOEs in the individual DEHP risk evaluation is 1.1 mg/kg (derived from a NOAEL of 4.8 mg/kg based on a spectrum of effects on the developing male reproductive system consistent with phthalate syndrome). The index chemical (DBP) POD is 1.9 times higher (*i.e.*, less sensitive) than the DEHP POD, which will contribute to less sensitive cumulative MOEs.

POD ↑ MOE ↑

- ***Addition of Non-Attributable Cumulative Exposure:*** This will add 6.2 to 15.5 percent to the risk cup, depending on the population and lifestage being assessed (Table 5-4) and will contribute to the more sensitive risk estimates.

5.3.2 Impact of the Cumulative Analysis on Phthalates being Evaluated Under TSCA Under Approach 2

The cumulative analysis approach outlined in Section 5.2 is another approach being used by EPA to supplement the individual phthalate risk evaluations. Unlike the first approach outlined in Section 5.1, which has varying impacts on the cumulative risk estimates for each of the individual phthalate risk evaluations as described in Section 5.3.1 based on the RPFs, the second approach has the same impact on cumulative risk estimates for every phthalate being evaluated under TSCA. The only impact of approach 2 is the addition of non-attributable cumulative exposure from NHANES to individual phthalate exposures, which will add 6.2 to 15.5 percent to the risk cup, depending on the population and lifestage being assessed (Table 5-4). Approach 2 will have a small overall effect for DBP, DCHP, DIBP, BBP, DINP, and DEHP. Cumulative risk estimates for all phthalates will be approximately 1.1× to 1.2× more sensitive than in the individual phthalate risk evaluations (Table 5-5).

Table 5-5. Summary of Impact of Cumulative Assessment on Phthalates Being Evaluated Under TSCA

Phthalate	Individual Phthalate Assessment			Cumulative Analysis			Approach 1: Conclusions	Approach 2: Conclusions
	Acute POD (mg/kg-day)	POD Type and Effect	Benchmark MOE	RPF	Index Chemical POD (mg/kg-day)	Cumulative Benchmark MOE		
DBP (index chemical)	2.1	$BMDL_5$ (↓ fetal testicular testosterone)	30	1	2.1	30	Cumulative MOEs will be ~1.1×–1.2× more sensitive (or lower) than aggregate MOEs in the individual DBP risk assessment	Cumulative MOEs will be ~1.1–1.2× more sensitive (or lower) than aggregate MOEs in each individual phthalate risk assessment
DEHP	1.1	NOAEL (Phthalate syndrome-related effects)	30	0.84			Cumulative MOEs will be less sensitive (higher) than aggregate MOEs in the individual DEHP risk assessment based on the lower (more sensitive) DEHP POD compared to the index chemical POD	
BBP	12	NOAEL (Phthalate syndrome-related effects)	30	0.52			Cumulative MOEs will be ~3.2× to 3.5× more sensitive (or lower) than aggregate MOEs in the individual BBP risk assessment	
DIBP	5.7	$BMDL_5$ (↓ fetal testicular testosterone)	30	0.53			Cumulative MOEs will be ~1.5× to 1.7× more sensitive (or lower) than aggregate MOEs in the individual DIBP risk assessment	
DCHP	2.4	NOAEL (Phthalate syndrome-related effects)	30	1.66			Cumulative MOEs will be ~2× to 2.2× more sensitive (or lower) than aggregate MOEs in the individual DCHP risk assessment	
DINP	12	$BMDL_5$ (↓ fetal testicular testosterone)	30	0.21			Cumulative MOEs will be ~1.3× to 1.4× more sensitive (or lower) than aggregate MOEs in the individual phthalate risk assessment	

5.4 Comparison of Two Approaches for Estimating Cumulative Risk

This section provides an overview of the similarities and differences between the two approaches for estimating cumulative risk outlined above in Section 5.1 (Approach 1) and Section 5.2 (Approach 2). There are several notable similarities and differences between the two approaches. For example, both approaches utilize NHANES urinary biomonitoring data and reverse dosimetry to estimate non-attributable cumulative phthalate exposure expressed in index chemical (DBP) equivalents which will contribute 6.2 to 15.5 percent to the risk cup, depending on the population and lifestage being assessed (Table 5-4). Key differences between the two approaches include differences in application of RPFs and hazard values. For example, for Approach 1 (Section 5.1), cumulative risk is estimated by first scaling each individual phthalate exposure for a consumer or occupational COU by relative potency before combining with non-attributable cumulative exposure (in index chemical equivalents) estimated using NHANES. The index chemical POD is then used to calculate cumulative risk. For Approach 2 (Section 5.2), individual phthalate exposures from individual consumer and occupational COUs are not scaled by relative potency. Instead, the individual phthalate POD is used to calculate risk for each individual COU, and then this risk is combined with non-attributable cumulative risk from NHANES.

Both approaches were subject to public comment and peer-reviewed by SACC during the August 2025 phthalate peer-review meeting (U.S. EPA, 2025ag), and this CRA TSD takes public comments and SACC recommendations into account. Overall, SACC concluded that both approaches have strengths and uncertainties, but that the two approaches together provide a complete picture of the potential cumulative risk and that EPA should present both approaches in the individual risk evaluations for each phthalate and select the most scientifically defensible approach for the final individual risk characterization and decision making process for each phthalate (U.S. EPA, 2025ag).

Based on SACC recommendations, EPA is including both cumulative risk characterization approaches in each individual phthalate risk evaluation. To determine which approach is most scientifically defensible for use in the final risk characterization and decision making for each individual phthalate, EPA considered the strengths, limitations, and uncertainties of underlying dose-response data supporting both approaches for each phthalate included in the CRA. To support transparent and consistent decision making, EPA developed a framework that outlines key considerations used by EPA to determine the most scientifically defensible approach for the contribution of cumulative risk to the individual risk characterization for each phthalate, which is provided in Section 5.4.1. The remainder of this section then discusses the strengths, limitations, and uncertainties associated with both approaches, as well as the approach selected by EPA for DBP (Section 5.4.2), DCHP (Section 5.4.3), DIBP (Section 5.4.4), BBP (Section 5.4.5), DINP (Section 5.4.6), and DEHP (Section 5.4.7). Table 5-7 summarizes the CRA approach selected by EPA for each phthalate.

5.4.1 Framework of Considerations for CRA Approach Selection

This section outlines the information considered by EPA to support selection of the most scientifically defensible CRA approach for each phthalate. Because non-attributable cumulative exposure and risk from NHANES biomonitoring data are factored into Approaches 1 and 2 in the same manner, non-attributable cumulative exposure and risk from NHANES is not a factor that contributes to differences in cumulative risk estimates between the two approaches. Instead, differences between the two approaches stem from how exposure estimates from each individual phthalate COU are handled. For Approach 1 (Section 5.1), exposure estimates from individual consumer or occupational COUs are scaled by relative potency, expressed in index chemical equivalents, and the index chemical POD is used to calculate risk. For Approach 2 (Section 5.2), exposure estimates from individual consumer or occupational COUs are

not scaled by relative potency, and the individual phthalate POD is used to calculate risk for each individual COU, resulting in risk estimates identical to those calculated in the individual phthalate risk assessment. Therefore, there are two primary factors that contribute to how closely cumulative risk estimates align between Approaches 1 and 2: the RPF for each phthalate and the POD selected for each individual phthalate.

Understanding the strengths, limitations, and uncertainties of the dose-response data supporting the RPF for each phthalate and the POD selected for each phthalate is key for selecting the most scientifically defensible CRA approach for use in the final risk characterization and for use in decision making for each phthalate. Factors considered by EPA for each phthalate in support of decision making are provided in Table 5-6.

Table 5-6. Considerations for Determining Confidence in Cumulative Risk Estimates for CRA Approaches 1 and 2

Factor	Consideration
Dose-Response Data Supporting RPF Derivation	• Quantity and quality of fetal testicular testosterone dose-response data • Availability of dose-response data in the low-end range of the dose-response curve (*i.e.,* doses below those eliciting a 40% response) • Similarity of candidate RPFs across 5, 10, and 40% response levels (*i.e.,* consideration of the parallelism) • Similarity of BMD results obtained via different approaches (*i.e.,* meta-analysis and/or BMD modeling of individual datasets using EPA's BMDS)
Dose-Response Data Supporting the Individual Phthalate POD	• Quantity and quality of dose-response data supporting the POD, whether it be a NOAEL (*i.e.,* for DEHP, BBP, DCHP) or $BMDL_5$ (*i.e.,* for DBP, DIBP, DINP) • For DEHP, BBP, and DCHP, the dose-range between the NOAEL and LOAEL • Comparison of BMD modeling and NOAEL/LOAEL approaches

5.4.2 Dibutyl Phthalate (DBP)

As discussed in Section 2.3, DBP was selected as the index chemical and the RPF for DBP is 1.0 (Section 2.4). Since DBP is the index chemical, Approaches 1 and 2 are mathematically identical and result in identical cumulative risk estimates. Application of Approaches 1 and 2 both lead to cumulative risk estimates that are approximately 1.1× to 1.2× more sensitive than risk estimates in the individual DBP risk evaluation (Sections 5.3.1.1 and 5.3.2). The only factor contributing to the more sensitive cumulative risk estimates for DBP is the addition of non-attributable cumulative phthalate exposure (from NHANES) expressed in index chemical (DBP) equivalents which will contribute 6.2 to 15.5 percent to the risk cup, depending on the population and lifestage being assessed (Table 5-4). Overall,

Approaches 1 and 2 result in identical cumulative risk estimates for DBP, and EPA will consider both approaches in the risk characterization of exposures and hazards discussed in the *Risk Evaluation of DBP* (U.S. EPA, 2025af).

5.4.3 Dicyclohexyl Phthalate (DCHP)

As discussed in Section 5.3.1.2, application of Approach 1 for DCHP leads to cumulative risk estimates that are approximately 2× to 2.2× more sensitive than risk estimates in the individual DCHP risk evaluation, while application of Approach 2 leads to risk estimates that are approximately 1.1× to 1.2× more sensitive than in the individual DCHP risk evaluation (Section 5.3.2). The reason for the difference in cumulative risk estimates between the two approaches is because the RPF of 1.66 based on reduced fetal testicular testosterone content (used in Approach 1) indicates DCHP is 66 percent more potent than DBP, while the index chemical (DBP) POD of 2.1 mg/kg-day (used in Approach 1) is very similar to the DCHP POD of 2.4 mg/kg-day (used in Approach 2), which indicates DCHP and DBP have similar potency for causing phthalate syndrome-related effects. The strengths, limitations, and uncertainties of the dose-response data supporting derivation of the DCHP RPF and the DCHP POD are provided below.

Dose-Response Data Supporting RPF Derivation

- ***Quantity and quality of fetal testicular testosterone dose-response data:*** The RPF of 1.66 was derived based on the ratio of the index chemical (DBP) BMD_{40} to the DCHP BMD_{40} (*i.e.*, 149/90 = 1.66) for reduced fetal testicular testosterone. The DCHP RPF was estimated via meta-analysis and BMD analysis of fetal testicular testosterone data from three studies reported in two high-quality publications (Gray et al., 2021; Furr et al., 2014).
- ***Availability of dose-response data in the low end range of the dose-response curve (i.e., doses below those eliciting a 40% response):*** One source of uncertainty associated with the meta-analysis and BMD analysis of DCHP is that there are limited testosterone data available for DCHP in the low-end range of the dose response curve. For example, the lowest dose evaluated for DCHP and included in the meta-analysis is 33 mg/kg-day, while BMD_5 and $BMDL_5$, BMD_{10} and $BMDL_{10}$, and BMD_{40} and $BMDL_{40}$ estimates from the meta-analysis are 8.4 and 6.0, 17 and 12, and 90 and 63 mg/kg-day, respectively (U.S. EPA, 2025t). This uncertainty is in part lessened by a fourth study not included in the meta-analysis in which pregnant rats were gavaged with 0, 10, 100, and 1000 mg/kg-day DCHP on GD 12–21 and then testicular testosterone content was measured on postnatal day 1 (Li et al., 2016). Since testosterone was not measured in the fetal lifestage, the study was not included in the meta-analysis, however, BMD analysis of testicular testosterone data from this study using EPA's BMD Software (Version 25.1) supports BMD_5/$BMDL_5$, BMD_{10}/$BMDL_{10}$ and BMD_{40}/$BMDL_{40}$ estimates of 6.9/1.2, 15/2.6, and 113/24 mg/kg-day, respectively. This study is limited by small sample size (N of 6 per group) and resulting large standard error, which is reflected in large BMD/BMDL ratios of approximately 5–6 and making the BMD results from the Li et al. study not appropriate for deriving a POD for the single chemical assessment. BMD estimates at the 5 and 10 percent response levels are very similar to those estimated for reduced fetal testosterone via meta-analysis (*i.e.*, 8.4 vs. 6.9 mg/kg-day and 17 vs. 15 mg/kg-day at the 5 and 10% response levels, respectively).
- ***Similarity of candidate RPFs across 5, 10, 40 percent response levels (i.e., consideration of the parallelism):*** Candidate RPFs for DCHP did not vary significantly at the 5, 10, and 40 percent response levels (*i.e.*, RPFs ranged from 1.66–1.71; Table 2-4). This indicates that the selected RPF of 1.66 derived from the 40 percent response level is expected to provide a reasonable estimate of potency at the 5 and 10 percent response levels, indicating parallel dose-response curves. This increases EPA's confidence in the selected RPF for DCHP.

- ***Similarity of BMD results obtained via different approaches:*** EPA also conducted BMD modeling of the individual DCHP fetal testicular testosterone data from each of the three studies included in the meta-analysis using EPA's BMDS Online software (Version 25.1) (U.S. EPA, 2025w). One benefit of this analysis is that BMDS includes a broader suite of models compared to those included in the meta-analysis approach (*i.e.*, Exponential, Hill, Polynomial, Power, Linear models vs. linear and linear-quadratic models in the meta-analysis). BMD modeling of individual fetal testicular testosterone data supported BMD_5 and $BMDL_5$ estimates nearly identical to those estimated via meta-analysis (see (U.S. EPA, 2025w) for further discussion). For example, BMD_5 and $BMDL_5$ estimates for reduced fetal testicular testosterone are 9.0 and 5.2 mg/kg-day for the best-fitting Exponential 3 model (Furr et al., 2014) and 13.7 and 10.0 mg/kg-day for the best-fitting Exponential 3 model (Gray et al., 2021), compared to 8.4 and 6.0 mg/kg-day for the best-fitting linear-quadratic model in the meta-analysis.

Dose-Response Data Supporting the Individual Phthalate POD

- ***Quantity and quality of dose-response data supporting the POD:*** The DCHP POD is an HED of 2.4 mg/kg-day and is derived from a NOAEL of 10 mg/kg-day based on a spectrum of effects on the developing male reproductive system consistent with phthalate syndrome (U.S. EPA, 2025w). The DCHP POD is supported by six gestational exposure studies of rats, including 2 high-quality (Ahbab and Barlas, 2015; Furr et al., 2014) and 4 medium-quality studies (Ahbab et al., 2017; Li et al., 2016; Ahbab and Barlas, 2013; Hoshino et al., 2005).
- ***Dose-range between the NOAEL and LOAEL:*** The six studies supporting the selected POD for DCHP support a narrow range of NOAEL (10–17 mg/kg-day) and LOAEL (20–33 mg/kg-day) values for phthalate syndrome-related effects in gestationally exposed rats (see Section 4 of (U.S. EPA, 2025w) for further discussion). This increases EPA's confidence in the selected POD for DCHP.
- ***Comparison of BMD modeling and NOAEL/LOAEL approaches:*** EPA's meta-analysis and BMD-analysis of fetal testicular testosterone data (including the analysis of individual datasets) supports $BMDL_5$ estimates ranging from 5.2 to 10 mg/kg-day, which further supports the selected NOAEL of 10 mg/kg-day (U.S. EPA, 2025w). Although 2 out of 3 of the $BMDL_5$ estimates are below (*i.e.*, more sensitive than) the selected NOAEL of 10 mg/kg-day, EPA selected the NOAEL over a $BMDL_5$ estimate because all $BMDL_5$ estimates for reduced fetal testicular testosterone were below the lowest dose included in each respective study by factors of approximately 5× to 10×. Consistent with EPA's *Benchmark Dose Technical Guidance* (U.S. EPA, 2012), the lack of data to inform the low-end of the dose-response curve reduces EPA's confidence in the $BMDL_5$ estimates for use in risk characterization in the individual DCHP risk evaluation. Finally, and as described further in Section 4 of the DCHP non-cancer human health hazard assessment (U.S. EPA, 2025w), EPA also considered BMD analysis of phthalate-syndrome-related outcomes other than reduced testosterone. However, studies were generally not amenable to modeling for several reasons due to data limitations, study sensitivity, or the magnitude of the observed response (*e.g.*, all or none response, with no data in the low-end range of the curve close to a BMR of 5%).

Based on the weight of scientific evidence considerations outlined in the developed framework (Section 5.4.1), EPA has weighed the strengths and uncertainties associated with the DCHP RPF (Approach 1) and the DCHP POD (Approach 2 and individual DCHP risk evaluation). EPA acknowledges there are strengths and uncertainties of both approaches and concludes that Approach 2 using the POD from the single chemical assessment is the most appropriate for deriving cumulative risks for DCHP. This conclusion is based on the following:

- The POD approach (*i.e.*, Approach 2) is based on 6 studies, including the Li et al. study with testosterone data measured postnatally, and considers the full spectrum of adverse outcomes relevant to phthalate syndrome across a broad degree of dose levels, including multiple studies are or near 10 mg/k/day. In contrast, the RPF approach (*i.e.*, Approach 1) is based on 3 studies using a single adverse outcome (fetal testosterone) where only high dose data are available reducing confidence the BMD estimates at the lower end of the dose-response curve. As a result, both from an adverse outcome pathway perspective and a dose-response perspective, the underlying data for the POD approach are more robust and more appropriate for extrapolating cumulative risk.

5.4.4 Diisobutyl Phthalate (DIBP)

For DIBP, approaches 1 and 2 lead to cumulative risk estimates that are similar. The reason for the difference in cumulative risk estimates between the two approaches is because the RPF of 0.53 based on reduced fetal testicular testosterone content (used in Approach 1) indicates DIBP is 47 percent less potent than DBP, while the difference between the index chemical (DBP) POD of 2.1 mg/kg-day (used in Approach 1) and DIBP POD of 5.7 mg/kg-day (used in Approach 2) indicates DIBP is 63 percent less potent than the index chemical (DBP). These small differences in relative potency (*i.e.*, 47 vs. 63 percent) lead to the differences in risk estimates between Approaches 1 and 2. The strengths, limitations, and uncertainties of the dose-response data supporting derivation of the DIBP RPF and the DIBP POD are provided below.

Dose-Response Data Supporting RPF Derivation

- ***Quantity and quality of fetal testicular testosterone dose-response data:*** The DIBP RPF of 0.53 is derived from the ratio of the DBP BMD_{40} to the DIBP BMD_{40} for reduced fetal testicular testosterone (*i.e.*, 149÷279 mg/kg-day = 0.53). The DIBP RPF was estimated via meta-analysis and BMD analysis of fetal testicular testosterone data from three studies (2 high- and 1 medium-quality) (Gray et al., 2021; Hannas et al., 2011; Howdeshell et al., 2008).
- ***Availability of dose-response data in the low end range of the dose-response curve (i.e., doses below those eliciting a 40% response):*** One source of uncertainty associated with the meta-analysis and BMD analysis of DIBP is that there are limited testosterone data available for DIBP in the low-end range of the dose-response curve. The lowest dose evaluated in all three of the available studies of DIBP was 100 mg/kg-day, while BMD_{10} and BMD_{40} estimates from the meta-analysis are 55 and 279 mg/kg-day, respectively (U.S. EPA, 2025t). Additionally, no BMD_5 estimate could be derived for DIBP via the meta-analysis approach.
- ***Similarity of candidate RPFs across 5, 10, 40 percent response levels (i.e., consideration of the parallelism):*** Candidate RPFs for DIBP were identical at the 10 and 40 percent response levels (*i.e.*, RPFs were 0.53 at both response levels; Table 2-4). Because no BMD_5 estimate could be derived for DIBP, no candidate RPF could be derived for DIBP at the 5 percent response level. There is some uncertainty in how representative the RPF of 0.53 derived at the 40 and 10 percent response levels is of the response at the 5 percent response level. However, this is somewhat addressed by the lack of variability in RPFs at the 10 and 40 percent response levels, indicating parallel dose-response curves. Further candidate RPFs for DEHP, DCHP, and DINP did not vary significantly across the 5, 10, and 40 percent response levels (Section 2.4), indicating parallel dose-response curves for these phthalates as well. This indicates that the selected RPF of 0.53 for DIBP derived from the 40 percent response level is expected to provide a reasonable estimate of potency at the 5 percent response level, increasing EPA's confidence in the selected RPF.

- ***Similarity of BMD results obtained via different approaches:*** EPA also conducted BMD modeling of fetal testicular testosterone data from each individual study included in the meta-analysis using EPA's BMD Software (BMDS Version 3.3.2). One benefit of this analysis is that BMDS includes a broader suite of models compared to those included in the meta-analysis approach (*i.e.*, Exponential, Hill, Polynomial, Power, Linear models vs. linear and linear-quadratic models in the meta-analysis). As discussed further in the *Non-cancer Human Health Hazard Assessment for DIBP* (U.S. EPA, 2025y), BMD analysis of individual datasets provided BMD/BMDL estimates generally consistent with the meta-analysis approach. For example, BMD_{40} estimates were 335 mg/kg-day from the best-fitting Exponential 3 model (Gray et al., 2021) and 298 mg/kg-day from the best-fitting Hill model (Howdeshell et al., 2008) versus 279 mg/kg-day from the best-fitting linear-quadratic model in the meta-analysis.

Dose-Response Data Supporting the Individual Phthalate POD

- ***Quantity and quality of dose-response data supporting the POD:*** The DIBP POD is an HED of 5.7 mg/kg-day and is derived from a $BMDL_5$ of 24 mg/kg-day based on reduced fetal testicular testosterone from one high-quality study (Gray et al., 2021). One uncertainty associated with the DIBP POD is that the $BMDL_5$ of 24 mg/kg-day is below the lowest dose of 100 mg/kg-day included in the study by Gray et al. (2021). However, there are no studies of DIBP that have evaluated doses below 100 mg/kg-day. Given the lack of studies of evaluating doses of DIBP less than 100 mg/kg-day, EPA considered the POD derived from the BMD analysis of data in the study by Gray et al. to have the least uncertainty and highest confidence upon examination of the weight of scientific evidence (U.S. EPA, 2025y). Notably, the SACC supported EPA's selection of a $BMDL_5$ of 24 mg/kg-day from Gray et al. (2021) for use as the basis for the POD and had no concerns for EPA's BMD modeling approach, given the lack of studies evaluating doses of DIBP less than 100 mg/kg-day (U.S. EPA, 2025ag).
- ***Comparison of BMD modeling and NOAEL/LOAEL approaches:*** As discussed in the *Non-cancer Human Health Hazard Assessment for DIBP* (U.S. EPA, 2025y), four gestational exposure studies (3 high- and 1 medium-quality) of DIBP support a narrow range of NOAEL and LOAEL values of 100 and 125 mg/kg-day, respectively, for phthalate syndrome related effects (Gray et al., 2021; Hannas et al., 2011; Howdeshell et al., 2008; Saillenfait et al., 2008). The selected $BMDL_5$ of 24 mg/kg-day is below the lowest NOAEL of 100 mg/kg-day. As discussed in Section 4 of the DIBP non-cancer human health hazard assessment (U.S. EPA, 2025y), the selected $BMDL_5$ of 24 mg/kg-day based on reduced fetal testicular testosterone is also below the lowest $BMDL_5$ of 60 mg/kg-day for apical effects on the developing male reproductive system consistent with phthalate syndrome (*i.e.*, increased incidence of azoospermia or oligospermia (Saillenfait et al., 2008)). However, as discussed above, there are no studies of DIBP that have evaluated doses below 100 mg/kg-day, and although the $BMDL_5$ estimate below the lowest dose with empirical data, EPA considers the BMD analysis of data in the study by Gray et al. to have the least uncertainty and highest confidence upon examination of the weight of scientific evidence (U.S. EPA, 2025y).

Based on the weight of scientific evidence considerations outlined in the developed framework (Table 5-6), EPA has weighed the strengths and uncertainties associated with the DIBP RPF (Approach 1) and the DIBP POD (Approach 2 and individual DIBP risk evaluation). EPA has concluded that the strengths and uncertainties of both approaches are well balanced. Both approaches are health-protective and align with input from SACC. MOEs from Approach 2 will be used to characterize cumulative risk for DIBP, simplifying the risk characterization as it is more consistent with the single chemical assessment.

5.4.5 Butyl Benzyl Phthalate (BBP)

As discussed in Section 5.3.1.4, application of Approach 1 for BBP leads to cumulative risk estimates that are approximately 3.2× to 3.5× more sensitive than risk estimates in the individual BBP risk evaluation, while application of Approach 2 leads to risk estimates that are approximately 1.1× to 1.2× more sensitive than in the individual BBP risk evaluation (Section 5.3.2). The reason for the difference in cumulative risk estimates between the two approaches is because the RPF of 0.52 based on reduced fetal testicular testosterone content (used in Approach 1) indicates BBP is 48 percent less potent than DBP, while the difference between the index chemical (DBP) POD of 2.1 mg/kg-day (used in Approach 1) and BBP POD of 12 mg/kg-day (used in Approach 2) indicates BBP is approximately 83 percent less potent than the index chemical (DBP). The strengths, limitations, and uncertainties of the dose-response data supporting derivation of the BBP RPF and the BBP POD are provided below.

Dose-Response Data Supporting RPF Derivation

- ***Quantity and quality of fetal testicular testosterone dose-response data:*** EPA calculated an RPF of 0.52 for BBP (Table 2-4). The RPF of 0.52 was derived based on the ratio of the index chemical (DBP) BMD_{40} to the BBP BMD_{40} (*i.e.,* 149/284 = 0.52) for reduced fetal testicular testosterone. The BBP RPF was estimated via meta-analysis and BMD analysis of fetal testicular testosterone data from four studies reported in three high-quality publications (Gray et al., 2021; Furr et al., 2014; Howdeshell et al., 2008).
- ***Availability of dose-response data in the low end range of the dose-response curve (i.e., doses below those eliciting a 40% response):*** One source of uncertainty associated with the meta-analysis and BMD analysis of BBP is that there are limited testosterone data available for BBP in the low-end range of the dose-response curve. For example, 1 study evaluated fetal testicular testosterone at doses of 11 and 33 mg/kg-day, while the lowest dose evaluated in the 3 remaining studies was 100 mg/kg-day. No BMD_5 or BMD_{10} estimates could be derived for BBP, presumably at least in part due to the limited dose-response data available in the low-end range of the dose-response curve (Section 2.4).
- ***Similarity of candidate RPFs across 5, 10, 40 percent response levels (i.e., consideration of the parallelism):*** The selected RPF for BBP is 0.52 and is derived at the 40 percent response level. Because no BMD_5 or BMD_{10} estimates could be derived for BBP, no candidate RPFs could be derived for BBP at the 5 or 10 percent response levels. There is some uncertainty in how representative the BBP RPF of 0.52 derived at the 40 percent response level is of the 5 and 10 percent response levels, and therefore there is some uncertainty in the parallelism of the BBP and index chemical (DBP) dose-response curves. Although, as discussed in Section 2.4, this uncertainty is somewhat addressed by the fact that RPFs calculated for DEHP, DIBP, DCHP, and DINP were consistent across evaluated response levels of 5, 10, and 40 percent, indicating parallel dose-response curves for these phthalates.
- ***Similarity of BMD results obtained via different approaches:*** EPA also conducted BMD modeling of fetal testicular testosterone data from each individual study included in the meta-analysis using EPA's BMDS (Version 3.3.2). One benefit of this analysis is that BMDS includes a broader suite of models compared to those included in the meta-analysis approach (*i.e.,* Exponential, Hill, Polynomial, Power, Linear models vs. linear and linear-quadratic models in the meta-analysis). However, fetal testicular testosterone data from individual studies did not model well as adequate model fits were only obtained for one of four datasets (U.S. EPA, 2025u). This is generally consistent with the meta-analysis approach, where no BMD_5 or BMD_{10} estimates could be derived for BBP. For the one fetal testicular testosterone dataset with an

adequate BMD model fit (Howdeshell et al., 2008), BMD_5 and $BMDL_5$ estimates were 138 and 81 mg/kg-day from the best-fitting Exponential 3 model (U.S. EPA, 2025u).

Dose-Response Data Supporting the Individual Phthalate POD

- ***Quantity and quality of dose-response data supporting the POD:*** The BBP POD is an HED of 12 mg/kg-day and is derived from a NOAEL of 50 mg/kg-day based on a spectrum of effects on the developing male reproductive system consistent with phthalate syndrome. Notably, the same NOAEL of 50 mg/kg-day has also been selected by U.S. CPSC (2014), Health Canada (Health Canada, 2020), ECHA (2017), NICNAS (2015), and EFSA (2019) for use for human health risk characterization of BBP. The BBP POD is supported by four studies (1 high- and 3 medium-quality), including two two-generation studies of reproduction of rats (Aso et al., 2005; Tyl et al., 2004) and two perinatal exposure studies of rats (Ahmad et al., 2014; Furr et al., 2014).
- ***Dose-range between the NOAEL and LOAEL:*** The four studies supporting the selected POD for BBP support a narrow range of NOAEL (50 mg/kg-day) and LOAEL (100 mg/kg-day) values for phthalate syndrome-related effects in gestationally exposed rats (see Section 4 of (U.S. EPA, 2025u) for further discussion). This increases EPA's confidence in the selected POD for BBP.
- ***Comparison of BMD modeling and NOAEL/LOAEL approaches:*** As discussed above, BBP fetal testicular testosterone data did not model well using either the meta-analysis or BMDS modeling approaches. A $BMDL_5$ estimate of 81 mg/kg-day for reduced *ex vivo* fetal testicular testosterone production was obtained from one study (Howdeshell et al., 2008). As described further in Section 4 of the BBP non-cancer human health hazard assessment (U.S. EPA, 2025u), EPA also considered BMD analysis of phthalate-syndrome-related outcomes other than reduced testosterone. This BMD analysis supported a $BMDL_5$ estimate of 55 mg/kg-day for increased incidence of testicular pathology (*e.g.*, seminiferous tubule atrophy) from a two-generation study of reproduction of rats (Aso et al., 2005). These $BMDL_5$ estimates fall between the selected NOAEL of 50 mg/kg-day and the LOAEL of 100 mg/kg-day, further increasing EPA's confidence in the selected NOAEL of 50 mg/kg-day. See Section 4 of the *Non-Cancer Human Health Hazard Assessment for BBP* for further discussion (U.S. EPA, 2025u).

Based on the weight of scientific evidence considerations outlined in the developed framework (Table 5-6), EPA has weighed the strengths and uncertainties associated with the BBP RPF (Approach 1) and the BBP POD (Approach 2 and individual BBP risk assessment). Given the strengths and uncertainties associated with the BBP RPF and the BBP POD, EPA has more confidence in the BBP POD compared to the BBP RPF and has concluded that Approach 2 is more appropriate for use in risk characterization in the *Risk Evaluation of BBP* (U.S. EPA, 2025ae).

- The BBP POD is supported by four studies (1 high- and 3 medium-quality) supporting a narrow range of NOAEL (50 mg/kg-day) and LOAEL (100 mg/kg-day) values for pthalate syndrome-related effects in gestationally exposed rats, which increases EPA's confidence in the selected POD. Further, the BBP POD is supported by benchmark dose modeling of several phthalate-syndrome related outcomes that provide $BMDL_5$ estimates ranging from 55–81 mg/kg-day, further increasing EPA's confidence in the selected BBP POD.
- In contrast, EPA has lower confidence in the BBP RPF. Although the BBP RPF was estimated via meta-analysis and BMD analysis of fetal testicular testosterone data from four studies reported in three high-quality publications, there are limited data available in the low-end range of the dose-response curve, and BMD estimates and candidate RPFs could not be generated at

the 5 or 10 percent response levels. Further, fetal testicular testosterone data from individual studies did not model well using EPA's BMD software, as adequate model fits were only obtained for one of four datasets, which is another source of uncertainty. Many of the uncertainties that reduce EPA's confidence in the BBP RPF, do not exist for RPFs derived for other phthalates (*e.g.,* candidate RPFs could be derived across all response levels and did not vary significantly).

5.4.6 Diisononyl Phthalate (DINP)

For DINP, Approaches 1 and 2 lead to cumulative risk estimates that are similar. The relatively small difference in cumulative risk estimates between the two approaches is because the RPF of 0.21 based on reduced fetal testicular testosterone content (used in Approach 1) indicates DINP is 79 percent less potent than DBP, while the difference between the index chemical (DBP) POD of 2.1 mg/kg-day (used in Approach 1) and DINP POD of 12 mg/kg-day (used in Approach 2) indicates DINP is approximately 83 percent less potent than the index chemical (DBP). A discussion of the strengths, limitations, and uncertainties of the dose-response data supporting derivation of the DINP RPF and the DINP POD is provided below.

Dose-Response Data Supporting RPF Derivation

- ***Quantity and quality of fetal testicular testosterone dose-response data:*** The DINP RPF of 0.21 was derived based on the ratio of the index chemical (DBP) BMD_{40} to the DINP BMD_{40} (*i.e.,* 149/699 = 0.21) for reduced fetal testicular testosterone. The DINP RPF was estimated via meta-analysis and BMD analysis of fetal testicular testosterone data from four publications (1 high- and 3 medium-quality) (Gray Jr et al., 2024; Furr et al., 2014; Boberg et al., 2011; Hannas et al., 2011).
- ***Availability of dose-response data in the low end range of the dose-response curve (i.e., doses below those eliciting a 40% response):*** One source of uncertainty associated with the meta-analysis and BMD analysis of DINP is that there are limited testosterone data available for DINP in the low-end range of the dose-response curve. For example, the lowest dose evaluated for DINP is 300 mg/kg-day, while BMD_5 and $BMDL_5$, BMD_{10} and $BMDL_{10}$, and BMD_{40} and $BMDL_{40}$ estimates for DINP are 74 and 47, 152 and 97, and 699 and 539 mg/kg-day, respectively (U.S. EPA, 2025t, z).
- ***Similarity of candidate RPFs across 5, 10, 40 percent response levels (i.e., consideration of the parallelism):*** Candidate RPFs for DINP did not vary significantly at the 5, 10, and 40 percent response levels (*i.e.,* RPFs ranged from 0.19–0.21; Table 2-4). This indicates that the selected RPF of 0.21 derived from the 40 percent response level is expected to provide a reasonable estimate of potency at the 5 and 10 percent response levels, indicating parallel dose-response curves. This increases EPA's confidence in the selected RPF for DINP.
- ***Similarity of BMD results obtained via different approaches:*** In the context of the CRA, the individual BMD analysis is important for deciding between Approaches 1 and 2. However, for DINP the meta-analysis of fetal testicular testosterone is the basis of the POD used in the individual DINP assessment and for deriving the DINP RPF, and there is little difference between Approaches 1 and 2 for DINP. Therefore, EPA did not conduct additional BMD analysis of individual studies. Additionally, of the four studies included in the meta-analysis of fetal testosterone data for DINP, two of the studies only evaluated a single dose level of DINP (Gray Jr et al., 2024; Furr et al., 2014) and are not amenable to BMD analysis, while of the

remaining two studies, neither had data available in the low-dose range. For example, the lowest dose evaluated by Boberg et al. (2011) was 300 mg/kg-day, while the lowest dose evaluated by Hannas et al. (2011) was 500 mg/kg-day.

Dose-Response Data Supporting the Individual Phthalate POD

- ***Quantity and quality of dose-response data supporting the POD:*** The DINP POD is an HED of 12 mg/kg-day and is derived from a $BMDL_5$ of 49 mg/kg-day based on meta-analysis and BMD modeling of fetal testicular testosterone data from 2 medium-quality studies (Boberg et al., 2011; Hannas et al., 2011). As discussed above, one uncertainty with the meta-analysis and BMD analysis of DINP is that there are limited testosterone data available for DINP in the low-end range of the dose-response curve. This means that the $BMDL_5$ estimate of 49 mg/kg-day for DINP is derived below the lowest dose with empirical data (*i.e.*, 300 mg/kg-day), which is a source of uncertainty.
- ***Comparison of BMD modeling and NOAEL/LOAEL approaches:*** As discussed further in the *Non-cancer Human Health Hazard Assessment for DINP* (U.S. EPA, 2025z), the selected POD for DINP is further supported by two additional developmental toxicity studies (1 high- and 1 medium-quality) of DINP that support NOAEL values of 50 and 56 mg/kg-day based on effects on the developing male reproductive system consistent with phthalate syndrome (Clewell et al., 2013a; Clewell et al., 2013b). These NOAELs are consistent with the $BMDL_5$ estimate of 49 mg/kg-day and support the selected DINP POD.

Based on the weight of scientific evidence considerations outlined in the developed framework (Table 5-6), EPA has weighed the strengths and uncertainties associated with the DINP RPF (Approach 1) and the DINP POD (Approach 2 and individual DINP risk evaluation). For DINP, the meta-analysis of fetal testicular testosterone is the basis of the POD used in the individual DINP assessment and for deriving the DINP RPF; as such there is little difference between Approaches 1 and 2 for DINP. Both approaches are health-protective and align with input from SACC. Because the meta-analysis is the basis of the POD and the DINP RPF, EPA will use MOEs from Approach 1 to characterize cumulative risk for DINP.

5.4.7 Diethylhexyl Phthalate (DEHP)

As discussed in Section 5.3.1.6, application of Approach 1 for DEHP leads to cumulative risk estimates that are less sensitive than risk estimates in the individual DEHP risk evaluation, while application of Approach 2 leads to risk estimates that are approximately 1.1× to 1.2× more sensitive than in the individual DEHP risk evaluation (Section 5.3.2). The reason for the difference in cumulative risk estimates between the two approaches is because the DEHP RPF of 0.84 based on reduced fetal testicular testosterone content (used in Approach 1) indicates DEHP is 16 percent less potent than DBP, while the difference between the index chemical (DBP) POD of 2.1 mg/kg-day (used in Approach 1) and DEHP POD of 1.1 mg/kg-day (used in Approach 2) indicates DEHP is 91 percent more potent than the index chemical (DBP). A discussion of the strengths, limitations, and uncertainties of the dose-response data supporting derivation of the DEHP RPF and the DEHP POD are provided below.

Dose-Response Data Supporting RPF Derivation

- ***Quantity and quality of fetal testicular testosterone dose-response data:*** EPA calculated an RPF of 0.84 for DEHP (Table 2-4). The DEHP RPF of 0.84 is derived from the ratio of the DBP BMD_{40} to the DEHP BMD_{40} for reduced fetal testicular testosterone (*i.e.*, 149÷178 mg/kg-day = 0.84). The DEHP RPF was estimated via meta-analysis and BMD analysis of a large and robust dataset of fetal testicular testosterone data from 8 studies (4 high- and 4 medium-quality) (Gray

et al., 2021; Furr et al., 2014; Saillenfait et al., 2013; Hannas et al., 2011; Culty et al., 2008; Howdeshell et al., 2008; Lin et al., 2008; Martino-Andrade et al., 2008).

- ***Availability of dose-response data in the low end range of the dose-response curve (i.e., doses below those eliciting a 40% response):*** One source of uncertainty associated with the meta-analysis and BMD analysis of DEHP is that there are limited testosterone data available for DEHP in the low-end range of the dose-response curve where the BMD_5/$BMDL_5$ and BMD_{10}/$BMDL_{10}$ estimates are derived. For example, the BMD_5 and $BMDL_5$ and BMD_{10} and $BMDL_{10}$ estimates for DEHP are 17/11 and 35/24 mg/kg-day, respectively, while one study of DEHP provides fetal testicular testosterone data at a dose of 10 mg/kg-day (Lin et al., 2008), one study of provides data at a dose of 50 mg/kg-day (Saillenfait et al., 2013), and all other studies provide testosterone data at doses of 100 mg/kg-day or higher (Section 2.3).
- ***Similarity of candidate RPFs across 5, 10, 40 percent response levels (i.e., consideration of the parallelism):*** Candidate RPFs for DEHP did not vary significantly at the 5, 10, and 40 percent response levels (*i.e.*, RPFs ranged from 0.82 to 0.84; Table 2-4). This indicates that the selected RPF of 0.84 derived from the 40 percent response level is expected to provide a reasonable estimate of potency at the 5 and 10 percent response levels, indicating parallel dose-response curves. This increases EPA's confidence in the selected RPF for DEHP.
- ***Similarity of BMD results obtained via different approaches:*** As discussed further below and in Section 4 of the DEHP non-cancer human health hazard TSD (U.S. EPA, 2025x), the $BMDL_5$ of 11 mg/kg-day for reduced testosterone is higher than the highest NOAEL of 4.8–5 mg/kg-day and is comparable to the lowest LOAEL of 10 mg/kg-day. This indicates that the $BMDL_5$ for reduced fetal testicular testosterone is not health protective, since it aligns with the LOAEL, and was therefore not selected for use as the POD in the individual chemical assessment. Since the meta-analysis includes testosterone data from eight studies, it is expected to provide more precise BMD/BMDL estimates than BMD analysis of data from individual studies and therefore BMD analysis of data from individual studies was not conducted. EPA did not conduct BMD modeling of individual fetal testicular testosterone datasets using EPA's BMDS for comparison to the meta-analysis results for DEHP.

Dose-Response Data Supporting the Individual Phthalate POD

- ***Quantity and quality of dose-response data supporting the POD:*** The DEHP POD is an HED of 1.1 mg/kg-day and is derived from a NOAEL of 4.8 mg/kg-day based on a spectrum of effects on the developing male reproductive system consistent with phthalate syndrome, including male reproductive tract malformations (U.S. EPA, 2025x). Notably, the same NOAEL of 4.8 mg/kg-day has also been selected by U.S. CPSC (2014), Health Canada (Health Canada, 2020), ECHA (2017), NICNAS (2010), and EFSA (2019) for use for human health risk characterization of DEHP. The DEHP POD is supported by four studies of rats, including one high-quality multi-generation study of reproduction (TherImmune Research Corporation, 2004), and three medium-quality gestational exposure studies of rats (Andrade et al., 2006b; Andrade et al., 2006a; Grande et al., 2006).
- ***Dose-range between the NOAEL and LOAEL:*** In addition to the four studies supporting the selected NOAEL of 4.8 mg/kg-day, an additional 13 studies reporting effects on the developing male reproductive system consistent with disrupted androgen action and phthalate syndrome support NOAEL and LOAEL values in a narrow dose-range of 1 to 5 mg/kg-day and 10 to 15 mg/kg-day, respectively (1 high-, 10 medium-, 2 low-quality) (Rajagopal et al., 2019; Guo et al., 2013; Kitaoka et al., 2013; Christiansen et al., 2010; Gray et al., 2009; Lin et al., 2009; Vo et al.,

2009b; Vo et al., 2009a; Lin et al., 2008; Ge et al., 2007; Akingbemi et al., 2004; Akingbemi et al., 2001; Ganning et al., 1990). The narrow dose-range between the NOAELs of 1–5 mg/kg-day and LOAELs of 10–15 mg/kg-day for effects consistent with phthalate syndrome increases EPA's confidence in the selected POD for DEHP.

- ***Comparison of BMD modeling and NOAEL/LOAEL approaches:*** Available studies of DEHP support NOAELs of 1–5 mg/kg-day and LOAELs of 10–15 mg/kg-day for effects consistent with phthalate syndrome. Comparatively, meta-analysis and BMD modeling of decreased fetal testicular testosterone data from 8 studies (4 high- and 4-medium quality) supports a BMD_5/$BMDL_5$ of 17/11 mg/kg-day. The $BMDL_5$ of 11 mg/kg-day is higher than the highest NOAEL of 4.8–5 mg/kg-day and is comparable to the lowest LOAEL of 10 mg/kg-day. This indicates that the $BMDL_5$ for reduced fetal testicular testosterone is not health protective and was therefore not selected for use as the POD in the individual chemical assessment. This decision is further supported by BMD analysis of male rat reproductive tract malformation (RTM) data from Blystone et al. (2010), which is the key study supporting the NOAEL of 4.8 mg/kg-day selected as the POD for use in risk characterization. BMD modeling of litter incidences of total RTM data by Blystone et al. supports BMD_5/$BMDL_5$ estimates of 11.6/7.0 mg/kg-day for the F1 generation, 10.4/2.2 mg/kg-day for the F2 generation, and 8.5/5.6 mg/kg-day for combined F1 and F2 generations. $BMDL_5$ estimates from Blystone et al. range from 2.2 to 7 mg/kg-day and are less than the $BMDL_5$ of 11 mg/kg-day for reduce fetal testicular testosterone from the meta-analysis, further indicating that the $BMDL_5$ for reduced fetal testicular testosterone is not health protective for use in risk assessment.

Based on the weight of scientific evidence considerations outlined in the developed framework (Table 5-6), EPA has weighed the strengths and uncertainties associated with the DEHP RPF (Approach 1) and the DEHP POD (Approach 2 and individual DIBP risk evaluation). Given the strengths and uncertainties associated with the DEHP RPF and the DEHP POD, EPA has more confidence in the DEHP POD compared to the DEHP RPF and has concluded that Approach 2 is more appropriate for use in risk characterization for DEHP. This conclusion is based on the following:

- EPA has confidence in the DEHP POD used in the individual DEHP risk assessment and as part of CRA Approach 2 because it is supported by 17 studies that support a narrow range of NOAEL (1–5 mg/kg-day) and LOAEL (10–15 mg/kg-day) values.
- Meta-analysis and BMD analysis of fetal testicular testosterone data from 8 studies supports a $BMDL_5$ of 11 mg/kg-day, which is comparable to the lowest LOAEL of 10 mg/kg-day, which indicates the $BMDL_5$ for reduced fetal testicular testosterone is not health protective for use in risk characterization.

Table 5-7. Summary of CRA Approach Selected for Each Phthalate

Phthalate	CRA Approach Selected for Use in Risk Characterization	Rationale (Section Reference for Further Details)
DBP (Index Chemical)	Approach 1 and 2	Approaches 1 and 2 are mathematically identical, since DBP is the index chemical (Section 5.4.2)
DCHP	Approach 2	EPA has more confidence in the DCHP POD compared to the DCHP RPF (Section 5.4.3)

Phthalate	CRA Approach Selected for Use in Risk Characterization	Rationale (Section Reference for Further Details)
DIBP	Approaches 2	Both approaches are health-protective and align with input from SACC. MOEs from Approach 2 will be used to characterize cumulative risk for DIBP, simplifying the risk characterization as it is more consistent with the single chemical assessment. (Section 5.4.4)
BBP	Approach 2	EPA has more confidence in the BBP POD compared to the BBP RPF (Section 5.4.5)
DINP	Approaches 1	Both approaches are health-protective and align with input from SACC. Because the meta-analysis is the basis of the DINP POD and the DINP RPF, EPA will use MOEs from Approach 1 to characterize cumulative risk for DINP (Section 5.4.6)
DEHP	Approaches 2	EPA has more confidence in the DEHP POD compared to the DEHP RPF (Section 5.4.7)

6 SUMMARY AND CONCLUSIONS

The Agency has developed this TSD for the cumulative risk assessment of six toxicologically similar phthalates being evaluated under Section 6 of TSCA, including DEHP, BBP, DBP, DCHP, DIBP, and DINP. This TSD provides the supporting information for the implementation of cumulative risk assessment within each individual phthalate risk evaluation and subsequent risk management based on SACC recommendations from the May 2023 CRA peer-review meeting (U.S. EPA, 2023c) and August 2025 phthalate peer-review meeting (U.S. EPA, 2025ag).

EPA describes its CRA as focusing on acute exposure durations (Section 1.5) for pregnant women/women of reproductive age, and male infants, male toddlers, and male children (Section 1.4) to six toxicologically similar phthalates (*i.e.*, DEHP, DBP, BBP, DIBP, DCHP, DINP) that induce effects on the developing male reproductive system consistent with a disruption of androgen action and phthalate syndrome. For cumulative risk estimates for each phthalate assessed under TSCA, EPA supported adding non-attributable cumulative phthalate exposure estimated using reverse dosimetry on the NHANES dataset (Section 4) to the relevant exposure scenarios for individual TSCA COUs to calculate a cumulative MOE. The non-attributable cumulative MOE is estimated using the RPFs for phthalate syndrome based on the shared endpoint and pooled dataset for assessing fetal testicular testosterone health endpoint for each of the six chemical substances using DBP as an index chemical (Section 2).

In this technical support document, EPA presented two approaches for how to apply this quantitative approach for evaluating cumulative risk resulting from aggregate exposure to a single phthalate from an exposure scenario or COU plus non-attributable cumulative risk from NHANES (Section 5). Both approaches were subject to public comment and peer-reviewed by SACC during the August 2025 phthalate peer-review meeting (U.S. EPA, 2025ag). Overall, SACC concluded that both approaches have strengths and uncertainties, but that the two approaches can complete one another and that EPA should present both approaches in the individual risk evaluations for each phthalate and select the most scientifically defensible approach for the final individual risk characterization and decision making process for each phthalate (U.S. EPA, 2025ag). Based on SACC recommendations, EPA considered both cumulative risk characterization approaches.

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APPENDICES

Appendix A FETAL TESTICULAR TESTOSTERONE DATA FOR DEHP AND DBP

Table_Apx A-1. Summary of Fetal Testicular Testosterone Data for DEHP

Brief Study Description, Measured Outcome (Reference)	Dose (mg/kg-day)															
	0	10	50	100	117	150	234	300	469	500	600	625	750	875	900	938
Long-Evans rats gavaged with 0, 10, 100, 750 mg/kg-day DEHP on GD 2-20. Fetal testis testosterone content on GD 21 (Lin et al., 2008)	100% (N=6)	157%* (N=6)	–	78% (N=6)	–	–	–	–	–	–	–	–	33%* (N=9)	–	–	–
Pregnant Wistar rats gavaged with 0, 150 mg/kg-day DEHP on GD 13-21. Fetal testis testosterone content on GD 21 (Martino-Andrade et al., 2008)	100% (N=7)	–	–	–	–	71%* (N=7)	–	–	–	–	–	–	–	–	–	–
Pregnant Wistar rats (3-6 dams/group) gavaged with 0, 100, 300, 500, 625, 750, 875 mg/kg-day DEHP on GD 14-18. *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Hannas et al., 2011)	100% (N=6)	–	–	100% (N=3)	–	–	–	50%* (N=3)	–	36%* (N=6)		24%* (N=4)	14%* (N=4)	18%* (N=3)	–	–
Pregnant SD rats (3-6 dams/group) gavaged with 0, 100, 300, 500, 625, 750, 875 mg/kg-day DEHP on GD 14-18. *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Hannas et al., 2011)	100% (N=6)	–	–	107% (N=3)	–	–	–	61%* (N=3)	–	40%* (N=6)		21%* (N=4)	29%* (N=4)	48%* (N=4)	–	–
Pregnant SD rats (3 dams/group) gavaged with 0, 117, 234, 469, 938 mg/kg-day DEHP on GD 14-20. *Ex vivo* fetal testicular testosterone production (24-hour incubation) on GD 21 (Culty et al., 2008)	100% (N=3)	–	–	–	41%* (N=3)	–	37%* (N=3)	–	23%* (N=3)	–	–	–	–	–	–	8.5% (N=3)
Pregnant SD rats (2-3 dams/group) gavaged with 0, 100, 300, 600, 900 mg/kg-day DEHP on GD 14-18 (Block 31). *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Furr et al., 2014)	100% (N=3)	–	–	37%* (N=2)	–	–	–	18%* (N=3)	–	–	7.1%* (N=3)	–	–	–	6.0%* (N=2)	–
Pregnant SD rats (2-3 dams/group) gavaged with 0, 100, 300, 600, 900 mg/kg-day DEHP on GD 14-18 (Block 32). *Ex vivo* fetal testicular	100% (N=2)	–	–	79%* (N=3)	–	–	–	35%* (N=3)	–	–	15%* (N=3)	–	–	–	12%* (N=2)	–

Brief Study Description, Measured Outcome (Reference)	Dose (mg/kg-day)															
	0	10	50	100	117	150	234	300	469	500	600	625	750	875	900	938
testosterone production (3-hour incubation) on GD 18 (Furr et al., 2014)																
Pregnant SD rats (4 dams/group) gavaged with 0, 100, 300, 600, 900 mg/kg-day DEHP on GD 14-18. *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Howdeshell et al., 2008)	100% (N=4)	–	–	82% (N=4)	–	–	–	58%* (N=4)	–	–	41%* (N=4)	–	–	–	22%* (N=4)	–
Pregnant SD rats (8-16 dams/group) gavaged with 0, 50, 625 mg/kg-day DEHP on GD 12-19. *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 19 (Saillenfait et al., 2013)	100% (N=16)	–	72%* (N=8)	–	–	–	–	–	–	–	–	16%* (N=8)	–	–	–	–
Pregnant SD rats (2-3 dams/group) gavaged with 0, 100, 300, 600, 900 mg/kg-day DEHP on GD 14-18 (Block 76). *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Gray et al., 2021)	100% (N=3)	–	–	104% (N=3)	–	–	–	75% (N=2)	–	–	30% (N=3)	–	–	–	20% (N=3)	–
Pregnant SD rats (3 dams/group) gavaged with 0, 100, 300, 600, 900 mg/kg-day DEHP on GD 14-18 (Block 77). *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Gray et al., 2021)	100% (N=3)	–	–	99% (N=3)	–	–	–	67% (N=3)	–	–	25% (N=3)	–	–	–	25% (N=3)	–
* Indicates a statistically significant effect compared to the concurrent control as calculated by original study authors. Percent testosterone values indicate the percent testosterone or testosterone production compared to the concurrent control as calculated by EPA.																

Table_Apx A-2. Summary of Fetal Testicular Testosterone Data for DBP

Brief Study Description, Measured Outcome (Reference)	Dose (mg/kg-day)											
	0	1	10	33	50	100	112	300	500	581	600	900
Pregnant Wistar rats gavaged with 0, 100, 500 mg/kg-day DBP on GD 13-21. Fetal testis testosterone content on GD 21 (Martino-Andrade et al., 2008)	100% (N=7)	–	–	–	–	71% (N=8)	–	–	37%* (N=7)	–	–	–
Pregnant SD rats (2-3 dams/group) gavaged with 0, 33, 50, 100, 300 mg/kg-day DBP on GD 14-18 (Block 18). *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Furr et al., 2014)	100% (N=3)	–	–	32% (N=3)	86% (N=2)	65%* (N=3)	–	23%* (N=3)	–	–	–	–
Pregnant SD rats (3–4 dams/group) gavaged with 0, 1, 10, 100 mg/kg-day DBP on GD 14-18 (Block 22). *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Furr et al., 2014)	100% (N=3)	88% (N=3)	80% (N=4)	–	–	64%* (N=4)	–	–	–	–	–	–
Pregnant SD rats (3–4 dams/group) gavaged with 0, 1, 10, 100 mg/kg-day DBP on GD 14-18 (Block 26). *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Furr et al., 2014)	100% (N=3)	160% (N=4)	119% (N=4)	–	–	75% (N=3)	–	–	–	–	–	–
Pregnant SD rats (3-4 dams/group) gavaged with 0, 33, 50, 100, 300, 600 mg/kg-day DBP on GD 8-18. *Ex vivo* fetal testicular testosterone production (2-hour incubation) on GD 18 (Howdeshell et al., 2008)	100% (N=3)	–	–	94% (N=4)	78% (N=4)	84% (N=4)	–	66%* (N=4)	–	–	33%* (N=4)	–
Pregnant SD rats (3-4 dams/group) gavaged with 0, 100, 500 mg/kg-day DBP on GD 18. Fetal testis testosterone content on GD 19. (Kuhl et al., 2007)	100% (N=10)	–	–	–	–	71% (N=10)	–	–	33%* (N=10)	–	–	–
Pregnant SD rats (7–9 dams/group) gavaged with 0, 112, 581 mg/kg-day DBP on GD 12-19. Fetal testis testosterone content on GD 19 (4 hour post-exposure) (Struve et al., 2009)	100% (N=9)	–	–	–	–	–	56% (N=7)	–	–	3.7%* (N=7)	–	–
Pregnant SD rats (7–9 dams/group) gavaged with 0, 112, 581 mg/kg-day DBP on GD 12-19. Fetal testis testosterone content on GD 19 (24 hour post-exposure) (Struve et al., 2009)	100% (N=9)	–	–	–	–	–	29%* (N=7)	–	–	7.1%* (N=7)	–	–
Pregnant SD rats (5-6 dams/group) gavaged with 0, 100 mg/kg-day DBP on GD 12-20. Fetal testis testosterone content on GD 20 (Johnson et al., 2011)	100% (N=5)	–	–	–	–	77% (N=6)	–	–	–	–	–	–
Pregnant SD rats (5–6 dams/group) gavaged with 0, 500 mg/kg-day DBP on GD 12-20. Fetal testis testosterone content on GD 20 (Johnson et al., 2011)	100% (N=6)	–	–	–	–	–	–	–	15%* (N=5)	–	–	–
Pregnant SD rats (5 dams/group) gavaged with 0, 1, 10, 100 mg/kg-day DBP on GD 19. Fetal testis testosterone content on GD 19 (Johnson et al., 2007)	100% (N=5)	109% (N=5)	67% (N=5)	–	–	84% (N=5)	–	–	–	–	–	–

Brief Study Description, Measured Outcome (Reference)	Dose (mg/kg-day)											
	0	**1**	**10**	**33**	**50**	**100**	**112**	**300**	**500**	**581**	**600**	**900**
Pregnant SD rats (3–4 dams/group) gavaged with 0, 300, 600, 900 mg/kg-day DBP on GD 14-18 (Block 70). *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Gray et al., 2021)	100% (N=3)	–	–	–	–	–	–	62% (N=4)	–	–	25% (N=4)	16% (N=4)
Pregnant SD rats (3–4 dams/group) gavaged with 0, 300, 600, 900 mg/kg-day DBP on GD 14-18 (Block 71). *Ex vivo* fetal testicular testosterone production (3-hour incubation) on GD 18 (Gray et al., 2021)	100% (N=4)	–	–	–	–	–	–	47% (N=3)	–	–	22% (N=4)	13% (N=4)
* Indicates a statistically significant effect compared to the concurrent control as calculated by original study authors. Percent testosterone values indicate the percent testosterone or testosterone production compared to the concurrent control as calculated by EPA.												

Appendix B CONSIDERATIONS FOR BENCHMARK RESPONSE (BMR) SELECTION FOR REDUCED FETAL TESTICULAR TESTOSTERONE

B.1 Purpose

EPA has conducted an updated meta-analysis and benchmark dose modeling (BMD) analysis of decreased fetal rat testicular testosterone (U.S. EPA, 2025t). During the July 2024 Science Advisory Committee on Chemicals (SACC) peer-review meeting of the draft risk evaluation of diisodecyl phthalate (DIDP) and draft human health hazard assessments for diisononyl phthalate (DINP), the SACC recommended that EPA should clearly state its rationale for selection of benchmark response (BMR) levels evaluated for decreases in fetal testicular testosterone (U.S. EPA, 2024e). This appendix describes EPA's rationale for evaluating BMRs of 5, 10, and 40 percent for decreases in fetal testicular testosterone.

B.2 Methods

As described in EPA's *Benchmark Dose Technical Guidance* (U.S. EPA, 2012), "Selecting a BMR(s) involves making judgments about the statistical and biological characteristics of the dataset and about the applications for which the resulting BMDs/BMDLs will be used." For the updated meta-analysis and BMD modeling analysis of fetal rat testicular testosterone, EPA evaluated BMR values of 5, 10, and 40 percent based on both statistical and biological considerations (U.S. EPA, 2025t).

In 2017, NASEM (2017) modeled BMRs of 5 and 40 percent for decreases in fetal testicular testosterone. NASEM did not provide explicit justification for selection of a BMR of 5 percent. However, justification for the BMR of 5 can be found elsewhere. As discussed in EPA's *Benchmark Dose Technical Guidance* (U.S. EPA, 2012), a BMR of 5 percent is supported in most developmental and reproductive studies. Comparative analyses of a large database of developmental toxicity studies demonstrated that developmental NOAELs are approximately equal to the $BMDL_5$ (Allen et al., 1994a, b; Faustman et al., 1994).

EPA also evaluated a BMR of 10 percent as part of the updated BMD analysis. BMD modeling of fetal testosterone conducted by NASEM (2017) indicated that BMD_5 estimates are below the lowest dose with empirical testosterone data for several of the phthalates (*e.g.*, DIBP, BBP). As discussed in EPA's *Benchmark Dose Technical Guidance* (U.S. EPA, 2012) "For some datasets the observations may correspond to response levels far in excess of a selected BMR and extrapolation sufficiently below the observable range may be too uncertain to reliably estimate BMDs/BMDLs for the selected BMR." Therefore, EPA modeled a BMR of 10 percent because datasets for some of the phthalates may not include sufficiently low doses to support modeling of a 5 percent response level.

NASEM (2017) also modeled a BMR of 40 percent using the following justification: "previous studies have shown that reproductive-tract malformations were seen in male rats when fetal testosterone production was reduced by about 40% *(*Gray et al., 2016*;* Howdeshell et al., 2015*)*."

Further description of methods and results for the updated meta-analysis and BMD modeling analysis that evaluated BMRs of 5, 10, and 40 percent for decreased fetal testicular testosterone are provided in EPA's *Meta-Analysis and Benchmark Dose Modeling of Fetal Testicular Testosterone for Di(2-ethylhexyl) Phthalate (DEHP), Dibutyl Phthalate (DBP), Butyl Benzyl Phthalate (BBP), Diisobutyl Phthalate (DIBP), and Dicyclohexyl Phthalate (DCHP)* (U.S. EPA, 2025t).

B.3 Results

BMD estimates, as well as 95 percent upper and lower confidence limits, for decreased fetal testicular testosterone for the evaluated BMRs of 5, 10, and 40 percent are shown in Table_Apx B-1. BMD_5 estimates ranged from 8.4 to 74 mg/kg-day for DEHP, DBP, DCHP, and DINP; however, a BMD_5 estimate could not be derived for BBP or DIBP. Similarly, BMD_{10} estimates ranged from 17 to 152 for DEHP, DBP, DCHP, DIBP and DINP; however, a BMD_{10} estimate could not be derived for BBP. BMD_{40} estimates were derived for all phthalates (*i.e.*, DEHP, DBP, DCHP, DIBP, BBP, DINP) and ranged from 90 to 699 mg/kg-day.

In the mode of action (MOA) for phthalate syndrome, which is described elsewhere (U.S. EPA, 2023b) and in Section 1.1 of this document, decreased fetal testicular testosterone is an early, upstream event in the MOA that precedes downstream apical outcomes such as male nipple retention, decreased anogenital distance, and reproductive tract malformations. Decreased fetal testicular testosterone should occur at lower or equal doses than downstream apical outcomes associated with a disruption of androgen action. Because the lower 95 percent confidence limit on the BMD, or BMDL, is used for deriving a point of departure (POD), EPA compared BMDL estimates at the 5, 10, and 40 percent response levels for each phthalate (DEHP, DBP, DCHP, DIBP, BBP, DINP) to the lowest identified apical outcomes associated with phthalate syndrome to determine which response level is protective of downstream apical outcomes.

Table_Apx B-1 provides a comparison of BMD and BMDL estimates for decreased fetal testicular testosterone at BMRs of 5, 10, and 40 percent, the lowest LOAEL(s) for apical outcomes associated with phthalate syndrome, and the POD selected for each phthalate for use in risk characterization. As can be seen from Table_Apx B-1, $BMDL_{40}$ values for DEHP, DBP, DIBP, BBP, DCHP, and DINP are all well above the PODs selected for use in risk characterization for each phthalate by 3× (for BBP) to 25.4× (for DEHP). Further, $BMDL_{40}$ values for DEHP, DBP, DIBP, BBP, and DCHP, but not DINP, are above the lowest LOAELs identified for apical outcomes on the developing male reproductive system. *These results clearly demonstrate that a BMR of 40 percent is not appropriate for use in human health risk assessment*.

As can be seen from Table_Apx B-1, $BMDL_{10}$ values for DBP ($BMDL_{10}$, POD, LOAEL = 20, 9, 30 mg/kg-day, respectively) and DCHP ($BMDL_{10}$, POD, LOAEL = 12, 10, 20 mg/kg-day, respectively) are slightly higher than the PODs selected for use in risk characterization and slightly less than the lowest LOAELs identified based on apical outcomes associated with the developing male reproductive system. This indicates that a BMR of 10% may be protective of apical outcomes evaluated in available studies for both DBP and DCHP. $BMDL_{10}$ values could not be derived for DIBP or BBP (Table_Apx B-1). Therefore, no comparisons to the POD or lowest LOAEL for apical outcomes could be made for either of these phthalates at the 10 percent response level.

For DEHP, the $BMDL_{10}$ is greater than the POD selected for use in risk characterization by 5× ($BMDL_{10}$ and POD = 24 and 24.8 mg/kg-day, respectively) and is greater than the lowest LOAEL identified for apical outcomes on the developing male reproductive system by 2.4× ($BMDL_{10}$ and LOAEL = 24 and 10 mg/kg-day, respectively). *This indicates that a BMR of 10 percent for decreased fetal testicular testosterone is not health protective for DEHP*. For DEHP, the $BMDL_5$ (11 mg/kg-day) is similar to the selected POD (NOAEL of 4.8 mg/kg-day) and the lowest LOAEL identified for apical outcomes on the developing male reproductive system (10 mg/kg-day).

B.4 Weight of Scientific Evidence Conclusion

As discussed elsewhere (U.S. EPA, 2023b), DEHP, DBP, BBP, DIBP, DCHP, and DINP are toxicologically similar and induce effects on the developing male reproductive system consistent with a disruption of androgen action. Because these phthalates are toxicologically similar, it is more appropriate to select a single BMR for decreased fetal testicular testosterone to provide a consistent basis for dose-response analysis and for deriving PODs relevant to the single chemical assessments and CRA. *EPA has reached the conclusion that a BMR of 5 percent is the most and health protective response level for evaluating decreased fetal testicular testosterone* when sufficient dose-response data are available to support modeling of fetal testicular testosterone in the low-end range of the dose-response curve. This conclusion is supported by the following weight of scientific evidence considerations.

- For DEHP, the $BMDL_{10}$ estimate is greater than the POD selected for use in risk characterization by 5× and is greater than the lowest LOAEL identified for apical outcomes on the developing male reproductive system by 2.4×. *This indicates that a BMR of 10 percent is not protective for DEHP*.
- The $BMDL_5$ estimate for DEHP is similar to the selected POD and lowest LOAEL for apical outcomes on the developing male reproductive system.
- $BMDL_{10}$ estimates for DBP ($BMDL_{10}$, POD, LOAEL = 20, 9, 30 mg/kg-day, respectively) and DCHP ($BMDL_{10}$, POD, LOAEL = 12, 10, 20 mg/kg-day, respectively) are slightly higher than the PODs selected for use in risk characterization and slightly less than the lowest LOAELs identified based on apical outcomes associated with the developing male reproductive system. This indicates that a BMR of 10 percent may be protective of apical outcomes evaluated in available studies for both DBP and DCHP. However, this may be a reflection of the larger database of studies and wider range of endpoints evaluated for DEHP, compared to DBP and DCHP.
- NASEM (2017) modeled a BMR of 40 percent using the following justification: "previous studies have shown that reproductive-tract malformations were seen in male rats when fetal testosterone production was reduced by about 40% *(*Gray et al., 2016*;* Howdeshell et al., 2015*)*." However, publications supporting a 40 percent response level are relatively narrow in scope and assessed the link between reduced fetal testicular testosterone in SD rats on GD 18 and later life reproductive tract malformations in F1 males. More specifically, Howdeshell et al. (2015) found reproductive tract malformations in 17 to 100 percent of F1 males when fetal testosterone on GD 18 was reduced by approximately 25 to 72 percent, while Gray et al. (2016) found dose-related reproductive alterations in F1 males treated with dipentyl phthalate (a phthalate not currently being evaluated under TSCA) when fetal testosterone was reduced by about 45 percent on GD 18. Although NASEM modeled a BMR of 40 percent based on biological considerations, there is no scientific consensus on the biologically significant response level and no other authoritative or regulatory agencies have endorsed the 40 percent response level as biologically significant for reductions in fetal testosterone.
- $BMDL_{40}$ values for DEHP, DBP, DIBP, BBP, DCHP, and DINP are above the PODs selected for use in risk characterization for each phthalate by 3× to 25.4× (Table_Apx B-1). $BMDL_{40}$ values for DEHP, DBP, DIBP, BBP, and DCHP, but not DINP, are above the lowest LOAELs identified for apical outcomes on the developing male reproductive system. These results clearly demonstrate that a BMR of 40 percent is not health protective.

Table_Apx B-1. Comparison of BMD/BMDL Values Across BMRs of 5%, 10%, and 40% with PODs and LOAELs for Apical Outcomes for DEHP, DBP, DIBP, BBP, DCHP, and DINP

Phthalate	POD (mg/kg-day) Selected for use in Risk Characterization (Effect)	Lowest LOAEL(s) (mg/kg-day) for Apical Effects on the Male Reproductive System	BMD_5 Estimate [a] (mg/kg-day) [95% CI]	BMD_{10} Estimate [a] (mg/kg-day) [95% CI]	BMD_{40} Estimate [a] (mg/kg-day) [95% CI]	Reference For Further Details on the Selected POD and Lowest Identified LOAEL,
DEHP	NOAEL = 4.8 (↑ Male RTM in F1 and F2 males)	10 to 15 (NR, ↓ AGD, RTMs)	17 [11, 31]	35 [24, 63]	178 [122, 284]	(U.S. EPA, 2025x)
DBP	$BMDL_5$ = 9 (↓ Fetal testicular testosterone)	30 (↑ Testicular pathology)	14 [9, 27]	29 [20, 54]	149 [101, 247]	(U.S. EPA, 2025v)
DIBP	$BMDL_5$ = 24 (↓ Fetal testicular testosterone)	125 (↑ Testicular pathology)	–[b]	55 [NA, 266][b]	279 [136, 517]	(U.S. EPA, 2025y)
BBP	NOAEL = 50 (Phthalate syndrome-related effects)	100 (↓ AGD)	–[b]	–[b]	284 [150, 481]	(U.S. EPA, 2025u)
DCHP	NOAEL = 10 (Phthalate syndrome-related effects)	20 (↑ Testicular pathology)	8.4 [6.0, 14]	17 [12, 29]	90 [63, 151]	(U.S. EPA, 2025w)
DINP	$BMDL_5$ = 49 (↓ Fetal testicular testosterone)	600 (↓ Sperm motility)	74 [47, 158]	152 [97, 278]	699 [539, 858]	(U.S. EPA, 2025z)

Abbreviations: AGD = anogenital distance; BMD = benchmark dose; BMDL = lower 95% confidence limit on BMD; CI = 95% confidence interval; LOAEL = lowest observable-adverse-effect level; NOAEL = no observable-adverse-effect level; NR = nipple retention; POD = point of departure; RTM = reproductive tract malformations

[a] The linear-quadratic model provided the best fit (based on lowest Akaike information criterion [AIC]) for DEHP, DBP, DIBP, BBP, DCHP, and DINP.

[b] BMD and/or BMDL estimate could not be derived.

Appendix C NHANES URINARY BIOMONITORING

C.1 Urinary Biomonitoring: Methods and Results

EPA analyzed urinary biomonitoring data from the U.S. Centers for Disease Control and Prevention (CDC) National Health and Nutrition Evaluation Surveys (NHANES), which reports urinary concentrations for 15 phthalate metabolites specific to individual phthalate diesters.

DEHP: Four urinary metabolites of DEHP, mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHP), mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono(2-ethyl-5-carboxypentyl) phthalate (MECPP), and mono(2-ethyl-5-oxohexyl) phthalate (MEOHP) have been reported in the NHANES data. MEHP has been reported in NHANES beginning with the 1999 cycle and measured in 26,740 members of the general public, including 7,331 children under age 16 and 19,409 adults aged 16 and over. MEHHP was added starting in the 2001 to 2002 NHANES cycle and has been measured in 24,199 participants, including 6,617 children and 17,852 adults. MEOHP was added starting in the 2001 to 2002 NHANES cycle and has been measured in 24,199 participants, including 6,617 children and 17,582 adults. MECPP was added starting in the 2003 to 2004 NHANES cycles and has been measured in 21,417 participants, including 5,839 children and 15,578 adults. Metabolites of DEHP were quantified in urinary samples from a one-third subsample of all participants aged 6 and older. Beginning with the 2005 to 2006 cycle of NHANES, all participants between 3 to 5 years were eligible for DEHP metabolite urinary analysis. Urinary DEHP metabolite concentrations were quantified using high performance liquid chromatography-electrospray ionization-tandem mass spectrometry. Limits of detection (LOD) for each cycle of NHANES are provided in Table_Apx C-1. Values below the LOD were replaced by the lower limit of detection divided by the square root of two (NCHS, 2021). As can be seen from Table_Apx C-2, MEHHP, MEOHP, and MECPP were above the LOD in the urine of more than 99 percent of all NHANES participants (N=2,762) in the most recent survey (2017 to 2018), while MEHP was above the LOD in approximately 46 percent of samples.

DBP: Two urinary metabolites of DBP, mono-n-butyl phthalate (MnBP) and mono-3-hydroxybutyl phthalate (MHBP), have been reported in the NHANES data. MnBP has been reported in NHANES beginning with the 1999 cycle and was measured in 26,740 members of the general public, including 7,331 children under age 16 and 19,409 adults aged 16 and over. Although MHBP was measured in the 2013 to 2018 NHANES cycles, the data for the 2013 to 2014 NHANES cycle was determined to be inaccurate due to procedural error and only released as surplus data, which is not readily publicly available (https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/2013/DataFiles/SSPHTE_H.htm; accessed December 17, 2025). As a result, the present analysis only includes urinary MHBP data from the 2015 to 2018 NHANES cycles. The present analysis of MHBP includes data from the 2015 to 2018 NHANES cycles and has been measured in 5,737 participants, including 1,961 children under age 16 and 3,776 adults aged 16 and older. Urinary MnBP and MHBP concentrations were quantified using high performance liquid chromatography-electrospray ionization-tandem mass spectrometry. LODs for each cycle of NHANES are provided in Table_Apx C-1. Values below the LOD were replaced by the lower limit of detection divided by the square root of two (NCHS, 2021). As can be seen from Table_Apx C-2, MnBP was above the LOD in the urine of more than 99 percent of all NHANES participants (N=2,762) in the most recent survey (2017 to 2018), while MHBP was above the LOD in approximately 75 percent of samples.

BBP: One urinary metabolite of BBP, mono-benzyl phthalate (MBzP), has been reported in the NHANES dataset. MBzP has been reported in NHANES beginning with the 1999 cycle and measured in 26,740 members of the general public, including 7,331 children aged 15 and under and 19,409 adults

aged 16 and over. Urinary MBzP concentrations were quantified using high performance liquid chromatography-electrospray ionization-tandem mass spectrometry. LODs for each cycle of NHANES are provided in Table_Apx C-1. Values below the LOD were replaced by the lower limit of detection divided by the square root of two (NCHS, 2021). As can be seen from Table_Apx C-2, MBzP was above the LOD in the urine of 96.2 percent of all NHANES participants (N=2,762) in the most recent survey (2017 to 2018).

DIBP: Two urinary metabolites of DIBP, mono-2-methyl-2-hydroxypropyl phthalate (MHiBP) and mono-isobutyl phthalate (MIBP), have been reported in the NHANES dataset. MIBP has been reported starting in the 2001 to 2002 NHANES cycle and has been measured in 24,199 participants, including 6,617 children and 17,582 adults. Although MHiBP was measured in the 2013 to 2018 NHANES cycles, the data for the 2013 to 2014 NHANES cycle was determined to be inaccurate due to procedural error and only released as surplus data, which is not readily publicly available (https://wwwn.cdc.gov/Nchs/Data/Nhanes/Public/2013/DataFiles/SSPHTE_H.htm; accessed December 17, 2025). As a result, the present analysis only includes urinary MHiBP data from the 2015 to 2018 NHANES cycles. From 2015 to 2018, MHiBP and has been measured in 5,737 members of the general public, including 1,961 children aged 15 and under and 3,776 adults aged 16 and over. Urinary MIBP and MHiBP concentrations were quantified using high performance liquid chromatography-electrospray ionization-tandem mass spectrometry. LODs for each cycle of NHANES are provided in Table_Apx C-1. Values below the LOD were replaced by the lower limit of detection divided by the square root of two (NCHS, 2021). As can be seen from Table_Apx C-2, MHiBP was above the LOD in the urine of approximately 98 percent of all NHANES participants (N=2,762) in the most recent survey (2017 to 2018), while MIBP was above the LOD in approximately 95 percent of samples.

DINP: Three metabolites of DINP, mono-isononyl phthalate (MINP), mono-oxoisononyl phthalate (MONP), and mono-(carboxyoctyl) phthalate (MCOP) have been reported in the NHANES dataset. MINP has been reported in NHANES beginning with the 1999 cycle and measured in 26,740 members of the general public, including 7,331 children aged 15 and under and 19,409 adults aged 16 and over. MCOP was added starting in the 2005 to 2006 NHANES cycle and has been measured in 18,812 participants, including 5,123 children and 13,689 adults. Most recently (in 2017 to 2018), NHANES began reporting concentrations of MONP, which has been measured in 2,762 participants, including 866 children and 1,896 adults. Urinary MINP, MONP, and MCOP concentrations were quantified using high performance liquid chromatography-electrospray ionization-tandem mass spectrometry. LODs for each cycle of NHANES are provided in Table_Apx C-1. Values below the LOD were replaced by the lower limit of detection divided by the square root of two (NCHS, 2021). As can be seen from Table_Apx C-2, MCOP was above the LOD in the urine of greater than 99 percent of all NHANES participants (N=2,762) in the most recent survey (2017 to 2018), while MINP and MONP were above the LOD in approximately 87 percent of samples.

DCHP: One metabolite of DCHP, mono-cyclohexyl phthalate (MCHP), has been reported in the NHANES dataset. MCHP has been reported in NHANES beginning with the 1999 cycle and measured in 15,829 members of the general public, including 4,130 children aged 15 and under and 11,699 adults aged 16 and over. However, MCHP was excluded from the NHANES survey due to low detection levels and a low frequency of detection in human urine after the 2009 to 2010 survey cycle (CDC, 2013a). Urinary MCHP concentrations were quantified using high performance liquid chromatography-electrospray ionization-tandem mass spectrometry. LODs for each cycle of NHANES are provided in Table_Apx C-1. Values below the LOD were replaced by the lower limit of detection divided by the square root of two (NCHS, 2021). In the 1999 to 2000 NHANES survey, MCHP was above the LOD in

100 percent of urine samples; however, the percent of samples with levels of MCHP above the LOD dropped precipitously in subsequent survey years. In the 2009 to 2010 survey year (last survey in which MCHP was monitored), MCHP was above the LOD in 4.3 percent of samples for all adults aged 16 years and older, and 7.9 percent of samples for all children 3 to less than 16 years of age (see Appendix B of the *Environmental Media, General Population, and Environmental Exposure for Dicyclohexyl Phthalate (DCHP)* (U.S. EPA, 2025h)).

Table_Apx C-1. Limit of Detection (ng/mL) of Urinary Phthalate Metabolites by NHANES Survey Year

Phthalate	Urinary Metabolite	NHANES Survey Year									
		1999–2000	2001–2002	2003–2004	2005–2006	2007–2008	2009–2010	2011–2012	2013–2014	2015–2016	2017–2018
DEHP	MEHP	0.86	0.86	0.9	1.2	1.2	0.5	0.5	0.8	0.8	0.8
	MEHHP	–	–	0.32	0.7	0.7	0.2	0.2	0.4	0.4	0.4
	MECPP	–	–	0.25	0.6	0.6	0.2	0.2	0.4	0.4	0.4
	MEOHP	–	–	0.45	0.7	0.7	0.2	0.2	0.2	0.2	0.2
DBP	MnBP	0.94	0.94	0.4	0.6	0.6	0.4	0.2	0.4	0.4	0.4
	MHBP	–	–	–	–	–	–	–	–	0.4	0.4
BBP	MBzP	0.47	0.47	0.11	0.3	0.3	0.216	0.3	0.3	0.3	0.3
DIBP	MiBP	–	0.94	0.26	0.3	0.3	0.2	0.2	0.8	0.8	0.8
	MHiBP	–	–	–	–	–	–	–	–	0.4	0.4
DCHP	MCHP	0.93	0.93	0.2	0.3	0.3	0.402	–	–	–	–
DINP	MiNP	0.79	0.79	1.54	1.23	1.23	0.77	0.5	0.9	0.9	0.9
	MCOP	–	–	–	0.7	0.7	0.2	0.2	0.3	0.3	0.3
	MONP	–	–	–	–	–	–	–	–	–	0.4

Table_Apx C-2. Summary of Phthalate Metabolite Detection Frequencies in NHANES[a]

Parent Phthalate	Urinary Metabolite	Percentage Below the Limit of Detection		
		2017–2018 NHANES (All Participants; N=2,762)	2017–2018 NHANES (Women Aged 16–49; N=470)	2017–2018 NHANES (Children Aged 6–17; N=866)
BBP	Mono-benzyl phthalate (MBzP)	3.8%	6.25%	0.81%
DBP	Mono-n-butyl phthalate (MnBP)	0.69%	0.81%	0.58%
	Mono-3-hydroxybutyl phthalate (MHBP)	24.91%	27.82%	15.82%
DEHP	Mono-2-ethylhexyl phthalate (MEHP)	43.77%	41.13%	36.84%
	Mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)	0.98%	1.21%	0.12%
	Mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP)	0.83%	1.21%	0.12%
	Mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP)	0.18%	–	–
DIBP	Mono-isobutyl phthalate (MiBP)	4.89%	7.46%	1.5%
	Mono-2-methyl-2-hydroxypropyl Phthalate (MHiBP)	2.17%	2.34%	1.03%
DINP	Mono-isononyl phthalate (MiNP)	12.57%	14.37%	18.01%
	Mono-(carboxyoctyl) phthalate (MCOP)	0.51%	0.40%	0.11%
	Mono-oxoisononyl phthalate (MONP)	12.85%	11.06%	7.62%

– Indicates that the metabolite was not included as part of the analysis.
[a] Collection of the urinary DCHP metabolite, MCHP, was discontinued after the 2009–2010 NHANES cycle and is not included in this table.

C.2 Urinary Biomonitoring: Temporal Trends Analysis

C.2.1 DEHP

Temporal trends in urinary MEHP, MEHHP, MEOHP, and MEOCP, which are metabolites of DEHP, are summarized below and discussed in detail in Section 10.2 of EPA's *Environmental Media and General Population and Environmental Exposure for Diethylhexyl Phthalate (DEHP)* (U.S. EPA, 2025j). *Overall, 50th and 95th percentile urinary MEHP, MEHPP, MEOHP and MEOCP concentrations have significantly decreased over time (1999–2018) for all lifestages.* Note temporal trends discussed in this section pertain to population level trends, not an individual's time course of exposure.

For MEHP (NHANES reporting years: 1999–2018), the following trends were observed:

- Overall, median and 95th percentile MEHP urinary concentrations have decreased over time (1999–2018) for all lifestages.

- Median and 95th percentile urinary MEHP concentrations decreased significantly among all children under age 16, as well as among children aged 3 to less than 6 years, 6 to less than 11 years, and 11 to less than 16 years from 1999 to 2018. There were also significant decreases in median and 95th percentile urinary MEHP concentrations for all male children and all female children under age 16 from 1999 to 2018.
- Median and 95th percentile urinary MEHP concentrations decreased significantly among all adults, female adults, and male adults 16 years and older from 1999 to 2018. Among women of reproductive age, there were statistically significant decreases in 50th and 95th percentile MEHP urinary concentrations from 1999 to 2018.

For MEHHP and MEOHP (NHANES reporting years for both metabolites: 2001–2018), the following trends were observed:

- Overall, median and 95th percentile MEHHP and MEOHP concentrations have decreased over time (2001–2018) for all lifestages.
- Statistically significant decreases in 50th and 95th percentile urinary MEHHP and MEOHP concentrations were observed among all children under age 16, as well as among children aged 3 to less than 6 years, 6 to less than 11 years, and 11 to less than 16 years from 1999 to 2018. Median and 95th percentile urinary MEHHP and MEOHP concentrations also decreased significantly for all male and all female children, and female children under age 16, from 1999 to 2018.
- Median and 95th percentile MEHHP and MEOHP urinary concentrations decreased significantly among all adults, as well as among adult males, and among adult females 16 years and older from 2001 to 2018. Among women of reproductive age, there were statistically significant decreases in 50th and 95th percentile MEHHP and MEOHP urinary concentrations from 2001 to 2018.

For MECPP (NHANES reporting years: 2003–2018), the following trends were observed:

- Overall, median and 95th percentile MECPP concentrations have decreased over time (2003–2018) for all lifestages.
- Statistically significant decreases in 50th and 95th percentile urinary MECPP concentrations were observed among all children under age 16, as well as among children aged 3 to less than 6 years, 6 to less than 11 years, and 11 to less than 16 years from 2003 to 2018. Median and 95th percentile urinary MECPP concentrations also decreased significantly for all male and all female children and female children under age 16 from 1999 to 2018.
- Median and 95th percentile MECPP urinary concentrations decreased significantly among all adults, as well as among adult males, and among adult females 16 years and older from 2003 to 2018. Among women of reproductive age, there were statistically significant decreases in 50th and 95th percentile MECPP urinary concentrations from 2003 to 2018.

C.2.2 DBP

Temporal trends in urinary MnBP and MHBP, which are metabolites of DBP, are summarized below and discussed in detail in Section 10.2 of EPA's *Environmental Media and General Population and Environmental Exposure for Dibutyl Phthalate (DBP)* (U.S. EPA, 2025i). *Overall, 50th and 95th percentile urinary MnBP concentrations have decreased over time (1999–2018) for all life stages.* For urinary MHBP, consistent temporal trends across populations are less apparent; however, MHBP has only been measured in NHANES from 2015 to 2018. This shorter sampling period may account for some of the observed variability and inconsistency. Note temporal trends discussed in this section pertain to population level trends, not an individual's time course of exposure.

For MnBP (NHANES reporting years: 1999–2018), the following trends were observed:

- Overall, 50th and 95th MnBP urinary concentrations have decreased over time (1999–2018) for all life stages.
- From 1999 to 2018, 50th and 95th percentile urinary MnBP concentrations significantly decreased over time for all children under 16 years of age, as well as for children aged 3 to less than 6 years, 6 to less than 11 years, and 11 to less than 16 years; all adults, all female adults, and all male adults 16 years and older; and women of reproductive age (16 to 49 years of age).

For MHBP (NHANES reporting years: 2015–2018), the following trends were observed:

- While 95th percentile MHBP concentrations tended to decrease over time for children and adults, they increased over time among women of reproductive age. Meanwhile, 50th percentile MHBP concentrations tended to increase over time among children under 16, decrease for adults, and have no significant changes for women of reproductive age.
- From 2015 to 2018, 50th percentile MHBP concentrations increased over time among all children under 16, and among adolescents aged 11 to less than 16 years old. However, 95th percentile MHBP concentrations decreased over time among all children under 16, male children under 16, children aged 6 to less than 11 years, and adolescents aged 11 to less than 16 years.
- Additionally, 50th percentile MHBP concentrations decreased over time among all adults and for adult females. During this period, 95th percentile MHBP concentrations also decreased among all adults, adult males, and adult females. Among women of reproductive age, 95th percentile MHBP concentrations increased significantly, though no significant changes were observed at the 50th percentile.

C.2.3 BBP

Temporal trends in urinary MBzP, a metabolite of BBP, are summarized below and discussed in detail in Section 10.2 of EPA's *Environmental Media and General Population and Environment Exposure for Butyl benzyl phthalate (BBP)* (U.S. EPA, 2025l). *Overall, 50th and 95th percentile urinary MBzP concentrations significantly decreased over time (1999–2018) for all lifestages.* Note temporal trends discussed in this section pertain to population level trends, not an individual's time course of exposure.

For MBzP (NHANES reporting years: 1999–2018), the following trends were observed:

- Overall, MBzP urinary concentrations have decreased over time across all life stages between 1999 and 2018.
- From 1999 to 2018, 50th and 95th percentile MBzP concentrations decreased significantly for all children under 16 over time, as well as for male children and female children. This significant trend held for all age groups: 3 to less than 6 years, 6 to less than 11, and 11 to less than 16 years. The 50th and 95th percentile MBzP urinary concentrations also decreased significantly amongst all adults, adult males, and adult females ages 16 years and older.
- From 1999 to 2018, both 50th and 95th percentile MBzP urinary concentrations decreased amongst women of reproductive age (16 to 49 years of age) over time.

C.2.4 DIBP

Temporal trends in urinary MIBP and MHiBP, which are metabolites of DIBP, are summarized below and in more detail in Section 10.2 of EPA's *Environmental Media and General Population and Environmental Exposure for Diisobutyl phthalate (DIBP)* (U.S. EPA, 2025m). *Overall, 50th and 95th percentile urinary MIBP concentrations significantly increased over time (1999–2018) for all lifestages, while 50th and 95th percentile MHiBP urinary concentrations decreased over time (2015–2018) for most life stages.* Note temporal trends discussed in this section pertain to population level trends, not an individual's time course of exposure.

For MIBP (NHANES reporting years: 2001–2018), the following trends were observed:

- Overall, median and 95th percentile MIBP urinary concentrations significantly increased over time for all life stages from 2001 to 2018.
- From 2001 to 2018, median and 95th percentile urinary MIBP concentrations significantly increased among all children 3 to less than 16 years, as well as for children 6 to less than 11 years and children 11 to less than 16 years. MIBP concentrations also significantly increased among toddlers 3 to less than 6 years at the 95th percentile. Similarly, median and 95th percentile MIBP concentrations significantly increased among all adults, adult males, and adult females, females ages 16 years and older, as well as for women of reproductive age (16 to 49 years).

For MHiBP (NHANES reporting years: 2015–2018), the following trends were observed:

- Overall, median and 95th percentile MHiBP urinary concentrations decreased over time for most life stages.
- From 2015 to 2018, median MHiBP urinary concentrations decreased among all children 3 to less than 16 years, as well as for the children 6 to less than 11 years. However, median MHiBP urinary concentrations increased among adolescents 11 to less than 16 years. During this time, 95th percentile MHiBP urinary concentrations decreased significantly over time among all children 3 to less than 16 years, male children, female children, and among the following age groups: toddlers 3 to less than 6 years, children 6 to less than 11 years, and adolescents 11 to less than 16 years.
- Significant decreases in median MHiBP urinary concentrations were observed among all adults aged 16 and older, adult females, adult males, and women of reproductive age (16 to 49 years). Additionally, 95th percentile MHiBP urinary concentrations decreased significantly among all adults aged 16 and older, as well as for male adults, and women of reproductive age (16 to 49 years).

C.2.5 DINP

Temporal trends in urinary MINP and MCOP, which are metabolites of DINP, are summarized below and in more detail in Section 10.2 of EPA's *Environmental Media and General Population Screening for Diisononyl Phthalate (DINP)* (U.S. EPA, 2025k). For MONP, no temporal trends analysis was conducted because MONP has only been measured in the most recent NHANES survey (2017 to 2018). Note temporal trends discussed in this section pertain to population level trends, not an individual's time course of exposure.

For MINP (NHANES reporting years: 1999–2018), the following trends were observed:

- Among all NHANES participants, the direction of the trend of MiNP concentrations changed over time. MiNP significantly increased ($p<0.001$ for both 50th and 95th percentile exposures) between 1999 and 2014, but decreased between 2015 and 2018; the decrease was statistically significant at the 95th percentile ($p=0.007$), but not at the 50th percentile.
- Overall, urinary concentrations of MINP have generally decreased over time for most lifestages.
- Among all children under 16, significant changes were observed in 50th and 95th percentile MINP concentrations (50th percentile, $p < 0.001$; 95th percentile, $p < 0.001$), as well as a significant increase in 95th percentile concentrations among male children under 16 ($p < 0.001$), and a significant decrease among female children under 16 ($p < 0.001$). Within age groups, MINP concentrations significantly decreased among children aged 3 to less than 6 years of age (95th percentile, $p < 0.001$) and significantly increased among adolescents 11 to less than 16 years of age (50th percentile, $p < 0.001$; 95th percentile, $p < 0.001$); no significant changes in 50th or 95th percentile MINP concentrations over time were observed among children aged 6 to less than 11.
- MINP concentrations significantly decreased among all adults (50th percentile, $p < 0.001$; 95th percentile, $p < 0.001$), adult males (95th percentile, $p < 0.001$), and adult females (50th percentile, $p < 0.001$). A significant increase in MINP concentrations were observed among adult females (50th percentile, $p < 0.001$; 95th percentile, $p < 0.001$) and in 50th percentile concentrations among women of reproductive age ($p = 0.03$).

For MCOP (NHANES reporting years: 2005–2018), the following trends were observed:

- Among all NHANES participants, the direction of the trend of MCOP concentrations changed over time. Between 2005 and 2014, MCOP concentrations significantly increased among all NHANES participants (50th percentile, $p<0.001$). After 2014, MCOP concentrations significantly decreased at both the 50th and 95th percentile for all participants ($p<0.001$ for both analyses).
- Overall, median MCOP concentrations have decreased over time for all lifestages, while 95th percentile concentrations increased over time for all lifestages.
- There was a significant decrease in 50th percentile urinary MCOP concentrations among all children under 16 ($p < 0.001$), as well as among children aged 6 to less than 11 years ($p < 0.001$). Increases in 95th percentile urinary MCOP concentrations were observed among all children under 16 ($p < 0.001$), all male children under 16 ($p < 0.001$), and all female children under 16 ($p < 0.001$). Additionally, a significant increase in 95th percentile concentrations over time was observed among toddlers aged 3 to less than 6, and a significant decrease in MCOP concentrations was observed among children aged 6 to less than 11 years old ($p < 0.001$). At both the 50th and 95th percentile, significant differences in urinary MCOP concentrations were

observed between male and female children under 16 over time (50th percentile, $p < 0.001$; 95th percentile, $p < 0.001$).

- Among adults, 50th percentile MCOP concentrations significantly decreased over time for all adults, but significantly increased over time for adults at the 95th percentile of exposure. Significant decreases in MCOP were also observed among adult males (50th percentile, $p < 0.001$) and adult females (50th percentile, $p < 0.001$; 95th percentile, $p = 0.005$) but not for women of reproductive age. Additionally, a significant difference in 95th percentile MCOP concentrations were observed between adult men and women ($p < 0.001$), but no difference was observed for 50th percentile MCOP concentrations.

C.3 Reverse Dosimetry: Methods and Results

Using urinary metabolite concentrations for DEHP, DBP, BBP, DIBP, and DINP measured in the most recently available NHANES sampling cycle (2017 to 2018), EPA estimated phthalate daily intake through reverse dosimetry. Reverse dosimetry approaches that incorporate basic pharmacokinetic information are available for phthalates (Koch et al., 2007; Koch et al., 2003; David, 2000) and have been used in previous phthalate risk assessments conducted by U.S. CPSC (2014) and Health Canada (Health Canada, 2020) to estimate daily intake values for exposure assessment. For phthalates, reverse dosimetry can be used to estimate a daily intake (DI) value for a parent phthalate diester based on phthalate monoester metabolites measured in human urine using Equation_Apx C-1 (Koch et al., 2007).

Equation_Apx C-1. Calculating the Daily Intake Value from Urinary Biomonitoring Data

$$Phthalate\ DI = \frac{(\mathrm{UE}_{Sum} \times \mathrm{CE})}{\mathrm{Fue}_{sum}} \times MW_{Parent}$$

Where:

- Phthalate DI = Daily intake ($\mu g/kg_{bw}/day$) value for the parent phthalate diester
- UE_{sum} = The sum molar concentration of urinary metabolites associated with the parent phthalate diester (in units of µmole per gram creatinine).
- CE = The creatinine excretion rate normalized by body weight (in units of mg creatinine per kg body weight per day). CE can be estimated from the urinary creatinine values reported in biomonitoring studies (*i.e.,* NHANES) using the equations of Mage et al. (2008) based on age, gender, height, and race, as was done by Health Canada (Health Canada, 2020) and U.S. CPSC (2014).
- Fue_{sum} = The summed molar fraction of urinary metabolites. The molar fraction describes the molar ratio between the amount of metabolite excreted in urine and the amount of parent compound taken up. Fue values used for daily intake value calculations are shown in Table_Apx C-3.
- MW_{parent} = The molecular weight of the parent phthalate diester (in units of g/mole).

Daily intake values were calculated for each participant from NHANES. A creatinine excretion rate for each participant was calculated using equations provided by Mage et al. (2008). The applied equation is dependent on the participant's age, height, race, and sex to accommodate variances in urinary excretion

rates. Creatinine excretion rate equations were only reported for people who are non-Hispanic Black and non-Hispanic White, so the creatinine excretion rate for participants of other races were calculated using the equation for non-Hispanic White adults or children, in accordance with the approach used by U.S. CPSC (2015).

Table_Apx C-3. Fue Values Used for the Calculation of Daily Intake Values of DEHP, BBP, DBP, DIBP, and DINP

Parent Phthalate	Study Population	Metabolite(s)	Fue[a]	Fue Sum	Reference
DEHP	N = 10 men (20–42 years of age) and 10 women (18–77 years of age)	MEHP	0.062	0.452	(Anderson et al., 2011)
		MEHHP	0.149		
		MEOHP	0.109		
		MECPP	0.132		
BBP	N = 14 volunteers (gender and age not provided)	MBzP	0.73	0.73	(Anderson et al., 2001)
DBP	N = 13 volunteers (gender and age not provided)	MBP	0.69	0.69	(Anderson et al., 2001)
DIBP	N = 13 volunteers (gender and age not provided)	MiBP	0.69[b]	0.69[b]	(Anderson et al., 2001)
DINP	N = 10 men (20–42 years of age) and 10 women (18–77 years of age)	MINP	0.030	0.192	(Anderson et al., 2011)
		MONP	0.063		
		MCOP	0.099		

[a] Fue values are presented on a molar basis and were estimated by study authors based on metabolite excretion over a 24-hour period (DINP, DBP, DIBP).
[b] Fue value of 0.69 based on excretion of DBP urinary metabolite MnBP.

C.4 Statistical Analysis of Cumulative Phthalate Exposure

Table_Apx C-4. Statistical Analysis (t-test) of Cumulative Phthalate Exposure for Women of Reproductive Age by Race[a]

Variable	Method	Variances	tValue	DF	Probt	Race 1[b]	Race 2[b]
50th Percentile	Pooled	Equal	-0.7049	8	0.5009	white	black
50th percentile	Pooled	Equal	-0.2509	8	0.8082	white	mexic
50th percentile	Pooled	Equal	0.5053	8	0.6270	white	other
50th percentile	Pooled	Equal	-0.4905	8	0.6369	black	mexic
50th percentile	Pooled	Equal	-1.0495	8	0.3246	black	other
50th percentile	Pooled	Equal	-0.7143	8	0.4954	mexic	other
50th percentile	Pooled	Equal	0.5780	8	0.5792	white	black
50th percentile	Pooled	Equal	-0.4230	8	0.6834	white	mexic
50th percentile	Pooled	Equal	1.0271	8	0.3344	white	other
50th percentile	Pooled	Equal	0.8771	8	0.4060	black	mexic
50th percentile	Pooled	Equal	-0.6560	8	0.5302	black	other
50th percentile	Pooled	Equal	-1.1843	8	0.2703	mexic	other
50th percentile	Pooled	Equal	-0.7049	8	0.5009	white	black
50th percentile	Pooled	Equal	-0.2509	8	0.8082	white	mexic
50th percentile	Pooled	Equal	0.5053	8	0.6270	white	other
50th percentile	Pooled	Equal	-0.4905	8	0.6369	black	mexic
50th percentile	Pooled	Equal	-1.0495	8	0.3246	black	other
50th percentile	Pooled	Equal	-0.7143	8	0.4954	mexic	other
95th percentile	Pooled	Equal	0.5780	8	0.5792	white	black
95th percentile	Pooled	Equal	-0.4230	8	0.6834	white	mexic
95th percentile	Pooled	Equal	1.0271	8	0.3344	white	other
95th percentile	Pooled	Equal	0.8771	8	0.4060	black	mexic
95th percentile	Pooled	Equal	-0.6560	8	0.5302	black	other
95th percentile	Pooled	Equal	-1.1843	8	0.2703	mexic	other
95th percentile	Pooled	Equal	-0.7049	8	0.5009	white	black
95th percentile	Pooled	Equal	-0.2509	8	0.8082	white	mexic
95th percentile	Pooled	Equal	0.5053	8	0.6270	white	other
95th percentile	Pooled	Equal	-0.4905	8	0.6369	black	mexic
95th percentile	Pooled	Equal	-1.0495	8	0.3246	black	other
95th percentile	Pooled	Equal	-0.7143	8	0.4954	mexic	other
95th percentile	Pooled	Equal	0.5780	8	0.5792	white	black
95th percentile	Pooled	Equal	-0.4230	8	0.6834	white	mexic
95th percentile	Pooled	Equal	1.0271	8	0.3344	white	other
95th percentile	Pooled	Equal	0.8771	8	0.4060	black	mexic
95th percentile	Pooled	Equal	-0.6560	8	0.5302	black	other
95th percentile	Pooled	Equal	-1.1843	8	0.2703	mexic	other

[a] Independent t-test with pooled variance (assuming equal variance in exposures among both racial groups) to assess differences in mean phthalate exposure between different racial groups.
[b] Racial groups include White non-Hispanic, Black non-Hispanic, Mexican American, and Other.

Table_Apx C-5. Statistical Analysis (ANOVA with Tukey Post-Hoc Test) of Cumulative Phthalate Exposure for Women of Reproductive Age by Race[a]

Dependent	Source	DF	SS	MS	F Value	ProbF
50th percentile	Model	3	0.053263348	0.017754449	0.491687573	0.693011899
	Error	16	0.577747344	0.036109209		
	Corrected Total	19	0.631010692			
95th percentile	Model	3	7.932713778	2.644237926	0.850142129	0.486666284
	Error	16	49.76556906	3.110348067		
	Corrected Total	19	57.69828284			

Abbreviations: DF = Degrees of freedom; MS = mean squares; SS = sum-of-squares
[a] ANOVA to determine whether there are significant differences in phthalate exposure among racial groups among women of reproductive age. Post-hoc tests were performed to examine differences in exposure between races. No differences were observed and output was not generated.

Table_Apx C-6. Statistical Analysis (ANOVA with Tukey Post-Hoc Test) of Cumulative Phthalate Exposure for Women of Reproductive Age by Socioeconomic Status[a]

Dependent	Source	DF	SS	MS	F Value	ProbF
50th percentile	Model	2	0.058905	0.029453	0.299768	0.74638
	Error	12	1.179014	0.098251		
	Corrected Total	14	1.237919			
95th percentile	Model	2	6.019748	3.009874	0.085482	0.918624
	Error	12	422.5295	35.21079		
	Corrected Total	14	428.5493			

Abbreviations: DF = Degrees of freedom; MS = mean squares; SS = sum-of-squares;
[a] ANOVA to determine whether there are significant differences in phthalate exposure among socioeconomic status groups among women of reproductive age. Post-hoc tests were performed to examine differences in exposure between socioeconomic status. No differences were observed and output was not generated.

Table_Apx C-7. Statistical Analysis (ANOVA with Tukey Post-Hoc Test) of Cumulative Phthalate Exposure for Women of Reproductive Age and Male Children by Age[a]

Dependent	Source	DF	SS	MS	F Value	ProbF
50th percentile	Model	3	0.527705678	0.175901893	1.061407322	0.393002372
	Error	16	2.651602472	0.165725155		
	Corrected Total	19	3.17930815			
95th percentile	Model	3	6.568006156	2.189335385	1.403496422	0.278192271
	Error	16	24.95864302	1.559915189		
	Corrected Total	19	31.52664917			

Abbreviations: DF = Degrees of freedom; MS = mean squares; SS = sum-of-squares;
[a] ANOVA to determine whether there are significant differences in phthalate exposure among age groups (women aged 16–49, boys age 3–5, boys age 6–11, and boys age 12–15). Post-hoc tests were performed to examine differences in exposure between races. No differences were observed and output was not generated.

C.5 Limitations and Uncertainties of Reverse Dosimetry Approach

Controlled human exposure studies have been conducted and provide estimates of the urinary molar excretion factor (*i.e.*, the Fue) to support use of a reverse dosimetry approach. These studies most frequently involve oral administration of an isotope-labelled (*e.g.*, deuterium or carbon-13) phthalate diester to a healthy human volunteer and then urinary excretion of monoester metabolites is monitored over 24 to 48 hours. Fue values estimated from these studies have been used by both U.S. CPSC (2014) and Health Canada (Health Canada, 2020) to estimate phthalate daily intake values using urinary biomonitoring data.

Use of reverse dosimetry and urinary biomonitoring data to estimate daily intake of phthalates is consistent with approaches employed by both U.S. CPSC (2014) and Health Canada (Health Canada, 2020). However, there are challenges and sources of uncertainty associated with the use of reverse dosimetry approaches. U.S. CPSC considered several sources of uncertainty associated with use of human urinary biomonitoring data to estimate daily intake values and conducted a semi-quantitative evaluation of uncertainties to determine the overall effect on daily intake estimates (see Section 4.1.3 of (CPSC, 2014)). Identified sources of uncertainty include: (1) analytical variability in urinary metabolite measurements; (2) human variability in phthalate metabolism and its effect on metabolite conversion factors (*i.e.*, the Fue); (3) temporal variability in urinary phthalate metabolite levels; (4) variability in urinary phthalate metabolite levels due to fasting prior to sample collection; (5) variability due to fast elimination kinetics and spot samples; and (6) creatinine correction models for estimating daily intake values.

In addition to some of the limitations and uncertainties discussed above and outlined by U.S. CPSC (2014), the short half-lives of phthalates can be a challenge when using a reverse dosimetry approach. Phthalates have elimination half-lives on the order of several hours and are quickly excreted from the body in urine and to some extent feces (ATSDR, 2022; EC/HC, 2015). Therefore, spot urine samples, as collected through NHANES and many other biomonitoring studies, are representative of relatively recent exposures. Spot urine samples were used by Health Canada (Health Canada, 2020) and U.S. CPSC (2014) to estimate daily intake values. However, due to the short half-lives of phthalates, a single spot sample may not be representative of average urinary concentrations that are collected over a longer term or calculated using pooled samples (Shin et al., 2019; Aylward et al., 2016). Multiple spot samples provide a better characterization of exposure, with multiple 24-hour samples potentially leading to better characterization, but are less feasible to collect for large studies (Shin et al., 2019). Due to rapid elimination kinetics, U.S. CPSC concluded that spot urine samples collected at a short time (2 to 4 hours) since last exposure may overestimate human exposure, while samples collected at a longer time (greater than 14 hours) since last exposure may underestimate exposure (see Section 4.1.3 of (CPSC, 2014) for further discussion).

Appendix D Supporting Analyses for Occupational Exposure to Phthalates

D.1 Trends in National Aggregate Production Volume

EPA also considered whether trends in national aggregate production volume data may mirror temporal trends noted in NHANES urinary biomonitoring data. To do this, EPA extracted national aggregate production volume (PV) data for DEHP, DBP, DIBP, BBP, DCHP, and DINP from the 2016 and 2020 Chemical Data Reporting (CDR), which is shown in Table_Apx D-1. In CDR, national aggregate PV data are reported as a range to protect PV data claimed as confidential business information (CBI). Given the large ranges in reported PV data for each phthalate, it is difficult to definitively conclude whether there are any trends in PV for any phthalate. Based on available CDR data, there is no evidence of a trend in national aggregate PV for DEHP (PV ranged from 10,000,000 lbs to less than 50,000,000 lbs in 2012 through 2019), DBP (PV ranged 1,000,000 lbs to less than 10,000,000 lbs in 2012 through 2019), or DCHP (PV ranged from 500,000 lbs to less than 1,000,000 lbs in 2012 through 2019). For BBP, there is some limited evidence of a decline in PV, which was reported as 10,000,000 to less than 50,000,000 lbs from 2012 to 2015 and declined to 10,000,000 to less than 20,000,000 lbs from 2016 through 2019. For DIBP, there is some limited evidence of a decline in PV, with PV reported as ranging from 1,000,000 to less than 20,000,000 lbs in 2012 and declining to less than 1,000,000 lbs in 2013 through 2019. For DINP (CASRN 28553-12-0), there is some limited evidence of a decline in PV with PV reported as 100,000,000 to less than 250,000,000 lbs in 2012 through 2018 and declining to 50,000,000 to less than 100,000,000 lbs in 2019. In contrast, there is some limited evidence of an increase in PV for DINP (CASRN 68515-48-0), with PV reported as 100,000,000 to less than 250,000,000 lbs in 2012 through 2015 and 100,000,000 to less than 1,000,000,000 lbs in 2016 through 2019.

Overall, given the large ranges in reported PV, it is difficult to conclude whether there are any trends in PV data for any phthalate.

Table_Apx D-1. Trends in Nationally Aggregated Production Volume (lbs) Data for DEHP, DBP, BBP, DIBP, DCHP, and DINP

Phthalate	CASRN	2019	2018	2017	2016	2015	2014	2013	2012
DEHP	117-81-7	10,000,000 – <50,000,000	10,000,000 – <50,000,000	10,000,000 – <50,000,000	10,000,000 – <50,000,000	10,000,000 – <50,000,000	10,000,000 – <50,000,000	10,000,000 – <50,000,000	10,000,000 – <50,000,000
DBP	84-74-2	1,000,000 – <10,000,000	1,000,000 – <10,000,000	1,000,000 – <10,000,000	1,000,000 – <10,000,000	1,000,000 – <10,000,000	1,000,000 – <10,000,000	1,000,000 – <10,000,000	1,000,000 – <10,000,000
BBP	85-68-7	1,000,000 – <20,000,000	1,000,000 – <20,000,000	1,000,000 – <20,000,000	1,000,000 – <20,000,000	10,000,000 – <50,000,000	10,000,000 – <50,000,000	10,000,000 – <50,000,000	10,000,000 – <50,000,000
DIBP	84-69-5	407,303	403,833	384,591	440,833	<1,000,000	<1,000,000	<1,000,000	1,000,000 – <20,000,000
DCHP	84-61-7	500,000 – <1,000,000	<1,000,000	500,000 – <1,000,000	500,000 – <1,000,000	500,000 – <1,000,000	500,000 – <1,000,000	500,000 – <1,000,000	500,000 – <1,000,000
DINP	28553-12-0	50,000,000 – <100,000,000	100,000,000 – <250,000,000	100,000,000 – <250,000,000	100,000,000 – <250,000,000	100,000,000 – <250,000,000	100,000,000 – <250,000,000	100,000,000 – <250,000,000	100,000,000 – <250,000,000
	68515-48-0	100,000,000 – <1,000,000,000	100,000,000 – <1,000,000,000	100,000,000 – <1,000,000,000	100,000,000 – <1,000,000,000	100,000,000 – <250,000,000	100,000,000 – <250,000,000	100,000,000 – <250,000,000	100,000,000 – <250,000,000

D.2 Industrial and Commercial Products Containing Multiple Phthalates

Table_Apx D-2. Summary of Industrial and Commercial Products that Contain Multiple Phthalates

Manufacturer	Product	Physical State	Source	Use	DEHP	DBP	BBP	DIBP	DINP	DCHP
Restek Corporation	33227 / EPA Method 8061A Phthalate Esters Mixture	No data available	Restek Corporation (2019)	Laboratory chemical	0.10%	0.10%	0.10%	0.10%		0.10%
Phenova	BN Extractables – Skinner List	Liquid	Phenova (2017a)	Laboratory chemical	0.20%	0.20%	0.20%			
Phenova	Custom 8061 Phthalates Mix	Liquid	Phenova (2017)	Laboratory chemical	0.10%	0.10%	0.10%	0.10%		
Phenova	Custom 8270 Cal Mix 1	Liquid	Phenova (2018a)	Laboratory chemical	0.10%	0.10%	0.10%			
Phenova	Custom 8270 Cal Standard	Liquid	Phenova (2017c)	Laboratory chemical	0.20%	0.20%	0.20%			
Phenova	Custom 8270 Plus Cal Mix	Liquid	Phenova (2017d)	Laboratory chemical	0.10%	0.10%	0.10%			
Phenova	Custom Low ICAL Mix	Liquid	Phenova (2017e)	Laboratory chemical	0.10%	0.10%	0.10%			
Phenova	Custom SS 8270 Cal Mix 1	Liquid	Phenova (2018b)	Laboratory chemical	0.10%	0.10%	0.10%			
Phenova	EPA 525.2 Semivolatile Mix	Liquid	Phenova (2018c)	Laboratory chemical	0.10%	0.10%	0.10%			
Lord Corporation	Fusor 108B, 109B Metal Bonding ADH PT B	Paste	LORD Corporation (2017)	Adhesive (acrylic)		1–5%				1–5%
SPEX CertiPrep LLC	Phthalate Standard	Liquid	SPEX CertiPrep LLC (2017b)	Laboratory chemical	0.10%	0.10%	0.10%		0.10%	
SPEX CertiPrep LLC	Phthalates in Poly(vinyl chloride)	Solid	SPEX CertiPrep LLC (2017c)	Laboratory chemical	0.30%	0.30%	0.30%		3.00%	
SPEX CertiPrep LLC	Phthalates in Polyethylene Standard	Solid	SPEX CertiPrep LLC (2017c)	Laboratory chemical	0.30%	0.30%	0.30%		3.00%	
SPEX CertiPrep LLC	Phthalates in Polyethylene Standard w/BPA	Solid	SPEX CertiPrep LLC (2017d)	Laboratory chemical	0.10%	0.10%	0.10%		0.10%	
Penn State Industries	PSI PolyClay Canes and PSI PolyClay Bricks	Solid	Penn State Industries (2016)	Polymer clay bricks, canes	<2.5%	<2.5%	<2.5%		<2.5%	

D.3 Parent Company Overlap in Phthalate Manufacture and Processing

Data from CDR provide manufacture and processing information from parent companies, including overall production volume and number of facilities, and all phthalates considered in this cumulative assessment are reported to CDR. Though these data provide a broad overview of the various businesses involved in the phthalate industry, the CDR data provide information about the parent company only and are not granular enough to determine if multiple phthalates are being processed within a singular facility. Therefore, there is uncertainty associated with assigning co-exposures based on parent company reporting data from CDR. Table_Apx D-3 characterizes the various parent companies from 2016 and 2020 CDR that report use of multiple phthalates considered in this cumulative assessment, as well as parent companies reporting use of DEHP and DBP under the 2017 to 2022 Toxics Release Inventory (TRI).

Table_Apx D-3. Parent Companies Reporting Use of Multiple Phthalates (DEHP, DBP, BBP, DIBP, DINP, DCHP) to 2016 and 2020 CDR and 2017 through 2022 TRI

CDR or TRI Year	Use Category	Domestic Parent Company Name	Address	City	State	Postal Code	Reported in TRI		Reported in CDR					
							DEHP	DBP	DBP	DEHP	DINP	DCHP	BBP	DBP
2016 CDR; 2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	ALAC International Inc	350 Fifth Avenue	New York	NY	10118				X	X			
2016 CDR; 2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Allchem Industries Holding Corp	6010 NW First Place	Gainesville	FL	32607			X	X				
2017–2022 TRI	Processing	American Polymers Corp	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2016 CDR; 2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	BASF Corporation	100 Park Avenue	Florham Park	MI	7932					X		X	
2016 CDR: 2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	CBI[b]	CBI[b]	CBI[b]	CBI[b]	CBI[b]			X		X		X	
2016 CDR	Industrial Processing and Use; Consumer and Commercial Use	CBI[c] (reporting site name is Air Prod & Chem Hamilton Blvd Fac)	CBI[c]	CBI[c]	CBI[c]	CBI[c]			X	X	X			
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	CBI[c] (reporting site name is Exxon Mobil BR Chemical Plant)	CBI[c]	CBI[c]	CBI[c]	CBI[c]			X	X	X			
2016 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	CBI[c] (reporting site name is Greenchem)	CBI[c]	CBI[c]	CBI[c]	CBI[c]			X	X	X			
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	CBI[c] (reporting site name is M. Argueso & Co., Inc.)	CBI[c]	CBI[c]	CBI[c]	CBI[c]			X	X	X		X	
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	CBI[c] (reporting site name is Mak Chemicals)	CBI[c]	CBI[c]	CBI[c]	CBI[c]			X	X	X		X	
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	CBI[c] (reporting site name is Tremco Incorporated)	CBI[c]	CBI[c]	CBI[c]	CBI[c]			X	X	X		X	
2016 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	CBI[c] (reporting site name is Tricon International, Ltd)	CBI[c]	CBI[c]	CBI[c]	CBI[c]			X	X	X			
2016 CDR; 2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	ChemSpec, Ltd.	1559 Corporate Woods Parkway	Uniontown	OH	44685				X	X			
2017–2022 TRI	Waste Handling	Clean Harbors Inc	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						

CDR or TRI Year	Use Category	Domestic Parent Company Name	Address	City	State	Postal Code	Reported in TRI		Reported in CDR					
							DEHP	DBP	DBP	DEHP	DINP	DCHP	BBP	DBP
2020–2022 TRI	Processing	Danfoss Power Solutions (US) Co	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2017 TRI	Processing	DOW Inc	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X			X[d]			
2017–2019 TRI	Processing	EATON Corp	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Formosa Plastics Corporation, U.S.A.	9 Peach Tree Hill Rd.	Livingston	NJ	7039				X	X			
2016 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	FRP Services & Co. (America) INC	25 West 45th Street	New York	NY	10036				X	X			
2016 CDR; 2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	G.J. Chemical Co., Inc.	40 Veronic Ave.	Somerset	NJ	8873			X	X				
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	GEON Performance Solutions LLC	25777 Detroit Road, Suite 202	Westlake	OH	44145				X	X			
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Greenchem Industries LLC	222 Clematis St.	West Palm Beach	FL	33401			X		X			
2016 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	H I G Capital LLC	7500 East Pleasant Valley Road	Independence	OH	44131			X				X	
2016 CDR; 2020 CDR; 2017–2018 TRI	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Hallstar Co	120 S. Riverside Drive	Chicago	IL	60606	X		X	X	X			
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Harwick Standard Distribution Corporation	60 S. Seiberling St.	Akron	OH	44305				X	X			
2017–2021 TRI	Processing	Henkel of America Inc	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X			X[d]			
2017–2022 TRI	Waste Handling	Heritage-WTI LLC	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2016 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	ICC Industries Inc.	460 Park Ave	New York	NY	10022			X	X	X			
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	ICC Industries Inc.	725 Fifth Avenue	New York	NY	10022			X	X	X			
2016 CDR; 2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Industrial Chemicals Inc.	2042 Montreat Dr.	Birmingham	AL	35216			X	X	X			
2016 CDR; 2020 CDR;	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Lanxess Corporation	111 RIDC Park West Dr.	Pittsburgh	PA	15275	X	X	X			X		X

CDR or TRI Year	Use Category	Domestic Parent Company Name	Address	City	State	Postal Code	Reported in TRI		Reported in CDR					
							DEHP	DBP	DBP	DEHP	DINP	DCHP	BBP	DBP
2017–2022 TRI														
2017–2022 TRI	Waste Handling	Lehigh Hanson	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	M.A. Global Resources Inc	1028 Branch Line Lane	Apex	NC	27502				X	X			
2016 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	MC International, LLC	2 Ne 40th St	Miami	FL	33137			X	X	X			
2016 CDR; 2017–2022 TRI	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Mexichem SAB DE CV	170 Pioneer Drive	Leominster	MA	01453	X			X	X		X	
2017–2022 TRI	Processing	Parker Hannifin Corp	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2016 CDR; 2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	POLYONE CORPORATION	33587 Walker Rd	Avon Lake	OH	44012				X	X			
2017–2022 TRI	Waste Handling	RC Lonestar Inc	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2017–2022 TRI	Waste Handling	RI Technologies Inc	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2016 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Royce International	3400 Tamiami Trail, Suite 300	Sarasota	FL	34239			X		X			
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Shrieve Chemical Company	1755 Woodstead Court	The Woodlands	TX	77380			X	X				
2020 CDR; 2018–2022 TRI	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Sika Corporation	201 Polito Avenue	Lyndhurst	NJ	7071		X	X					X
2016 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Silver Fern Chemical	2226 Queen Anne Avenue N.	Seattle	WA	98109				X	X			
2016 CDR; 2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Soyventis North America LLC	100 Town Square Pl.	Jersey City	NJ	07310			X		X			
2018–2022 TRI	Processing	Superior Industrial Solutions Inc	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2020 CDR; 2016 CDR (under different address);	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Teknor Apex Co	505 Central Ave	Pawtucket	RI	02861	X			X	X			

CDR or TRI Year	Use Category	Domestic Parent Company Name	Address	City	State	Postal Code	Reported in TRI		Reported in CDR					
							DEHP	DBP	DBP	DEHP	DINP	DCHP	BBP	DBP
2017–2022 TRI														
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	The Chemical Company	44 Southwest Avenue	Jamestown	RI	2835				X	X			
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Tribute Energy, Inc.	2100 W. Loop South	Houston	TX	77027				X	X			
2020 CDR; 2016 CDR (under different address); 2017–2022 TRI	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Univar Solutions Inc.	3075 Highland Pkwy., Ste. 200	Downers Grove	IL	60515-5560	X	X	X	X	X			
2017–2020 TRI	Waste Handling	US Ecology Inc	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Valtris	7500 East Pleasant Valley	Independence	OH	44131			X				X	
2017 TRI	Waste Handling	Veolia Environmental Services North America LLC	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2017–2022 TRI	Processing	W R Grace & Co	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2017–2019 TRI	Waste Handling	Waste Management Inc	n/a [a]	n/a [a]	n/a [a]	n/a [a]	X	X						
2016 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Wego Chemical Group	239 Great Neck Road	Great Neck	NY	11021			X		X			
2020 CDR	Manufacture; Industrial Processing and Use; Consumer and Commercial Use	Wilbur-Ellis Company LLC	345 California Street	San Francisco	CA	94104				X	X			

[a] 'n/a' = not applicable, parent company address not provided in TRI.
[b] Because all information is claimed as CBI, it is possible that this row represents multiple parent companies that reported some combination of the flagged phthalates.
[c] Because parent company information is claimed as CBI, it is possible that there are fewer parent companies than rows with CBI parent companies but non-CBI reporting site names.
[d] In TRI, these companies reported releases of DBP and/or DEHP and used a different parent company name than in CDR. In CDR, these sites only reported for DINP. As well, the physical reporting sites themselves have different addresses. Therefore, there is uncertainty in whether the same parent company applies to both the TRI and CDR reports.

D.4 Conditions of Use Listed in Final Scopes for Individual Phthalate Risk Evaluations

Table_Apx D-4. Categories of Conditions of Use for High-Priority Phthalates and a Manufacturer-Requested Phthalate

Use	Conditions of Use	DBP	BBP	DEHP	DCHP	DIBP	DINP
Industrial	Adhesive and sealants		X		X	X	X
	Automotive care products		X				X
	Building/construction materials not covered elsewhere		X			X	X
	Castings		X				
	Chemical intermediate		X				
	Fabric, textile, and leather products not covered elsewhere		X			X	
	Finishing agent				X		
	Floor coverings		X			X	
	Fuels and related products					X	
	Hydraulic fluid		X				
	Hydraulic fracturing			X			
	Ink, toner, and colorant products		X		X	X	
	Laboratory chemicals		X	X			
	Paints and coatings		X	X		X	
	Plastic and rubber products not covered elsewhere		X		X	X	
	Plasticizer						X
	Solvent	X					
	Transportation equipment manufacturing			X			
	Adhesives and sealants	X	X	X	X	X	X
Commercial	Air care products					X	X
	Arts, crafts and hobby materials			X			X
	Automotive care products		X	X			X
	Batteries			X			
	Building/construction materials not covered elsewhere		X	X	X		X
	Castings		X				
	Chemical intermediate		X				
	Chemiluminescent light stick	X					

Use	Conditions of Use	DBP	BBP	DEHP	DCHP	DIBP	DINP
Commercial	Cleaning and furnishing care products	X					X
	Dyes and pigments			X			
	Electrical and electronic products			X			X
	Explosive materials	X					
	Fabric, textile, and leather products not covered elsewhere		X	X			X
	Floor coverings	X	X			X	X
	Foam seating and bedding products						X
	Furniture and furnishings not covered elsewhere	X		X			X
	Hydraulic fluid						X
	Ink, toner, and colorant products	X	X		X	X	
	Inspection penetrant kit	X					
	Laboratory chemical	X	X		X	X	X
	Lawn and garden care products			X			
	Lubricants	X					
	Paints and coatings	X	X	X	X	X	X
	Personal care products	X					
	Pigment						X
	Plastic and rubber products						X
	Plastic and rubber products not covered elsewhere	X	X	X	X	X	X
	Solvent						X
	Toys, playground, and sporting equipment			X			X
Consumer	Adhesives and sealants	X	X	X	X	X	X
	Air care products					X	X
	Arts, crafts and hobby materials	X	X	X	X		X
	Automotive Care products		X	X			X
	Batteries			X			
	Building/construction materials not covered elsewhere		X	X			X
	Chemiluminescent light stick	X					
	Cleaning and furnishing care products	X	X				X
	Dyes and pigments			X			
	Electrical and electronic products			X			X

Use	Conditions of Use	DBP	BBP	DEHP	DCHP	DIBP	DINP
Consumer	Fabric, textile, and leather products not covered elsewhere	X	X	X		X	X
	Floor coverings	X	X			X	X
	Foam seating and bedding products						X
	Furniture and furnishings not covered elsewhere	X		X			X
	Ink, toner, and colorant products		X		X	X	X
	Lawn and garden care products			X			
	Paints and coatings	X	X	X	X	X	X
	Paper products						X
	Plastic and rubber products						X
	Plastic and rubber products not covered elsewhere	X	X	X	X	X	X
	Reference material and/or laboratory reagent			X			
	Toys, playground, and sporting equipment	X	X	X		X	X

[a] Table taken from EPA's *Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the Toxic Substances Control Act* (U.S. EPA, 2023b). COU overlap based on COU tables presented in the final scoping documents for DEHP, DBP, BBP, DIBP, DCHP, and DINP.

Appendix E Calculation of Occupational Exposure Values Based on Cumulative Exposures and Relative Potency Assumptions

EPA typically derives an occupational exposure value (OEV) to represent the exposure concentration below which exposed workers and occupational non-users are not expected to exhibit any appreciable risk of adverse toxicological outcomes. For exposures to individual chemicals, this can be easily calculated based on the POD for the most sensitive human health effect supported by the weight of scientific evidence, expressed relative to benchmarks and standard occupational scenario assumptions.

A singular value cannot be applied across the board for application to cumulative risk analysis of all phthalates, given that neither the identity nor relative ratio of the phthalates present in a given exposure scenario can be generalized. Therefore, EPA derived an inhalation OEV for the index chemical (DBP), which can then incorporate RPFs to determine whether cumulative exposures result in risk relative to benchmark based on measurement of phthalates in air (Appendix E.2).

Similar to OEVs for individual chemicals, the index chemical (DBP) OEV may be used to support risk management efforts for phthalates under TSCA section 6(a), 15 U.S.C. 2605. TSCA requires risk evaluations to be conducted without consideration of cost and other non-risk factors, and thus this most sensitive OEV represents a risk-only number. If risk management is implemented following the final risk evaluation for any phthalates covered by the cumulative risk analysis TSD, EPA may consider cost and other non-risk factors, such as technological feasibility, the availability of alternatives, and the potential for critical or essential uses. Any existing chemical exposure limit (ECEL) used for occupational safety risk management purposes could differ from the OEVs used in these example calculations based on additional consideration of exposures and non-risk factors consistent with TSCA section 6(c).

The index chemical (DBP) OEV represents the exposure concentration below which exposed workers and occupational non-users are not expected to exhibit any appreciable risk for reduced fetal testicular testosterone, the basis of RPFs across the phthalates. This OEV accounts for PESS. This value is expressed relative to benchmarks and standard occupational scenario assumptions of 8 hours per day, 5 days per week exposures for a total of 250 days exposure per year, and a 40-year working life.

E.1 Occupational Exposure Value for the Index Chemical (DBP)

This section presents the calculations used to estimate a OEV for the index chemical, DBP, using inputs derived in this analysis. For DBP, the index chemical HED used for cumulative risk assessment and application of RPFs is 2.1 mg/kg-day, for reduced fetal testicular testosterone (Section 2.3). Based on average adult body weight of 80 kg and default resting breathing rate of 14.7 m^3/day (0.6125 m^3/hour for 24 hours) (U.S. EPA, 2011a), the inhalation HEC based on route-to-route extrapolation is 11.4 mg/m^3.

Occupational Exposure Value for DBP

The OEV was calculated as the concentration at which the MOE would equal the benchmark MOE of 30 for occupational exposures using Equation_Apx E-1. The OEV was derived based on acute exposures, the most sensitive exposure scenario relevant to reduced fetal testicular testosterone.

Equation_Apx E-1.

$$\mathrm{OEV_{index}(mg/m^3)} = \frac{\mathrm{HEC_{acute}}}{Benchmark\ MOE_{acute}} * \frac{\mathrm{AT_{HECacute}}}{ED} * \frac{\mathrm{IR_{resting}}}{\mathrm{IR_{workers}}} =$$

$$\frac{11.4\ \mathrm{mg/m^3}}{30} * \frac{\frac{24h}{d}}{\frac{8h}{d}} * \frac{0.6125\frac{\mathrm{m^3}}{h}}{1.25\frac{\mathrm{m^3}}{h}} = 0.56\ \mathrm{mg/m^3}$$

$$\mathrm{OEV_{index}}\ (ppm) = \frac{EV\ \frac{\mathrm{mg}}{\mathrm{m^3}} * Molar\ Volume}{MW} = \frac{0.56\ \mathrm{mg/m^3} * 24.45\ \frac{L}{mol}}{278\frac{g}{mol}} = 0.049\ \mathrm{ppm}$$

The parameters used in the above equations are described below.

Where:

$AT_{HECacute}$	=	Averaging time for the POD/HEC used for evaluating non-cancer, acute occupational risk, based on study conditions and/or any HEC adjustments (24 hrs/day)
Benchmark MOE_{acute} =		Acute non-cancer benchmark margin of exposure, based on the total uncertainty factor of 30
OEV_{index}	=	Occupational exposure value based on reduced fetal testicular testosterone
ED	=	Exposure duration (8 hrs/day)
HEC_{acute}	=	Human equivalent concentration for acute occupational exposure scenarios
IR	=	Inhalation rate (default is 1.25 m^3/hr for workers and 0.6125 m^3/hr for the general population at rest)
Molar Volume	=	24.45 L/mol, the volume of a mole of gas at 1 atm and 25 °C
MW	=	Molecular weight of DBP (278.0 g/mole)

E.2 Estimating Inhalation Risk to Air Mixtures using Cumulative and Individual OEVs

As stated above, the index chemical OEV alone cannot be used to summarize risk thresholds for cumulative exposures covering any mixture of phthalates. In EPA's proposed approach, adapted from the OSHA Technical Manual (OTM) - Section II: Chapter 1 | Occupational Safety and Health Administration, concentrations of the individual phthalates are compared to their respective OEV, and the ratios are summed together to determine if the cumulative concentration is greater than one (indicating potential risk). This is presented in the equation below:

$$\mathrm{E}_m = \frac{\mathrm{C}_1}{\mathrm{L}_1} + \frac{\mathrm{C}_2}{\mathrm{L}_2} + \cdots + \frac{\mathrm{C}_n}{\mathrm{L}_n}$$

Where:

E_m is the minimum equivalent exposure for the mixture (E_m should be less than or equal to 1 for compliance);
C_n is the measured concentration of a particular substance;
L_n is the corresponding occupational exposure value for a particular substance in the same units as the concentration.

The OSHA method has a few complications however when applied to the phthalates. First, the health endpoint and POD from the DBP dataset that is the basis of the RPF for comparison across phthalates is not always the most sensitive POD for each phthalate. Therefore, risks must be evaluated both for the individual phthalate OEV and also the cumulative hazard index based on RPFs. The equation above would therefore be applied to the RPF-adjusted OEVs (derived from the OEV_{index} of 0.049 ppm and represented by L_1, L_2 etc. in the above equation). Risk for the most sensitive endpoint would then also be considered independently for each individual phthalate. Individual OEVs for each phthalate are derived based on the most sensitive human health effect relative to benchmarks from their respective risk evaluation and human health hazard assessment.

Another major limitation is that only two phthalates (DEHP and DBP) currently have fully validated air monitoring methods, including OSHA Method 104 for DEHP and DBP and NIOSH Method 5020, which is fully validated for DBP and partially validated for DEHP. Although air monitoring methods for DIBP, BBP, and DCHP have been reported in the peer-reviewed literature (Chi et al., 2017), this approach is currently limited in its application to workplaces only for DEHP and DBP, until validated methods are available for BBP, DIBP, DCHP, and DINP. Additionally, an OEV based only on workplace air concentrations will not be inclusive of non-attributable national (non-occupational) exposure. As a possible alternative approach, urinary biomonitoring of phthalate metabolites in workers is available for all phthalate species and could be inclusive of both occupational and non-workplace exposures to phthalates (depending on whether a baseline/background comparison was implemented). Urinary biomonitoring and reverse dosimetry methods have been previously applied by NIOSH for measuring phthalate intake among workers (Hines et al., 2011).

Urinary biomonitoring is clearly limited in that it does not allow real-time workplace monitoring and could only be implemented either based on a regular schedule or some triggering event/air concentration limit. Baseline measurements would also be required to establish internal dose based on non-attributable national exposures. Despite these limitations this approach could be valuable for being able to measure all phthalate species and being inclusive of aggregate exposures, including non-attributable, non-occupational exposures. EPA will explore the possibility of developing a method for applying the RPF approach to urinary biomonitoring in addition to other alternative approaches.

Appendix F Supporting Analyses for Consumer Exposure to Phthalates

Table_Apx F-1. Sample of Consumer Products Containing Phthalates [f]

Phthalate	Product [a b c]	Manufacturer [d]
BBP	Sakrete Blacktop Repair Tube	Sakrete of North America
	Concrete Patching Compound	Quikrete Companies
	Mortar Repair Sealant	Quikrete Companies
	DAP Roof & Flashing Sealant, Polyurethane	DAP Products, Inc.
	Pre-Mixed Stucco Patch	Quikrete Companies
	Hercules Plumber's Caulk - White/Linen	HCC Holdings Inc.
	Wilsonart Color Matched Caulk	Wilsonart LLC
	Acrylic Caulk	Momentive Performance Materials - Daytona
	Silicone Fortified Window & Door Sealant	Henry Company
	Air Bloc 33	Henry Company
	PSI PolyClay Canes and PSI PolyClay Bricks [e]	Penn State Industries
	Double Bubble Urethane High Peel Strength D50 Part A (04022)	Royal Adhesives & Sealants
	Dymonic FC Anodized Aluminum	Tremco Canadian Sealants [Canada]
	GE7000	Momentive Performance Materials
	Hydrogel SX	Prime Resins Inc.
	Permatite Acrylic Sealant	Permatite / Division of DSI
	Protecto Sealant 25XL	Protecto Wrap Company
	Spectrem 3 Aluminum Stone - 30 CTG	Tremco Canadian Sealants [Canada]
	Spectrem 4	Tremco U.S Sealants
	STP 17925 Power Steering Fluid & Stop Leak	Armored AutoGroup Inc.
	126VR Disc Brake Quiet 0.25 Fl. Oz Pouch	ITW Permatex
	Steri-Crete SL Component A	Dudick, Inc.
	Stonclad UT Resin Polyol	Stonhard, Division of StonCor Group, Inc.
	ENSURE Sterilization Emulator	SciCan Ltd. [Canada]
	Phthalates in Poly(vinyl chloride)	SPEX CertiPrep, LLC
	Elmer's Model + Hobby Cement	Elmers Products, Inc.
	Accent MBRU 6pk Silver Metallic 2oz	Rust-Oleum Corporation
	Champion Sprayon Acrylic Matte Finish	Chase Products Co.
	6840 Ultra Black	BJB Enterprises, Inc.
	Handstamp - Blue	Identity Group
	Repair and Refinishing Spray	Multi-Tech Products Corp.
	Armacell WB Finish	Mon-Eco Industries, Inc.
	Black Tire Paint Concentrate	Akron Paint and Varnish (dba APV Engineered Coatings)

Phthalate	Product [a b c]	Manufacturer [d]
BBP	IC 1-gl 2pk Gray Shop Coat Primer	Rust-Oleum Corporation
	Klean-Strip Mask & Peel Paint Booth Coating	W. M. Barr
	Lacquer Touch-up Paint - Clear Topcoat	Ford Motor Company
	SK Clear-Seal Satin Sealer 5 Gal	Rust-Oleum Corporation
DBP	3M Bondo Glazing & Spot Putty	3M Company
	SureFlex Multi-Purpose Adhesive, SH-360	Barristo Enterprises, Inc. dba SureHold
	Lanco Seal	Lanco Mfg. Corp.
	PSI PolyClay Canes and PSI PolyClay Bricks [e]	Penn State Industries
	Hydrostop Premiumcoat Finish Coat	GAF
	Hydrostop Premiumcoat Foundation Coat	GAF
	Hydrostop Trafficcoat Deck Coating	GAF
	Pro 1-GL 2PK Flat Aluminum Primer	Rust-Oleum Corporation
	DURALAQ-WB WATERBORNE WHITE ACRYLIC FINISH DULL RUBBED	Benjamin Moore & Co.
	Hydrostop Premiumcoat Foundation Coat Summer	GAF
	Bondo Gray Filler Primer	3M Company
	Pettit XL Vivid 1861 Black	Kop-Coat, Inc. / Pettit Marine Paint
	Accurate Solo 1000, Accurate LT-30, Accurate LT-32, Accurate 2015, Accurate 2495, Accurate 4064, Accurate 4350	Western Powders, Inc.
	Cartridge 9 mm FX Marking, Toxfree primer	General Dynamics - Ordnance and Tactical Systems - Canada Inc. [Canada]
	Rimfire Blank Round - Circuit Breaker	Olin Corporation - Winchester Division, Inc.
	Wizard 31 Epoxy Ball Plug Hardener	Brunswick Bowling Products, LLC
DEHP	765-1553 BALKAMP VINYL REPAIR KIT	Permatex, Inc.
	Chocolate	Wellington Fragrance
	PSI PolyClay Canes and PSI PolyClay Bricks[e]	Penn State Industries
	DUPLI-COLOR BED ARMOR	Dupli-Color Products Company
	DUPLI-COLOR High Performance Textured Metallic Coating Charcoal	Dupli-Color Products Company
	264 BLACK TRUCK BED LNR 6UC	The Valspar Corporation
	RED GLAZING PUTTY 1# TUBE	The Valspar Corporation
	Prime WPC/Prime Essentials/Prime SPC	Carlton Hardwood Flooring
	Lenox MetalMax	Lenox Tools
	6.17 OZ 100040 FH FRESH SCENT PET TW 12PK	Fresh House
	KRYLON Fusion All-In-One Textured Galaxy	Krylon Products Group

Phthalate	Product [a b c]	Manufacturer [d]
DEHP	Self-cath pediatric 30 pack	Coloplast Corp.
	3M™ Economy Vinyl Electrical Tape 1400, 1400C	3M
	Pronto Putty	The Valspar Corporation
	Red Glazing Putty 1# Tube	Quest Automotive Products
	BD Loop Goop	Royal Adhesives and Sealants Canada Ltd.
	SCOFIELD® CureSeal 350	Sika Corporation
DCHP	Duco Cement (bottle and tube)1	ITW Consumer - Devcon/Versachem
	Fusor 108B, 109B Metal Bonding ADH PT B	LORD Corporation
DIBP	Blue Label Washable PVA Adhesive	Colorlord Ltd.
	BETAKRIL TEXTURE	Betek Boya ve Kimya Sanayi A.S [Turkey]
	Centerfire Pistol & Revolver and Rifle Cartridges	Companhia Brasileira de Cartuchos (CBC)
	Art Board	Ningbo Zhonghua Paper Co. Ltd.
	Glitter Boards	DJECO
	Painting - Oh, It's Magic	DJECO

[a] This table includes a sample of products listed in the Use Reports for each DBP, BBP, DIBP, DEHP, DCHP (Abt Associates, 2021; U.S. EPA, 2020a, b, c, d, e).
[b] This table may represent updated information with products listed that are not identified in the published Use Reports.
[c] This is not a comprehensive list of products containing each phthalate nor does the presence of a product on this list indicate its availability in the United States for consumer purchase.
[d] Some manufacturers may appear over-represented in this table. This may mean that they are more likely to disclose product ingredients online than other manufacturers, but this does not imply anything about use of the chemical compared to other manufacturers in this sector.
[e] The SDS for PSI PolyClay Canes and PSI PolyClay Bricks, which lists the product as containing multiple phthalates is available here: https://www.pennstateind.com/MSDS/POLYCLAY_MSDS.pdf (accessed December 17, 2025).
[f] Table from *Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the Toxic Substances Control Act* (U.S. EPA, 2023b).