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Draft 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

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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 draft 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)]. These conclusions were supported by the SACC in their final peer-review report to EPA (U.S. EPA, 2023c) and carried forward in this draft cumulative risk assessment TSD.

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. Analytical pieces from this TSD are elaborated 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 RPFs.** Section 2 calculates draft relative potency factors (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. This provides a more robust basis for assessing the dose-response to the shared hazard endpoint across all assessed phthalates. 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 or male children, which can augment specific acute scenarios described further in individual risk evaluations.
- **Examples for Calculating Cumulative Risk**. This TSD also elaborates an example 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. Most notably, an option is elaborated for considering a cumulative occupational exposure value (OEV). The calculated draft value is 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 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 risk evaluations.

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, 2024h), DBP (U.S. EPA, 2024f), DIBP (U.S. EPA, 2024i), BBP (U.S. EPA, 2024e), DCHP (U.S. EPA, 2024g), and DINP (U.S. EPA, 2025p), 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. These conclusions were supported by the SACC in their final peer-review report to EPA (U.S. EPA, 2023c) and carried forward in this draft cumulative risk assessment technical support document.

Sections 1.1 through 1.7 further outline the scope of this draft cumulative risk assessment technical support document.

This draft cumulative risk assessment technical support document is being released for public comment and peer-review by the SACC during the summer of 2025, when EPA will be soliciting feedback on the

implementation of its cumulative risk analysis approach. EPA will not solicit specific feedback on options previously considered by the SACC during its May 2023 peer-review meeting (U.S. EPA, 2023c).

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, 2024h), DBP (U.S. EPA, 2024f), DIBP (U.S. EPA, 2024i), BBP (U.S. EPA, 2024e), DCHP (U.S. EPA, 2024g), and DINP (U.S. EPA, 2025p). 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., 2013; 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., 2020).

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., 2020; Howdeshell et al., 2017; NASEM, 2017; NRC, 2008).

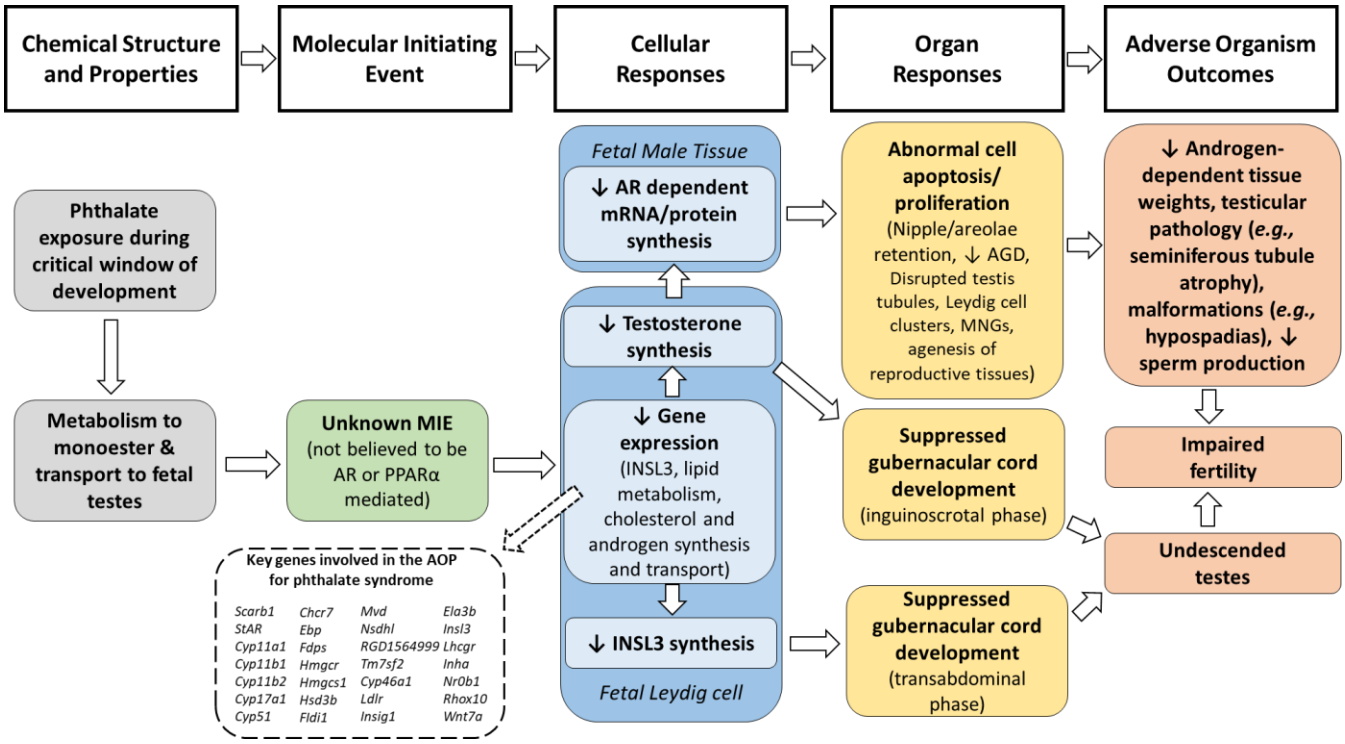


Figure 1-1. Phthalate Syndrome Mode of Action Following Gestational Exposure

Figure adapted from (Conley et al., 2021; Gray et al., 2021; Schwartz et al., 2021; Howdeshell et al., 2017). 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 (ECCC/HC, 2020) recently conducted a CRA of phthalates, which included the six 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. This conclusion was supported by the SACC in its the final peer-review report to EPA (U.S. EPA, 2023c). **Therefore, EPA is including DEHP, BBP, DBP, DCHP, DIBP, and DINP in its draft 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.

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 (*ex vivo* testosterone production via radioimmunoassay) of measurement.

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). Inconsistency in the DINP dataset reduces EPA's confidence in deriving RPFs based on this outcome.
- ***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
- ***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.
- ***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, hypospadias 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.

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 draft RPFs**.

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). **Therefore, 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, 2025p) and draft non-cancer human health hazard assessments for DEHP (U.S. EPA, 2024h), DBP (U.S. EPA, 2024f), BBP (U.S. EPA, 2024e), DIBP (U.S. EPA, 2024i), and DCHP (U.S. EPA, 2024g), 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, 2024q). 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 endorsed 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.

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 (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 5.1 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.

[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))

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.

2 RELATIVE POTENCY FACTORS

This section describes the approach used by EPA to derive draft relative potency factors (RPFs) for the six phthalates (*i.e.*, DEHP, DBP, BBP, DIBP, DCHP, DINP) that EPA is including in its draft 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 draft 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 draft 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 benchmark margin of exposure (benchmark MOE).
- Section 2.6 – Describes the applicability of the draft 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 (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 draft 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 a number of 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 was not included in the 2017 NASEM analysis. This new data was 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) 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 0. Readers are directed to EPA's *Draft 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, 2024d) and *Non-Cancer Human Health Hazard Assessment for Diisononyl Phthalate* (U.S. EPA, 2025p) 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 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, this data was included in EPA's updated analysis.

2.2.1 Results: Benchmark Dose Estimation

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 *Draft 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, 2024d) and *Non-Cancer Human Health Hazard Assessment for Diisononyl Phthalate* (U.S. EPA, 2025p) 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

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 Quadradic	14 [9, 27]	29 [20, 54]	149 [101, 247]
DEHP	Linear Quadradic	17 [11, 31]	35 [24, 63]	178 [122, 284]
DIBP	Linear Quadradic	--[b]	55 [NA, 266][b]	279 [136, 517]
BBP	Linear Quadradic	--[b]	--[b]	284 [150, 481]
DCHP	Linear Quadradic	8.4 [6.0, 14]	17 [12, 29]	90 [63, 151]
DINP	Linear Quadradic	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 draft non-cancer human health hazard assessments of DEHP (U.S. EPA, 2024h) and DBP (U.S. EPA, 2024f), 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 is 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 preliminarily selected DBP as the index chemical.**

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). 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. Using allometric body weight scaling to the three-quarters power (U.S. EPA, 2011b), **EPA extrapolated an 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 draft 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 preliminarily 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.

As discussed by the National Resource Council in 2008 (NRC, 2008), there may be challenges associated with the RPF approach because phthalates 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 their 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). However, EPA's current analysis demonstrates that for reduced fetal testicular testosterone, RPFs do not vary across a range of BMRs (*i.e.*, BMRs of 5, 10, and 40%), which provides confidence in the overall approach.

For input into the draft CRA of phthalates under TSCA, EPA is using RPFs calculated using BMD_{40} estimates 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 percent 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.

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

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.

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, 2025p) and draft non-cancer human health hazard assessments for DEHP (U.S. EPA, 2024h), DBP (U.S. EPA, 2024f), BBP (U.S. EPA, 2024e), DIBP (U.S. EPA, 2024i), and DCHP (U.S. EPA, 2024g), 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 draft 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 draft RPFs are based on reduced fetal testicular testosterone, EPA considers the draft RPFs most directly applicable to pregnant women, women of reproductive age, and male infants. Use of the draft RPFs for other lifestages (*e.g.*, adult males) may be conservative.

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

EPA has preliminary 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 draft 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 proposed index chemical (DBP) POD and the draft RPFs** based on the following weight of the 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 *Draft Non-cancer Human Health Hazard Assessment for Dibutyl Phthalate (DBP)* (U.S. EPA, 2024f), EPA has also preliminarily 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. EPA has robust overall confidence in the proposed POD selected for DBP. Overall, the same weight of evidence considerations apply to the POD selected for the individual DBP risk evaluation and the draft CRA. Readers are directed to the *Draft Non-cancer Human Health Hazard Assessment for Dibutyl Phthalate (DBP)* (U.S. EPA, 2024f) for a complete discussion of the weight of 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 draft 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, 2024d)).
- EPA derived candidate RPFs using BMD_5, BMD_{10}, and BMD_{40} estimates (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 percent 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.

3 SCENARIO-BASED PHTHALATE EXPOSURE AND RISK

This section provides a qualitative analysis of co-exposures expected for consumers, workers, and general population exposed to environmental releases for each individual phthalate under their 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 draft 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 preliminary 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, 2025l), DBP (U.S. EPA, 2025k), BBP (U.S. EPA, 2025j), DIBP (U.S. EPA, 2025m), DCHP (U.S. EPA, 2024c), and DINP (U.S. EPA, 2025o).

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), with the exception of 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 percent by weight fraction). The clay polymer product also has low phthalate concentrations (less than 2.5 percent by weight fraction) and solid physical form, and the material is commonly used in fashioning commercial

[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))

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 *Draft Summary of Facility Release Data for Di(2-ethylhexyl) Phthalate (DEHP), Dibutyl Phthalate (DBP), and Butyl Benzyl Phthalate (BBP)* (U.S. EPA, 2024p).

Overall, EPA identified 1,922 unique facilities that report releases of DEHP, DBP, or BBP to TRI, DMR, and NEI (U.S. EPA, 2024p). 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 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). 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. Instead, EPA has 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, 2025e), DBP (U.S. EPA, 2025c), BBP (U.S. EPA, 2025b), DIBP (U.S. EPA, 2025d), DCHP (U.S. EPA, 2024a), and DINP (U.S. EPA, 2025a). 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]	Ingestion (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 TSCA 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 risk estimates 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.

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 draft technical support documents for each chemical substance: DEHP (U.S. EPA, 2024m), BBP (U.S. EPA, 2024j), DBP (U.S. EPA, 2024k), DIBP (U.S. EPA, 2024n), DCHP (U.S. EPA, 2024l), DINP (U.S. EPA, 2025q). 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, 2024m)	BBP (U.S. EPA, 2024j)	DBP (U.S. EPA, 2024k)	DIBP (U.S. EPA, 2024n)	DCHP (U.S. EPA, 2024l)	DINP (U.S. EPA, 2025q)
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)	1.42×10^{-7}	8.25×10^{-6}	2.01×10^{-5}	4.76×10^{-5}	8.69×10^{-7}	5.40×10^{-7}
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)	1.71×10^{-5}	7.61×10^{-7}	1.81×10^{-6}	1.83×10^{-7}	9.446×10^{-8}	9.14×10^{-5}
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 Persistance	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 *Draft Summary of Facility Release Data for Di(2-ethylhexyl) Phthalate (DEHP), Dibutyl Phthalate (DBP), and Butyl Benzyl Phthalate (BBP)* (U.S. EPA, 2024p). 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)

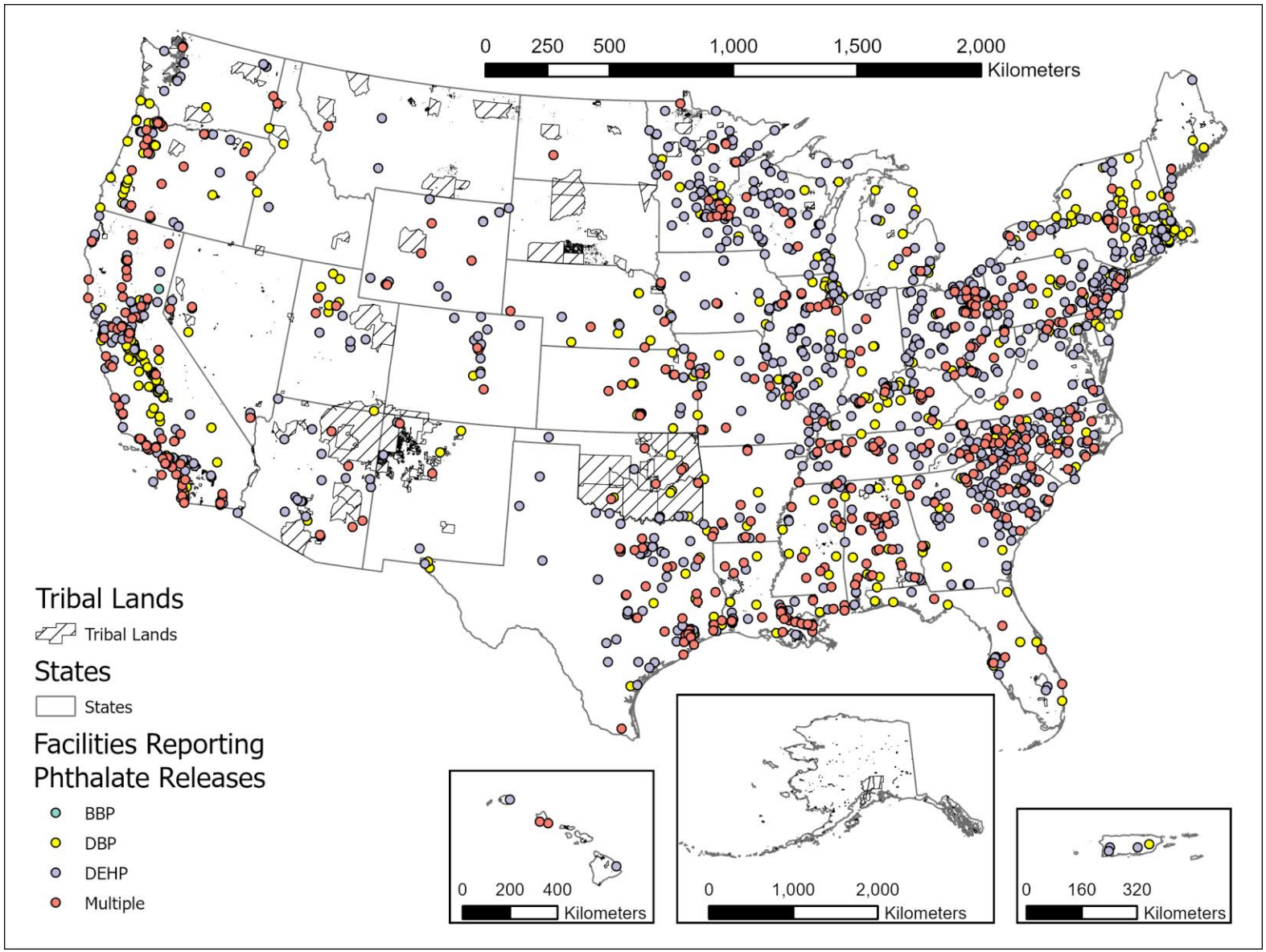
- 020301040205 in Hudson County, NJ and Kings County, NY (4 facilities)
- 020402010407 in Burlington County, NJ and Bucks County, PA (4 facilities)
- 020200041108 in Schenectady County, NY (4 facilities)

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.

1403



1404
1405 **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 modelled screening estimates without more refined exposure models or monitoring data.

3.4 Non-TSCA Exposure to Diet

Non-TSCA exposures to a combination of phthalates may occur through diet which includes the consumption of phthalates from food packaging. Using a scenario-based approach, U.S. Consumer Product Safety Commission (CPSC) found the majority of women's exposure to DEHP, DINP, and DIBP was from diet (DCHP was not included in their analysis). 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 (ECCC/HC, 2020). For their estimation of dietary intake of DIBP, BBP, DBP, and DEHP, Health Canada used the 2013 Canadian Total Diet Study (ECCC/HC, 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 (ECCC/HC, 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 (ECCC/HC, 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.

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. However, 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 percent 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, 2025h), DBP (U.S. EPA, 2025g), BBP (U.S. EPA, 2025f), DIBP (U.S. EPA, 2025i), DINP (U.S. EPA, 2025n), and DCHP (U.S. EPA, 2024b).

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%

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 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 (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 is not readily publicly available (https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/SSPHTE_H.htm). 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 (ECCC/HC, 2020). Consistent with EPA's decision to focus its draft 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; NCHS, 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 risk estimates 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.2. 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 (see Appendix C.2.4 for further details). However, urinary MHiBP data is 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 (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).

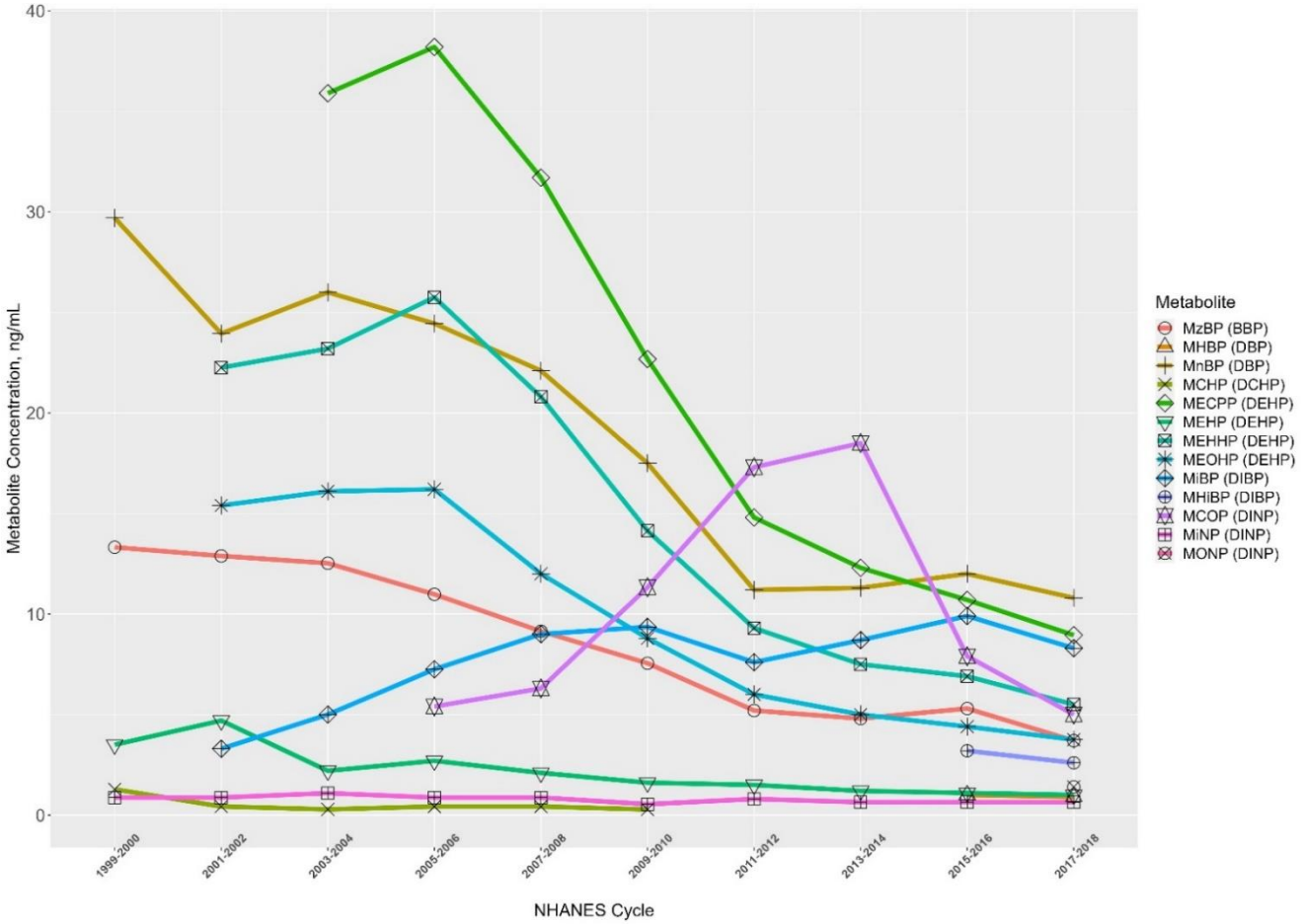


Figure 4-1. Median Phthalate Metabolite Concentrations Over Time for All NHANES Participants From 1999 Through 2018

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 is 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 or not 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 (ECCC/HC, 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, 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**. <u>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</u>**.

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. **<u>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</u>**.

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 preliminarily 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 the 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. 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]
		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] 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/kd-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.

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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]
		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] 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/kd-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.

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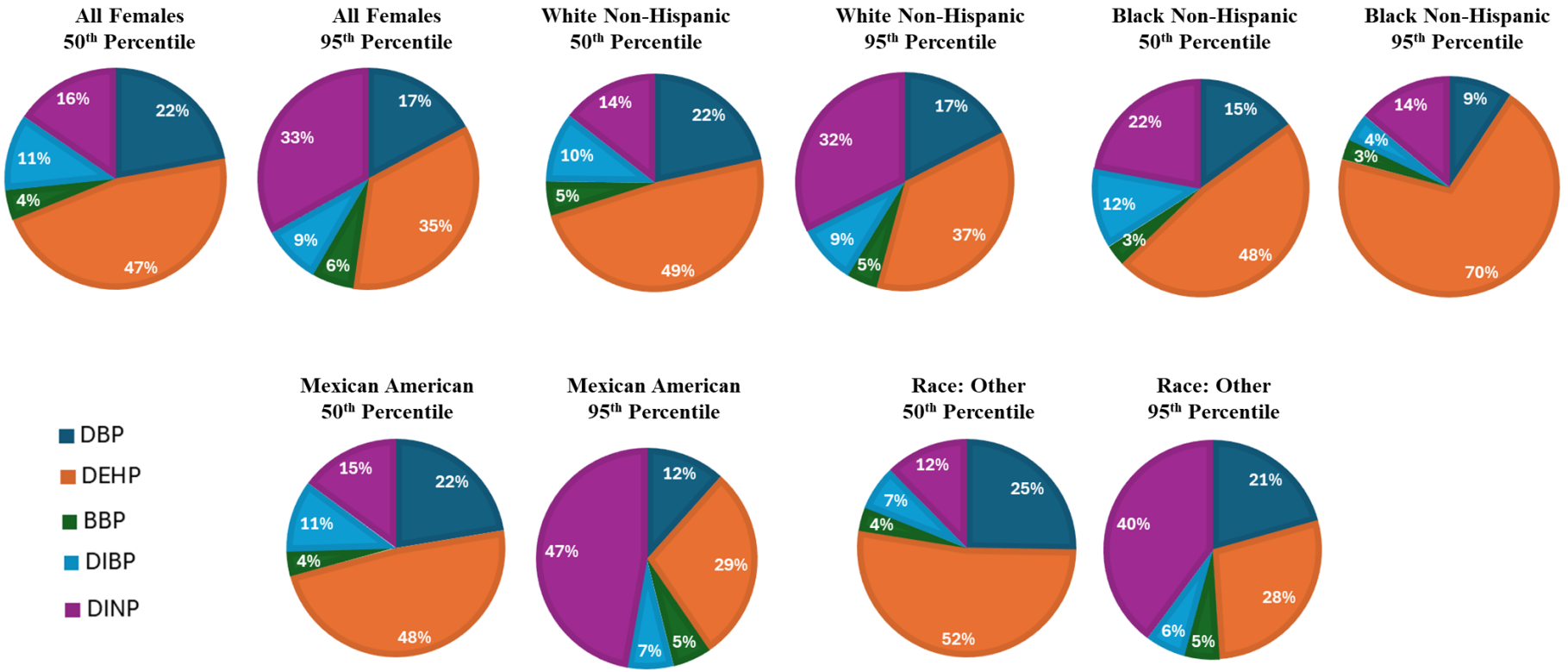

Figure 4-2. Percent Contribution to Cumulative Exposure for DEHP, DBP, BBP, DIBP, and DINP for Women of Reproductive Age (16 to 49 years) in 2017-2018 NHANES, Stratified by Race

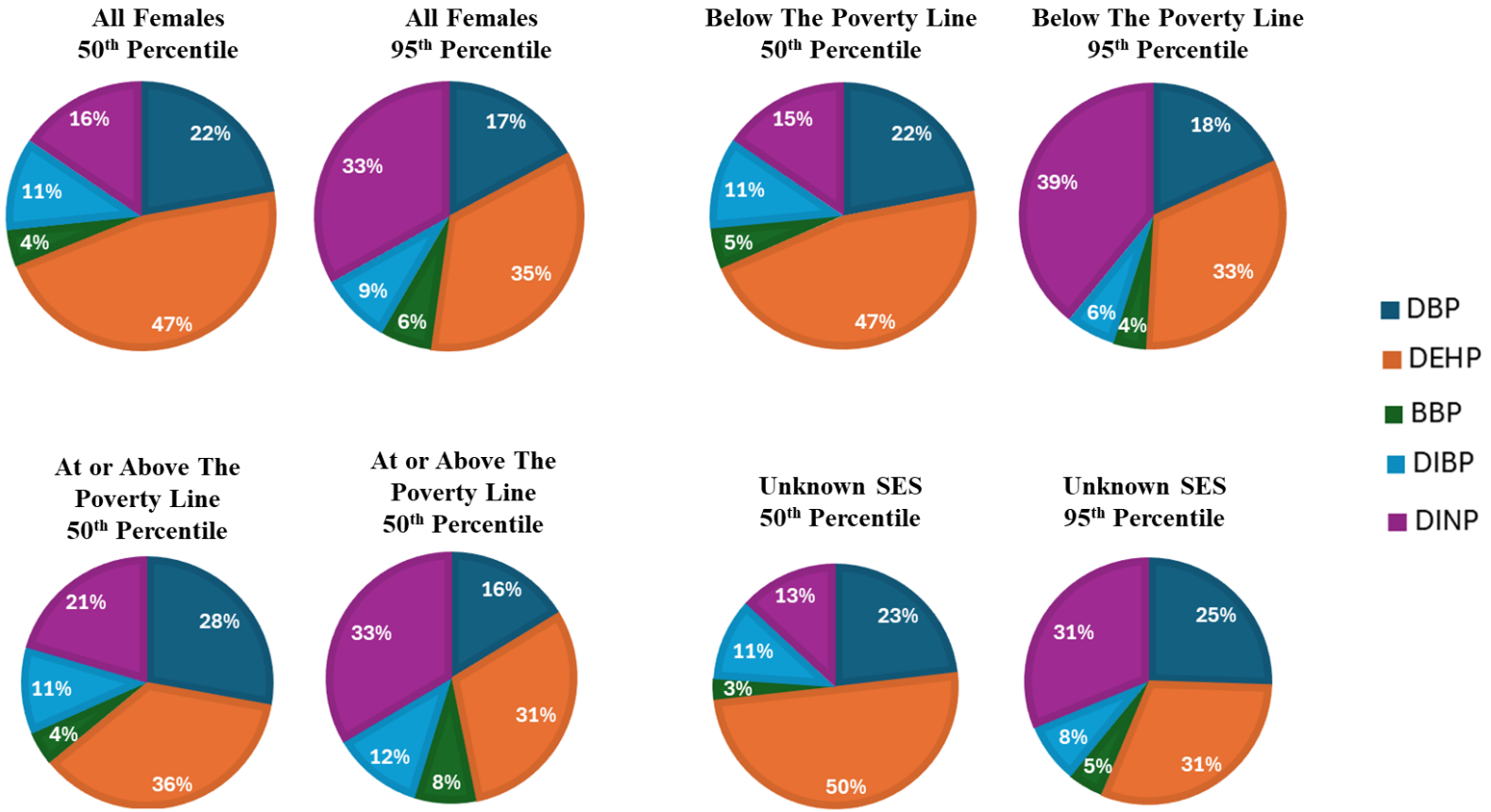

Figure 4-3. Percent Contribution to Cumulative Exposure for DEHP, DBP, BBP, DIBP, and DINP for Women of Reproductive Age (16 to 49 years) in 2017-2018 NHANES, Stratified by Socioeconomic Status

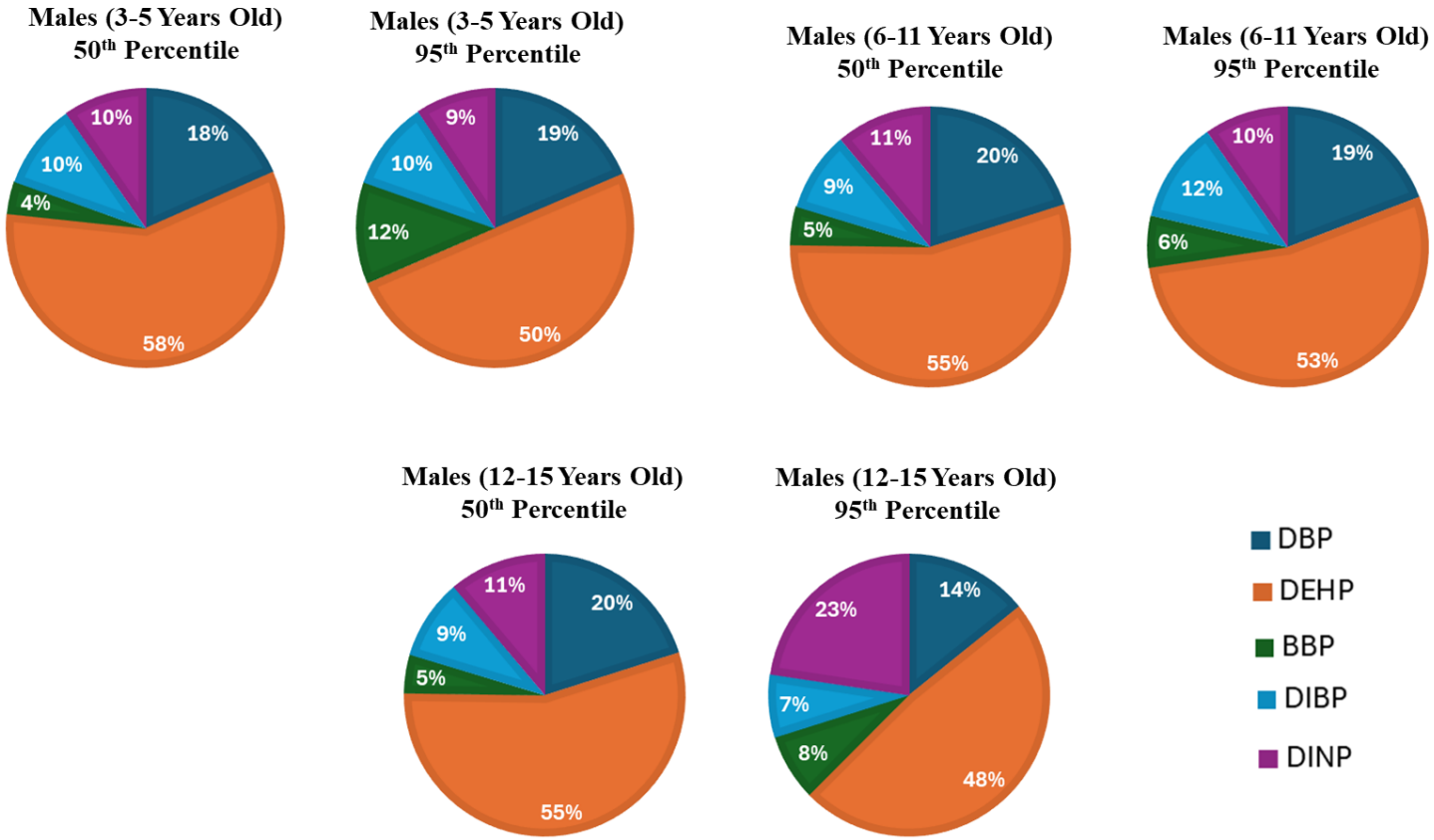

Figure 4-4. Percent Contribution to Cumulative Exposure for DEHP, DBP, BBP, DIBP, and DINP for Male Children Ages 3 to 5, 6 to 11, and 12 to 15 years in 2017–2018 NHANES

5 CONCLUSION AND NEXT STEPS

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 (scaled by relative potency and expressed in index chemical (DBP) equivalents), the relevant non-attributable cumulative exposures, and the non-TSCA 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 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 risk estimates are estimated using the draft 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.

Section 5.1 describes 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. This quantitative approach will be used in each of the individual relevant phthalate risk evaluations. Section 5.2 discusses the anticipated impact that this cumulative approach will have for each of the phthalates being evaluated under TSCA.

5.1 Estimation of Cumulative Risk

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 to estimate cumulative risk. Cumulative risk was estimated using the four-step process outlined below, along with one empirical example of how EPA calculated cumulative risk for one occupational OES for DCHP (*i.e.*, Application of Paints and Coatings (Solids)).

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: 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, 2024o). 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.

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

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

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

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 (Section 2.3).
- $Exposure_1$ is the exposure estimate in DBP equivalents for the pathway of interest (*i.e.,* from step 1 or 2 above).

Example: 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.

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

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

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

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: 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:

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

5.2 Anticipated Impact of the Cumulative Analysis on Phthalates being Evaluated Under TSCA

The cumulative analysis approach outlined in Section 5.1 is being used by EPA to supplement the individual phthalate risk evaluations. The cumulative analysis approach 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 5-1 and is discussed further in Section 5.2.1 through Section 5.2.6.

5.2.1 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 1.1x more sensitive than in the individual DBP risk evaluation (Table 5-1). This preliminary 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, 2024e) and as the index chemical POD for use in the CRA (Section 2.3), 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 5-2). This is the only factor that will contribute to the slightly more sensitive cumulative risk estimates for DBP.

5.2.2 Dicyclohexyl Phthalate (DCHP)

Application of the cumulative analysis outlined in Section 5.1 will lead to risk estimates that are approximately 2x to 2.2x more sensitive (Table 5-1). This preliminary 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 (Section 2.3), while the acute POD for DCHP used to calculate MOEs in the individual DCHP risk evaluation is 2.4 mg/kg (U.S. EPA, 2024g). The index chemical (DBP) POD is 12.5 percent 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 5-2) and will contribute to the more sensitive risk estimates.

5.2.3 Diisobutyl Phthalate (DIBP)

Application of the cumulative analysis outlined in Section 5.1 will lead to risk estimates that are approximately 1.5x to 1.7x more sensitive (Table 5-1). This preliminary 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 (Section 2.3), while the acute POD for DIBP used to calculate MOEs in the individual DIBP risk evaluation is 5.7 mg/kg (U.S. EPA, 2024i). 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 5-2) and will contribute to the more sensitive risk estimates.

5.2.4 Butyl Benzyl Phthalate (BBP)

Application of the cumulative analysis outlined in Section 5.1 will lead to risk estimates that are approximately 3.2x to 3.5x more sensitive (Table 5-1). This preliminary 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 (Section 2.3), while the acute POD for BBP used to calculate MOEs in the individual BBP risk evaluation is 12 mg/kg. 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 5-2) and will contribute to the more sensitive risk estimates.

5.2.5 Diisononyl Phthalate (DINP)

Application of the cumulative analysis outlined in Section 5.1 will lead to risk estimates that are approximately 1.3x to 1.4x more sensitive (Table 5-1). This preliminary 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 (Section 2.3), while the acute POD for DINP used to calculate MOEs in the individual DINP risk evaluation is 12 mg/kg. 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.
- ***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 5-2) and will contribute to the more sensitive risk estimates.

5.2.6 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 5-1). 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 preliminary 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 (Section 2.3), while the acute POD for DEHP used to calculate MOEs in the individual DEHP risk evaluation is 1.1 mg/kg. 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.
- ***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 5-2) and will contribute to the more sensitive risk estimates.

Table 5-1. Summary of Impact of Cumulative Assessment on Phthalates Being Evaluated Under TSCA

Phthalate	Individual Phthalate Assessment			Cumulative Analysis			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	Risk estimates will be ~1.1x more sensitive
DEHP	1.1	NOAEL (Phthalate syndrome-related effects)	30	0.84			Individual chemical assessment will be more sensitive based on slightly different endpoint
BBP	12	NOAEL (Phthalate syndrome-related effects)	30	0.52			Risk estimates will be ~3.2x to 3.5x more sensitive
DIBP	5.7	$BMDL_5$ (↓ fetal testicular testosterone)	30	0.53			Risk estimates will be ~1.5x to 1.7x more sensitive
DCHP	2.4	NOAEL (Phthalate syndrome-related effects)	30	1.66			Risk estimates will be ~2x to 2.2x more sensitive
DINP	12	$BMDL_5$ (↓ fetal testicular testosterone)	30	0.21			Risk estimates will be ~1.3x to 1.4x more sensitive

Table 5-2. 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)			

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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[a]

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 testosterone production (3-hour incubation) on GD 18 (Furr et al., 2014)	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**
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)	-

[a] Asterisk (*) 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.

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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)

[a] Asterisk (*) 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.

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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, 2024d). 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, 2024q). 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, 2024d).

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 modelled 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 *Draft 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, 2024d).

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 3x (for BBP) to 25.4x (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 5x ($BMDL_{10}$ 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 2.4x ($BMDL_{10}$ 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 preliminary conclusion that a BMR of 5 percent is the most appropriate 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 5x and is greater than the lowest LOAEL identified for apical outcomes on the developing male reproductive system by 2.4x. 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 3x to 25.4x (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, 2024h)
DBP	$BMDL_5$ = 9 (↓ fetal testicular testosterone)	30 (↑ Testicular Pathology)	14 [9, 27]	29 [20, 54]	149 [101, 247]	(U.S. EPA, 2024f)
DIBP	$BMDL_5$ = 24 (↓ fetal testicular testosterone)	125 (↑ Testicular Pathology)	–[b]	55 [NA, 266][b]	279 [136, 517]	(U.S. EPA, 2024i)
BBP	NOAEL = 50 (phthalate syndrome-related effects)	100 (↓ AGD)	–[b]	–[b]	284 [150, 481]	(U.S. EPA, 2024e)
DCHP	NOAEL = 10 (phthalate syndrome-related effects)	20 (↑ Testicular Pathology)	8.4 [6.0, 14]	17 [12, 29]	90 [63, 151]	(U.S. EPA, 2024g)
DINP	$BMDL_5$ = 49 (↓ fetal testicular testosterone)	600 (↓ sperm motility)	74 [47, 158]	152 [97, 278]	699 [539, 858]	(U.S. EPA, 2025p)

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; POD = point of departure; RTM = reproductive tract malformations

[a] The linear-quadratic model provided the best fit (based on lowest 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 2005–2006 cycle of NHANES, all participants between 3-5 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 on 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/Nhanes/2013-2014/SSPHTE_H.htm). 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. Limits of detection (LOD) for each cycle on 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=2762) 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. Limits of detection (LOD) for each cycle on 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=2762) 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/Nhanes/2013-2014/SSPHTE_H.htm). 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. 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, 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. Limits of detection (LOD) for each cycle on 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 age 15 and under and 11,699 adults age 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. Limits of detection (LOD) for each cycle on 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 *Draft Environmental Media, General Population, and Environmental Exposure for Dicyclohexyl Phthalate (DCHP)* (U.S. EPA, 2024b)).

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=2762)	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%	–	–

Parent Phthalate	Urinary Metabolite	Percentage Below the Limit of Detection		
		2017–2018 NHANES (All Participants; N=2762)	2017–2018 NHANES (Women Aged 16–49; N=470)	2017–2018 NHANES (Children Aged 6–17; N=866)
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 DCHP 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 *Draft Environmental Media and General Population and Environmental Exposure for Diethylhexyl Phthalate (DEHP)* (U.S. EPA, 2025h). **Overall, 50th and 95th percentile urinary MEHP, MEHPP, MEOHP and MEOCP concentrations have significantly decreased over time (1999–2018) for all lifestages.**

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 *Draft Environmental Media and General Population and Environmental Exposure for Dibutyl Phthalate (DBP)* (U.S. EPA, 2025g). **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.

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 *Draft Environmental Media and General Population and Environment Exposure for Butyl benzyl phthalate (BBP)* (U.S. EPA, 2025f). **Overall, 50th and 95th percentile urinary MBzP concentrations significantly decreased over time (1999–2018) for all lifestages.**

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 *Draft Environmental Media and General Population and Environmental Exposure for Diisobutyl phthalate (DIBP)* (U.S. EPA, 2025i). **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.**

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 *Draft Environmental Media and General Population Screening for Diisononyl Phthalate (DINP)* (U.S. EPA, 2025n). For MONP, no temporal trends analysis was conducted because MONP has only been measured in the most recent NHANES survey (2017 to 2018).

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 MiNP 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 (ECCC/HC, 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 (µg/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 bodyweight 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 (ECCC/HC, 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	0.69	(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;

Dependent	Source	DF	SS	MS	F Value	ProbF
[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 (ECCC/HC, 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 (ECCC/HC, 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 (U.S. 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 (ECCC/HC, 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 (U.S. 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 is 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 or not 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 or not 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 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.

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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			

Use	Conditions of Use	DBP	BBP	DEHP	DCHP	DIBP	DINP
	Electrical and electronic products			X			X
	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.

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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, 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 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 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 draft 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.

Draft Occupational Exposure Value for DBP

The draft OEV was calculated as the concentration at which the MOE would equal the benchmark MOE 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.

$$\mathrm{OEV_{index}} = \frac{\mathrm{HEC_{acute}}}{Benchmark\ MOE_{acute}} * \frac{\mathrm{AT_{HECacute}}}{ED} * \frac{\mathrm{IR_{resting}}}{\mathrm{IR_{workers}}} =$$

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

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

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 (24hrs/day)
Benchmark MOE_{acute}	=	Acute non-cancer benchmark margin of exposure, based on the total uncertainty factor of 30
OEV_{index}	=	Draft occupational exposure value based on reduced fetal testicular testosterone
ED	=	Exposure duration (8 hrs/day)
HEC_{acute}	=	Human equivalent concentration for acute, intermediate, or chronic 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 1 (indicating potential risk). This is presented in the equation below:

$$E_m = \frac{C_1}{L_1} + \frac{C_2}{L_2} + \cdots + \frac{C_n}{L_n}$$

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 therefore 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. Draft methods may be shared alongside future phthalate risk evaluations. EPA welcomes feedback for these and any other potential 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

Phthalate	Product [a b c]	Manufacturer [d]
	KRYLON Fusion All-In-One Textured Galaxy	Krylon Products Group
	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)
DIBP	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 (U.S. EPA, 2021, 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.
[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).

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