July 25, 2025

Dr. Alaa Kamel, Designated Federal Officer
Mission Support Division (7602M), Office of Program Support
Office of Chemical Safety and Pollution Prevention
Environmental Protection Agency

Submitted via: regulations.gov

RE: Science Advisory Committee on Chemicals (SACC) Peer Review; High-Priority Phthalates; Draft Risk Evaluations and Technical Support Documents; Notice of SACC Meeting; Availability of Draft Documents and Request for Comment
Docket No. EPA-HQ-OPPT-2024-0551

Dear Dr. Kamel,

On behalf of the American Chemistry Council High Phthalates Panel, I submit the attached comments on two draft cross-cutting documents for the cumulative risk assessment of high-priority phthalates and a manufacturer-requested phthalate under the Toxic Substances Control Act.

We request that these comments be considered by the Science Advisory Committee on Chemicals (SACC) for its upcoming peer review.

For any questions, please contact Eileen Conneely at 202-249-6711 or eileen_conneely@americanchemistry.com.

Sincerely,

Eileen Conneely

Eileen Conneely
Senior Director, Chemical Products & Technology
American Chemistry Council

American Chemistry Council High Phthalates Panel

Comments Related to Two Draft Cross-Cutting Documents for the Cumulative Risk Assessment of Six Phthalates

Executive Summary

The High Phthalates Panel of the American Chemistry Council (ACC) appreciates the opportunity to provide these comments to be considered during the upcoming August 4 – 8, 2025 public meeting as a part of the Science Advisory Committee on Chemicals' (SACC) peer review of Draft Risk Evaluations and Technical Support Documents for Phthalates. The comments herein address the EPA's approach to evaluation of the cumulative risk of the six phthalates and have been structured to respond to specific EPA Charge Questions to the SACC with relevance to the draft phthalates cumulative risk assessment (CRA). *Comments herein are limited to aspects related to the phthalates CRA meta-analysis modeling methods and selection of the index chemical; previously submitted comments have addressed other aspects of the CRA (ACC, 2025).*

The purpose of these comments is to provide feedback on the current draft CRA documentation and methods (whether the conduct of a CRA is appropriate for this set of phthalates is not in scope). **A summary of the key points, corresponding to SACC Charge Questions 5f, 5g, 9, 10 and 11 is provided Table ES-1**, and generally involve clarification and improvement in documentation and methods related to:

(1) Demonstration that the current draft meta-analysis modeling method is inconsistent with the state-of-the science and is not responsive to previous SACC comments regarding how the EPA will accommodate the mathematical aspects related to dose-response modeling and parallelism (US EPA, 2023b). The result of using the methods currently employed by EPA (versus methods that appropriately account for dose-response issues in assessing relative potency) is both an under- and over-estimation of risk. More appropriate, state-of-the-science modeling approaches are available and should be considered.

(2) The repeated use of assumptions that are not data-driven (particularly those related to exposure), results in an overly conservative approach that is more consistent with a screening-level risk assessment.

(3) Commentary and insights regarding the overall CRA process under TSCA are also provided.

Table ES-1: Summary of the key points in comments provided herein, organized by SACC charge questions.

SACC Charge Question	Summary of Key Points in Comment Document	Comment Document Section
5f. In the *Draft Meta-analysis and Benchmark Dose Modeling of Fetal Testicular Testosterone for DEHP, DBP, BBP, DIBP, and DCHP*, EPA conducted an updated meta-analysis and BMD modeling analysis of decreased fetal testicular testosterone in rats. The analysis represents an update of the analysis conducted by NASEM in 2017. As part of EPA's updated analysis, EPA conducted modeling using Metafor Version 2.0.0 (version originally used by NASEM in 2017) and Version 4.6.0 (most recent version available at the time of EPA's updated analysis); evaluated benchmark response (BMRs) of 5, 10, and 40 percent (NASEM evaluated BMRs of 5 and 40 percent); and included newly identified fetal testicular testosterone data. Overall, EPA selected BMD modeling results obtained using Metafor Version 4.6.0 for use in the single phthalate risk evaluations and phthalate cumulative risk assessment because these results were obtained using the most up-to-date version of the Metafor package available at the time of the updated meta-analysis and BMD modeling analysis. Please comment on the strengths and uncertainties associated with the methods and data used in the updated analysis. In your response, please comment on EPA's preliminary decision to use model results obtained using Metafor Version 4.6.0 vs. Version 2.0.0.	1. **The Charge Question does not address the inadequacies of Metafor when modeling these data**. While the Metafor version 4.6.0 should be superior to version 2.0.0, based on new features and bug fixes, the new version does not address inadequacies for assessing these data. **2. The phrasing of the Charge Question ignores concepts important in previous SACC reviews and the NASEM report – issues of the parallelism of the dose-response between the six phthalates – key concepts critical to developing RPFs that SACC and NASEM repeatedly issued.** *3.* EPA relies on Metafor in the CRA because NASEM (2017) utilized this approach; however, since that time, **science has made substantial advances and improved, and more appropriate modeling options are now available to describe heterogeneity demonstrated with the phthalates**. The R package Metafor was used by NASEM in 2017 because it was simple to implement and it could readily account for random effects and intra-study heterogeneity in the background response; as a result it was used to demonstrate the concepts in CRA of phthalates – *not to serve as the basis for regulatory decision-making.* 4. **Metafor does not allow for addressing heterogeneity in dose response (i.e., issues with parallelism, etc.),** which is necessary when appropriately evaluating potency. 5. **Metaphor does not let you evaluate the issue of parallelism using the Hill model, the standard methodology; this results both in under- and over-estimation of risk for each phthalate.** Furthermore, it does not allow for the modeling of sigmoidal dose-response curves, which is critical for RPF derivation. If the dose response is sigmoidal-shaped, the risk will be overestimated with the linear models used in Metaphor. In the case of sharp responses (e.g., one-hit models and the Michaelis-Menten model), the risk will be underestimated. 6. **Independent Bayesian Hierarchical Modeling (BHM) consistent with the state-of-the-science demonstrates that the dose-response data are not parallel for the six phthalates considered**. This modeling shows that using the BMD_{40} from the estimated dose-response curves to calculate RPFs leads to over- and underestimation of the risks for each phthalate. The Metafor software – regardless of version – does not allow for the assessment of this important aspect.	**1**

	7. **The previous SACC comments stated, "*the committee requested clarification from the EPA regarding how they will accommodate the mathematical aspects related to dose-response modeling*." In the current draft document, EPA has failed to clarify the mathematical aspects as requested by the previous SACC**. Previous comments submitted to the EPA on this topic have addressed the lack of consideration for these critical mathematical aspects. Herein, an alternative approach consistent with the state-of-the-science (i.e., the BHM), along with its mathematical details, is presented that challenges EPA's results. This approach involves modeling that addresses the lack of parallelism and accounts for inter-study heterogeneity.	
5g. In Section 4.3 of the *Draft Non-Cancer Human Health Hazard Assessment for DBP*, EPA has preliminarily selected an HED of 2.1 mg/kg-day (BMDL5 of 9 mg/kg-day) based on decreased fetal testicular testosterone for assessing risks from acute, intermediate, and chronic duration exposure to DBP. The BMDL5 that serves as the basis of the HED was derived through meta-analysis and benchmark dose modeling of fetal testicular testosterone data from eight studies of DBP with rats (Gray et al. 2021; Furr et al. 2014; Johnson et al. 2011; Struve et al. 2009; Howdeshell et al. 2008; Martino-Andrade et al. 2008; Johnson et al. 2007; Kuhl et al. 2007). Please comment on the strengths and uncertainties in the selected acute/intermediate/chronic HED for DBP. **9.** In Section 2.3 of the *Revised Draft Technical Support Document for the Cumulative Risk Analysis of DEHP, DBP, BBP, DIBP, DCHP, and DINP Under the Toxic Substances Control Act (TSCA)*, EPA preliminarily selected DBP to serve 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; is well characterized for the MOA	1. As noted in previous comments (ACC, 2025) and emphasized herein, **EPA has not transparently or sufficiently described its evidence identification process. Thus, the data selection and toxicity value derivation process cannot be reproduced in full.** The inability to do such prevents a robust recommendation related to the derived $BMDL_5$, resulting HED, and selection of DBP to serve as the index chemical. 2. Transparent and consistent data selection is essential to ensure that index chemicals are truly representative of their chemical group and are suitable for dose-response modeling. EPA's current approach to data selection suggests inconsistencies that undermine this tenet of CRA. **Re-evaluation of the meta-analysis inputs and critical appraisal process is warranted, supported by clear documentation of criteria and consistent application of such.** **3.** EPA has not adequately justified inclusions or exclusions of studies in its DBP meta-analysis; as a result, there is not a clear or reproducible approach to selecting studies upon which to derive and RPF. Thus, **it's likely that the derived RPFs do not reflect the full body of available evidence.** 4. **Study quality concerns appear to be selectively applied, with some datasets excluded for design limitations while others with more serious data transparency issues are retained and assigned high confidence**.	**2**

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. Please comment on the strengths and uncertainties of the selection of DBP as the index chemical.		
10. As described in Section 2.4 of the *Revised Draft Technical Support Document for the Cumulative Risk Analysis of DEHP, DBP, BBP, DIBP, DCHP, and DINP Under the Toxic Substances Control Act (TSCA)*, for input into the draft CRA of phthalates under TSCA, EPA has preliminarily selected relative potency factors (RPFs) calculated using BMD40 estimates based on reduced fetal testicular testosterone content and/or production. Please comment on the strengths and uncertainties of the derived RPFs.	1. BMD_{40} values are derived from the portions of the dose-response curves that are not parallel; therefore, **use of the BMD_{40} to calculate RFPs results in both over and underestimations of risk**. 2. Modeling with Metafor does not allow the evaluation of differences in slope (i.e., lack of parallelism) between dose-response curves; **independent analyses demonstrate the lack of parallelism** in the dose-response curves between the six phthalates herein. 3. **EPA needs to reconsider use of a modeling approach that is consistent with the state of the science and previous SACC recommendations** before using the BMD40 values to calculate RPFs.	**3**
11. In Section 5 of the *Revised Draft Technical Support Document for the Cumulative Risk Analysis of DEHP, DBP, BBP, DIBP, DCHP, and DINP Under the Toxic Substances Control Act (TSCA)A*, EPA describes two options for characterizing cumulative risk from exposure to phthalates under TSCA. Option 1 involves scaling each individual exposure by relative potency using RPFs to express all phthalate exposures in terms of index chemical (DBP) equivalents and then combining exposures from individual consumer or worker COUs/OES with non-attributable cumulative exposures estimated from NHANES biomonitoring data to estimate cumulative risk (Section 5.1). For Option 2, phthalate exposures from individual consumer and occupational COUs are not scaled by relative potency using RPFs but instead use the individual phthalate POD	1. **Screening-level exposure estimates used as inputs for Options 1 and 2 are inappropriate for definitive risk determinations.** EPA's reliance on worst-case exposure assumptions for the individual chemicals (e.g., maximum concentrations, simultaneous dermal and inhalation exposure, highest-use scenarios) combined with assumed co-exposure to all chemicals at maximum levels, may produce unrealistic exposure estimates. While this screening approach is useful to identify COUs that do not present unreasonable risk, it is not informative when potential risk is indicated due to the compounded conservativism of the assumptions. 2. **Neither Option 1 nor Option 2 presented by EPA adequately characterizes the cumulative risk given inherent issues with the meta-analysis modeling.** Because the dose-response curves are not parallel, estimating the RPFs with the BMD_{40} values from the areas of the curve that are not parallel mischaracterizes the potency of each phthalate using Option 1. 3. Option 2 presented by the EPA yields substantially different MOEs from Option 1 because it utilizes PODs from various endpoints. Thus, Option 2 is not directly relatable to risk from	**4**

to estimate risk, which is then combined with non-attributable cumulative exposure and risk estimated using NHANES (Section 5.2). Please comment on the strengths and uncertainties of Option 1. Please comment on the strengths and uncertainties of Option 2.	a specific outcome, and the impact on risk findings is challenging to categorize because it depends on the determination of the most sensitive endpoint per phthalate. **4. Using the state of the science BHM approach results in qualitatively similar MOEs following Option 1 and Option 2.**	
12. The *Draft Risk Evaluations* of DBP, DCHP, and DEHP contain three examples of the application of Phthalates Cumulative Risk Assessment (CRA) within an individual chemical risk evaluation. Please comment on the integration of the CRA approaches within the single chemical evaluations.	1. TSCA's statutory framework is structured around single-chemical evaluations, limiting the effective integration of CRA. Moreover, TSCA requires risk management of a chemical's specific conditions of use only to the extent necessary to address unreasonable risk. As a result, the utility of CRA within single-substance risk evaluations is significantly constrained. 2. The current CRA approach produces inconsistent and non-intuitive outcomes-such as directionally different impacts on the MOEs for DCHP and DEHP-that are difficult for risk managers to interpret. It also lacks clarity on which chemicals meaningfully contribute to cumulative risk under specific conditions of use, making it challenging for risk managers to simulate or evaluate the impact of potential regulatory actions. 3. To enhance CRA's utility in risk management, **EPA should move beyond single-substance integration and develop a risk communication tool that synthesizes CRA findings**, clarifies assumptions and uncertainties, and identifies chemical contributions to cumulative risk. This would help translate complex assessments into actionable insights for risk managers.	**5**

Background: Comments herein are limited to aspects related to the phthalates CRA meta-analysis modeling methods and selection of the index chemical; previously submitted comments have addressed other aspects of the CRA.

The High Phthalates Panel of the American Chemistry Council (ACC) appreciates the opportunity to provide these comments regarding cross-cutting documents developed for the U.S. Environmental Protection Agency's (EPA) draft cumulative risk assessment (CRA) of six select phthalates under the Toxic Substances Control Act (TSCA). Specifically, ACC is providing these comments for consideration by the Science Advisory Committee on Chemicals (SACC) for a select subset of the charge questions to be considered during the upcoming August 4 – 8, 2025 public meeting as a part of SACC's peer review of Draft Risk Evaluations and Technical Support Documents for Phthalates. The comments herein address the EPA's approach to evaluation of the cumulative risk of the six phthalates and have been structured to respond to specific EPA Charge Questions to the SACC with relevance to the draft phthalates CRA.

EPA is conducting a CRA of six ortho-phthalates (herein referred to as "phthalates") under TSCA: di(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), butyl benzyl phthalate (BBP), diisobutyl phthalate (DIBP), dicyclohexyl phthalate (DCHP), and diisononyl phthalate (DINP). EPA is seeking public comments on the draft risk evaluations (or portion of the draft risk evaluations) for five of these phthalates[1], and the cross-cutting documents related to the CRA for all six phthalates. The cross-cutting documents include:

- *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)* (referred to herein as "Draft TSD"; revised in June 2025)
- *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)* (referred to herein as "Draft Meta-analysis"; released in January 2025)

These comments are an extension of comments previously submitted to the DCHP docket (EPA-HQ-OPPT-2018-0504), specifically expanding upon aspects related to dose response modeling and relative potency factor (RPF) derivation and selection of the index chemical and its point of departure (POD) (ACC, 2025). Those comments also address

[1] Draft risk evaluations for DBP, DEHP, and DCHP; select draft technical support documents for DIBP and BBP.

other key aspects critical to the integrity of the CRA that need to be addressed, but which are not covered or not covered at length in this comment document, including:

- Procedural issues identified in the order of release of individual phthalate and cross-cutting phthalate documents
- Lack of cohesion and clarity across the Draft TSD, Draft Meta-analysis, and supporting documents posted to individual phthalate dockets
- Failure to sufficiently document and transparently describe the data identification process
- Lack of transparency in inclusion criteria and modeling choices and seemingly inconsistent exclusion of data from the meta-analysis within and across phthalates
- Insufficient documentation of the critical appraisal of studies and the impact of study reliability on meta-analysis modeling
- Failure to address certain key elements identified by the SACC in implementing an RPF approach, including toxicokinetic differences between phthalates, and differences in study reliability and data quality.
    - Key elements expanded upon the comments herein include
        - Dose-response issues, including lack of parallelism
        - Failure to account for the variability and uncertainty in the RPFs that arise from use of heterogenous datasets
- Lack of modeling multiple endpoints in multiple life stages
- Little to no qualitative and semi-quantitative assessment of uncertainty in the in CRA assessment
- Selection of an MOA that is not based on the best available science over more scientifically defensible MOAs
- Failure to identify the impacts of the previously identified uncertainties and conservative choices on the CRA

Collectively, the previously submitted comments pinpointed specific improvement areas to improve alignment with best practices in risk assessment and CRA (ACC, 2025).

1 Charge Question 5f re: Appropriateness of Metafor Version 4.6.0.

1.1 The fundamental limitations with using Metafor 2.0.0 in the meta-analysis of these fetal testicular testosterone data for the six phthalates in the CRA are not addressed by using Metafor 4.2.0; instead, a state-of-the-science approach with Bayesian hierarchical modeling, or equivalent random effect approach, is necessary

The EPA's updated meta-analysis and benchmark dose (BMD) modeling of decreased fetal testicular testosterone in rats for DEHP, DBP, BBP, DIBP, and DCHP was based on a 2017 NASEM meta-analysis conducted using the Metafor package for R (version 2.0.0). EPA used the updated Metafor package (version 4.6.0) in the phthalates CRA. However, the use of the updated Metafor package does not adequately address the limitations of the original NASEM analysis, because many of these limitations are inherent to the use of Metafor itself. That is to say, the uncertainties and limitations[2] in the original 2017 NASEM analysis persist in the updated EPA analysis: namely, the inability to adequately account for heterogeneity and assess parallelism of the dose-response curves for fetal testicular testosterone between phthalates. Independent modeling, based on the current state-of-the-science, reveals key issues with the updated EPA analysis in Metafor and highlights the critical need for the EPA to update its modeling approach.

1.1.1 Metafor does not adequately address key issues in dose-response meta-analysis modeling; therefore, the phthalate meta-analysis conducted using Metafor should be replaced with a modeling technique that better meets current state-of-the-science standards.

EPA updated NASEM's 2017 analysis of fetal testicular testosterone data through use of the newer Metafor package (version 4.6.0 compared to version 2.0.0). It is expected that version 4.6 will offer bug fixes and other improvements to model fitting over version 2.0; therefore, the most recent version is preferred. However, use of the newer version of Metafor does not adequately address the largest issues with the original Metafor package that still persist in the newest version – the inability to adequately account for study-to-study potency heterogeneity and assess parallelism. As explained in the NASEM report, its regression analysis "*focused on the dose-response relationship*" and the "*models were selected for illustration, as they are easily implemented with existing software meta-analysis*"; NASEM's analysis was not meant to serve as the basis for a risk analysis (2017; p. 49). Although the analysis with Metafor is adequate for illustrative purposes, it does not reflect the current state-of-the-science and should not be used in a regulatory risk assessment. The current science (Ring *et al.,* 2023; DeVito *et al*., 2024) incorporates the

2 Issues with the identified fetal testicular testosterone data included in the analysis are addressed in comments herein related to Charge Questions 5g and 9 and have been discussed extensively in comments previously submitted to the DCHP Docket by ACC (ACC, 2025).

inclusion of terms in the model that allow for study heterogeneity in the dose-response and the response at no exposure. As is demonstrated below, it also can be used as a starting point to determine parallelism. The issues of heterogeneity and parallelism are explored and demonstrated below.

Study heterogeneity, both in potency and non-exposed response, exists because responses are measured on different animals in different labs and are conducted at different times, which is all done using different protocols. Failing to account for both heterogeneity arising from these sources may lead to biases in understanding the dose-response relationship. By using the NASEM 2017 report, EPA correctly identifies the importance of accounting for the impact of intra-study heterogeneity. However, Metafor is a meta-analysis package that allows only for the inclusion of background heterogeneity through a study effect term and a meta-regression based on a linear term. Metafor does not account for heterogeneity in the chemicals' potency by study, as it can only include fixed-effect linear regression.

EPA, following the NASEM 2017 approach, models the dose-response as

$$y_{ij} = \mu + \mu_i + \beta f(dose) + \epsilon_{ij},$$

where μ is the overall mean, μ_i is the study random effect, $\beta f(dose)$ is the dose-response meta-regression component shared between all datasets, and ϵ_{ij} is the error term for observation ij in the meta-regression. This is a standard meta-analysis approach commonly used in the literature when comparing means or other reported summary measures (e.g., odds ratios). However, it does not allow for modeling heterogeneity in the potency. **Subsequently, the RPFs produced by the EPA do not represent the best available science.**

Beyond Metafor's inability to account for the heterogeneity in potency, Metafor cannot appropriately test for dose-response parallelism[3]. This issue arises because the Metafor package does not support non-linear[4] models, the primary models used in continuous dose-response analyses by the EPA BMDS software (US EPA, 2022). These models are used in dose-response because they are generally thought to represent the biology of chemical kinetics. That is, sigmoid-shaped curves represent plausible threshold behavior, and a plateaued response that represents saturation.

As an example of sigmoidal-shaped responses compared to Metafor, Figure 1 illustrates the fit of dose-response functions to the DEHP data (top) and contrasts this with the global

[3] Notably, in response to Charge Questions regarding the Proposed CRA Approach (US EPA, 2023), the SACC cautioned that "simply selecting a BMR to use for RPFs without accounting for dose-response parallelism and achieving maximum response will result in highly variable RPFs" (US EPA, 2023b: p. 68); nevertheless, EPA has proceeded with use of Metafor, which cannot test for parallelism.

[4] Linear models are not only defined as $y = mx + b$, where x is the observed dose. Instead, a linear model is a model where the quantity x is any known function of the observed dose. For example, $x = \log(dose)$ or even $x = dose^2$ is considered linear model. Models such as $x = dose^{\rho}$, where ρ is unknown, is a non-linear model because the quantity ρ must be estimated. Metafor cannot estimate unknown terms like ρ in non-linear models.

fit used by the Metafor package (bottom). This figure shows the study-to-study heterogeneity that can be accounted for when the state-of-the-science model is fit using the Exponential-5 model (Slob, 2002). It also displays the sigmoidal shapes observed in the data. In showing sigmoidal fits, this figure gives additional evidence that Metafor is inadequate because its linear fit does not reproduce this sigmoidal shape, and it cannot implement analyses that represent current best practice.

Beyond the ability to describe the data adequately, as shown in Figure 1, Metafor cannot fit non-linear sigmoidal shapes. As fitting such curves is a precondition for testing parallelism, the package cannot determine if dose responses are parallel between phthalates. **Metafor cannot answer the parallelism question emphasized by the previous SACC and NASEM reports**.

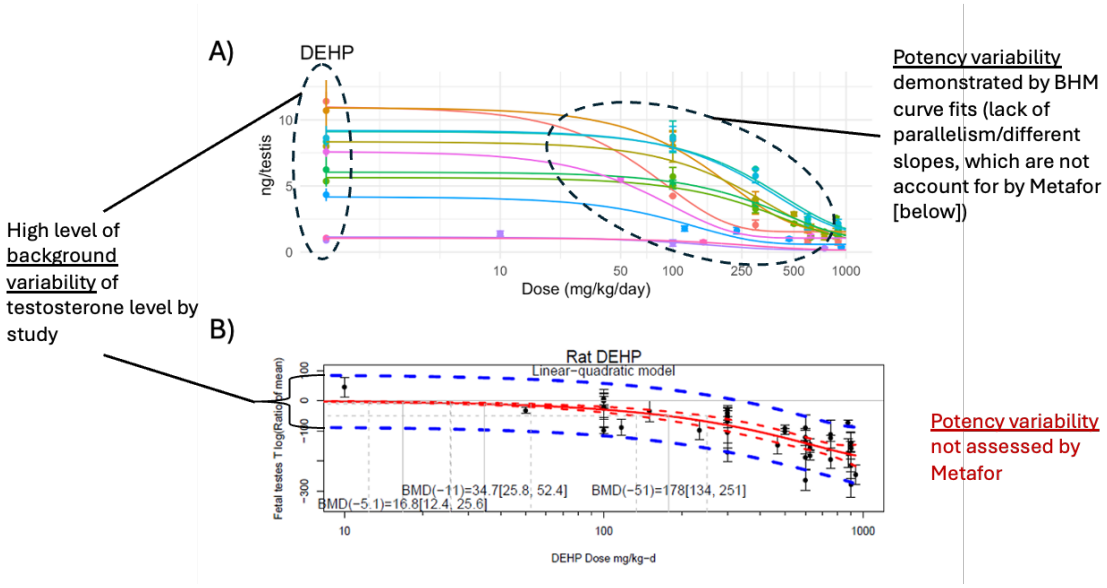

Figure 1: Comparison of the DEHP data-fit using A) the state-of-the-science BHM and B) the EPA's fit using the transformations $x_1 = \text{dose}$ and $x_2 = \text{dose}^2$ and meta-regression using the R package Metafor.

Consistent with the NASEM approach, use of the Metafor package to model the standardized mean difference relative to the background automatically removes the zero dose from the analysis. This is also not standard practice in modeling dose-responses, which assume independence in the error term (Crump, 1995). By subtracting the background response mean, each data point in this dataset becomes correlated. Consequently, the definition of the BMD used in this analysis is not standard and does not represent the best science.

The remedy for accounting for both background and potency heterogeneity is the introduction of random effect terms into the analysis, as both the response background and potency. For these data, the best science models the response as

$$y_{ij} = \mu + \mu_i + (\beta_i + \beta) f(dose) + \epsilon_{ij}.$$[5]

The key difference lies in the experiment-specific term β_i, which represents an experiment-specific slope indicating heterogeneity in the response. Unlike the NASEM report or the EPA approach, the dose-response term $f(dose)$ does not necessarily enter the model linearly, but linear options could be considered.

One could use the Hill model in this formulation, i.e.,

$$f(dose) = \frac{dose^d}{c^d + dose^d},$$

where the quantities like 'c' and 'd' must be estimated. Non-linear models, such as the Hill model allow for statistical testing of parallelism of the response by testing for the equality of the fit between different chemicals. It is standard practice to use the Hill model, as parameterized above, to test for parallelism (Dinse and Umbach, 2012); however, the current methods used by EPA cannot test parallelism in the dose-response's potency, which is necessary for dose-addition in CRA. Despite this, in the *Draft Phthalate CRA Approach,* EPA states, "available data indicate that DEHP, BBP, DBP, DIBP, DCHP, and DINP are toxicologically similar" (US EPA, 2023a; pg. 102). This conclusion cannot be supported using Metafor, and the data do not support this conclusion.

The state-of-the-science BHM modeling approach allows for testing for parallelism; using a standard dose-response function enables a definition consistent with risk assessment best practices. Further, CRA often estimates RPFs using the ED_{50}, which is the dose at which the response is halfway between the background level and the maximum change. To be congruent with this practice while also allowing for non-parallel dose-response curves, the relative effect definition defines the BMD as the percentage change (increase or decrease) from the background response. A lack of parallelism in dose-response curves may suggest differences in mode of action between phthalates, as the RPFs derived from these curves reflect. In such a case, if the RPF is used, it is important to select exposures at human relevant levels where the dose-responses are well approximated linearly at the exposure for additivity.[6]

If dose-responses are not parallel (as observed for the six phthalates in this assessment), realizing that the model form may impact the estimates of potency and ultimately the RPF, best practice includes considering model averaging (MA) (Raftery et al 1997; Wheeler and Bailer 2007; Shao and Gift 2014; Wheeler et al 2020; Wheeler et al 2022; EFSA 2022) to

[5] Here there is an implicit population dose response which is $\hat{f}(dose) = \int [\mu + \mu_i + (\beta + \beta_i) f(dose) d\mu_i d\beta_i$

[6] This implies that the function $f(dose)$ derivative is defined and the approximation defined by the first order Taylor series is a good approximation to $f(dose)$.

estimate the POD. MA quantifies uncertainty in the model form and allows it to propagate through the analysis.

In the phthalates CRA meta-analysis of fetal testicular testosterone, EPA should not rely on Metafor but instead use a modeling approach that incorporates potency heterogeneity, allows for evaluation of parallelism, and enables model averaging, which aligns with best scientific practice.

1.1.2 A state-of-the-science Bayesian Hierarchical Modeling approach addresses the key issues in EPA's modeling and yields RPF values substantially different from the current EPA-derived values.

Independent analysis using the fetal testosterone data provided by EPA was conducted with BHM that incorporates the best practices and is consistent with the current state-of-the-science capabilities. Table 1 provides a comparison between the state of the science and EPA (i.e., Metafor) approaches. As described previously, the EPA (Metafor) approach allows for incorporation of background heterogeneity and fit with linear models; however, the state of the science approach also allows incorporation of potency heterogeneity, use of non-linear models, consideration of MA, and evaluation of parallelism.

Table 1: Comparison between the state-of-the-science BHM and the capabilities of Metafor used in the US EPA's approach.

Capabilities	**BHM**	**Metafor**
Incorporation of Background Heterogeneity	✓	✓
Incorporation Potency Heterogeneity	✓	
Linear models	✓	✓
Non-linear models	✓	
Model Averaging	✓	
Testing parallelism	✓	

Key: BHM: Bayesian Hierarchical Modeling; ✓ – approach incorporates this capability; blank cells – approach does not incorporate this capability.

Herein, the linear and exponential Hill models, as well as the Exponential-5 models, from the state-of-the-science BHM approach are discussed. These two models are sigmoidal-shaped dose-response curves, which fit the dose-response data better than the linear model. MA models were investigated as described by EFSA (2022). Still, the Exponential-5 model was found to be superior to such an extent that the model weights for all other models are essentially zero. Note that, although the Exponential-5 model is superior, we use the Hill model described above and below to demonstrate the lack of parallelism, as this is the classical approach for determining parallelism (e.g., Dinse and Umbach, 2012). Figure 1 above provides an example of model fits derived from this BHM approach.

In this approach, the data are assumed to be distributed normally to avoid log-normal approximations. This is a standard assumption for continuous dose-response estimation (Crump, 1995) and because fetal testosterone levels decrease with exposure, the Hill model is parameterized as

$$f(dose) = \exp\left[\mu + \mu_i + (\beta + \beta_i)\left\{\frac{dose^d}{c^d + dose^d}\right\}\right]$$

and the Exponential-5 model as

$$f(dose) = \exp(\mu + \mu_i) \times \{c - (c - 1)\exp[(\beta + \beta_i) \times dose^d]\}.$$

These model forms ensure the positivity of the response whereby preventing biologically impossible situations where the dose-response relationship implies fetal testicular testosterone levels are less than zero.

To test for parallelism, the Hill model can be fit where the parameter *d* is shared between all phthalates and one where it is allowed to be unique for each chemical. As this approach is conducted in the Bayesian paradigm, Bayesian hypothesis testing should be performed using Bayes Factors (Kass and Raftery 1995). Under this testing paradigm, using the linear Hill model, the exponentialized Hill model, and the Exponential-5 model, the evidence is supportive of the conclusion that the dose-responses are not parallel. The fits of the linear Hill, exponential Hill, and Exponential-5 models are compared using Bayes Factors, the widely applicable information criterion (WAIC) (Watanabe 2013), and leave-one-out predictive modeling (Vehtari et al. 2017). Using all testing regimes, the Exponential-5 model is superior in modeling the data, leading to the conclusion that model averaging would not be a helpful tool. Thus, the Exponential-5 model is the basis for the state-of-the-science RPF derivations.

Table 2 presents BMD estimates based on benchmark responses (BMRs) of 5%, 10%, and 40% from the Exponential-5 model computed using the state-of-the-science BHM using the population average dose response computed by marginalizing out the random effects. Although a comparison between these estimates and those produced by EPA is not a congruous comparison because they are based on different versions of the BMD, they can be compared based on potency. In the state-of-the-science BHM approach, many phthalates have different potencies at low doses than the US EPA estimates. For example, at a 5% BMR, the DEHP estimates are approximately half as potent as those produced by the EPA model, while for DCHP, the estimates are approximately ***three times more potent***.

Table 2: Central (upper and lower quantiles) BMD estimates using the Exponential-5 model and BMRs of 5, 10, and 40% using the BHM. Estimates are compared to EPA's BMD estimates using the same data.

Phthalate	Model	BMD_5	BMD_{10}	BMD_{40}
BBP	BHM	115.1 (79.4, 158.2)	172.0 (126.8, 230.5)	416.8 (339.5, 541.2)
	EPA	--	--	284 (150, 481)
DBP	BHM	8.4 (4.1, 30.1)	20.3 (10.0, 65.6)	137.3 (71.7, 464.8)
	EPA	14 (9, 27)	29 (20, 54)	149 (101, 247)
DCHP	BHM	3.8 (2.3, 7.8)	9.6 (6.0, 18.7)	73.2 (47.4, 133.6)
	EPA	8.4 (6.0, 14)	17 (12, 29)	90 (63, 151)
DEHP	BHM	32.5 (13.6, 108.7)	58.0 (28.3, 214.4)	210.6 (119.6, 683.0)
	EPA	17 (11, 31)	35 (24, 63)	178 (122, 284)

DIBP	BHM	59.2 (39.3, 84.2)	99.6 (70.0, 130.8)	313.3 (251.8, 393.1)
	EPA	--	55 (NA, 266)	279 (136, 517)
DINP	BHM	86.1 (42.9, 242.1)	150.8 (82.1, 407.1)	514.3 (319.4, 1422.7)
	EPA	74 (47, 158)	152 (97, 278)	699 (539, 858)

Key: BMD – benchmark dose; BHM – Bayesian Hierarchical Modeling

The reason for the differences between the BMRs calculated by EPA and in this state-of-the-science approach is the model form. Linear models do not allow for sigmoidal-shaped curves, which are evident in the response data for BBP, DINP, and DIBP. When linear models are fitted, BMD estimates for these chemicals are overly conservative because they cannot account for the non-linearities in the data. Alternatively, the data suggest DEHP has a steep response at low doses. Here, the problem lies in the opposite direction: a linear model cannot adequately model the data in the low-dose region and underestimates the potency. Figure 2 shows these fits to the DCHP data.

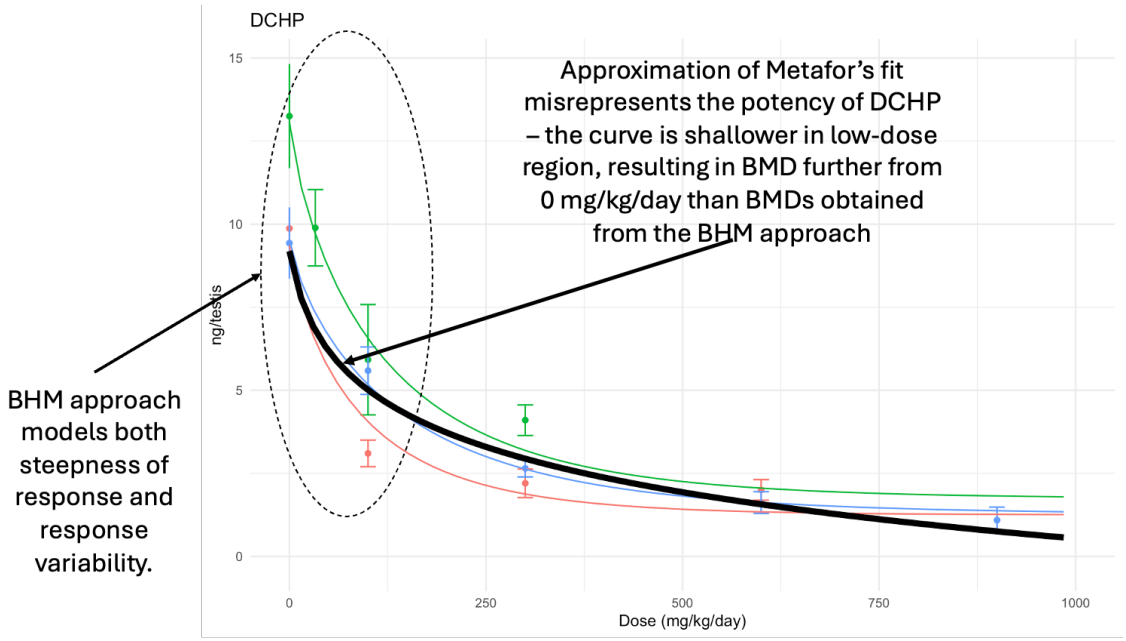

Figure 2: DCHP dose-response estimates using the state-of-the-science BHM approach (colored models). EPA's approach underestimates potency in the low-dose region for DCHP, as shown by the black line (approximation of the EPA linear model).

The DBP BMD estimates derived with the state-of-the-science BHM approach are very similar to EPA's approach. This similarity indicates a robustness in the approach used and the dataset overall, and it supports using DBP as the reference chemical, as we can be confident in the estimates.

A notable example of the effect of non-linearity is DINP. The response is shallow, resulting in an initial BMD at BMR of 5% being lower than that of BBP, but a BMD at BMR of 40% that is greater than that of BBP. This highlights the importance of using non-linear dose-response models when estimating the BMDs used in the calculation of the RPFs.

Using DBP as the index chemical, Table 3 presents RPF central estimates from the state-of-the-science BHM approach in comparison to EPA's RPF estimates, revealing substantial differences. Here, the recommended BHM RPF_5 estimates, which are in bold, are compared to the EPA estimates (also in bold). In this table, the recommended BHM RPFs that are less than EPA's recommended RPFs are in blue, and recommended BMH values greater than EPA's recommended RPFs are in burnt orange. Notably, although the EPA approach cannot compute the RPF_5 and RPF_{10} for some chemicals in the database, the presented BHM methodology produces RPFs for all BMRs, and the RPF values differ across BMRs. The ability to model non-linearities at low doses results in RPF derivations that are notably different than EPA's RPF estimates based on linear models by up to a factor of five. This difference highlights the importance of using state-of-the-science methods in the phthalate CRA. Failure to account for non-linearities while estimating the RPF at BMRs of 40% results in RPF estimates that are not fully health protective (e.g., DCHP) or overly conservative (e.g., BBP). Because the dose-responses are not parallel and chemicals have different potencies, EPA must consider the RPFs computed at BMRs of 5% using BHM.

Table 3: RPF central (median) estimates calculated from the distribution of BMDs for BMRs of 5, 10, and 40% using the state-of-the-science BHM approach compared to the RPF estimates given by EPA for each BMR. Recommended RPF values (both EPA and BHM) are color-coded and bolded. Blue represents RPFs that are lower than the EPA provided estimates, and burnt orange represents values that are greater than their EPA counterparts. The recommended RPFs via each method (i.e., BHM RPF_5 and EPA's RPF_{40}) are compared.

	RPF_5		**RPF_{10}**		**RPF_{40}**	
	BHM	**EPA**	**BHM**	**EPA**	**BHM**	**EPA**
BBP	**0.08**	--	0.12	--	0.33	**0.52**
DINP	**0.10**	0.19	0.13	0.19	0.26	**0.21**
DIBP	**0.15**	--	0.21	0.53	0.44	**0.53**
DEHP	**0.27**	0.82	0.34	0.83	0.65	**0.84**
DCHP	**2.19**	1.67	2.09	1.71	1.90	**1.66**

Key: RPF – relative potency factor; BHM – Bayesian Hierarchical Modeling

The approach mentioned above outlines how the best science produces BMDs and RPFs that are quantitatively and qualitatively different than EPA's approach with Metafor. A newer version of Metafor does not resolve inherent limitations of the EPA analysis that fall outside Metafor's capabilities. Metafor is designed to facilitate meta-analytic analysis on summary statistics provided in scientific manuscripts through a random-effects model, but not through general random-effect models. General random-effect models allow the model to account for heterogeneity, which Metafor cannot do; additionally, fitting features, beyond Metafor's capability, are required to test for parallelism. The differences between the models from Metaphor and the BHM approach ultimately lead to differences in the margin of exposure (MOE) estimates, as demonstrated below in response Charge Question 10.

2 Charge Questions 5g and 9 re: Selection of Index Chemical (DBP) and its POD

2.1 Assessment of the appropriateness of the index chemical selection and the adequacy of its underlying database cannot be performed due to the lack of consistent and transparent data selection and evaluation.

EPA acknowledges that informed selection of an index chemical is critical due to the impact of imprecision from an index chemical on other chemicals in the cumulative chemical group (US EPA, 2025c; US EPA, 2002). This is achieved, in part, by the index chemical having the highest quality toxicological database and high-quality dose-response data. As reflected in comments previously submitted by ACC (2025), EPA does not provide sufficient information in the publicly disseminated documents to determine whether the entire database of identified studies was considered for modeling. Specifically, inconsistent omissions of specific DBP data sets from meta-analysis inputs highlights that these data are not representative of the underlying evidence base.

2.1.1 EPA is inconsistent in its data selection criteria of DBP datasets for inclusion in the meta-analysis

An independent review of the DBP meta-analysis inputs was undertaken, identifying many inconsistencies and concerns in data quality. Based on this review, it is unlikely that the DBP meta-analysis and resulting RPFs are representative of the underlying body of evidence. As was noted in Comment 2.4 of comments previously submitted by ACC (2025), EPA identified 21 studies with fetal testicular testosterone content or production data in Table 3-3 of the Draft Non-cancer HHHA for DBP (US EPA, 2024c p. 37). Yet, EPA uses only eight of these studies in the meta-analysis for DBP, comprising the seven studies included by NASEM and one additional study by Gray et al. (2021). Thus, 13 studies reporting fetal testicular testosterone data for DBP were excluded from the meta-analysis. Of these 13, EPA provides justification for 7 studies; justification for the exclusion of the 6 remaining studies is not provided (Drake et al., 2009; Howdeshell et al., 2007; Macleod et al., 2010; Mylchreest et al., 2002; Spade et al., 2018; Wilson et al., 2004).

Other issues related to inconsistency in selection of data for inclusion were also noted:

- Johnson et al., 2007 reports exposure to dams on GD19, which is outside of the criteria for inclusion in the meta-analysis as reported by EPA's Draft meta-analysis document (EPA, 2024a: p. 9) that states the exposure must cover the "male programming window (defined by NASEM as gestational days (GD) 16-18)." Based on this, Johnson et al., 2007 should be considered for exclusion.
- Fetal testosterone data for DBP reported in a more recent publication by Gray et al. (2024) was not included in the EPA meta-analysis data inputs. An existing study quality evaluation is provided in EPA's DBP Data Quality Evaluation documentation (EPA, 2025b), indicating that EPA was aware of this dataset.

Further, data corresponding to the DINP exposure in the same block studies (Blocks 166 and 167) are included in the EPA meta-analysis data inputs.

- EPA's meta-analysis input includes a data row for fetal testosterone measures following 50 mg/kg bw/d *in utero* DBP exposure in F344 rats as reported by Johnson et al., 2011. The corresponding control (corn oil vehicle) data for this exposure is not included in the meta-analysis inputs. As a result, this data row appears to be excluded from the meta-analysis.

Based on the inconsistent data selection process as presented in the draft TSD, it is recommended that EPA re-evaluate the data inputs for the meta-analysis to be transparent and reproducible by being consistent with its reported inclusion and exclusion criteria. Further, it is recommended that EPA provide transparent exclusion decisions.

2.1.2 EPA did not consistently consider serious risks to study quality (bias) across the body of evidence identified for DBP

Study (and data) quality are important components of identifying the highest quality toxicological database and dose-response data. EPA has previously used study limitations as justification for excluding specific datasets from use in the meta-analysis. For example, in the Draft Non-cancer HHHA for DBP, EPA states that Clewell et al. (2009) is "limited by the fact that only one dose (i.e., the LOAEL of 50 mg/kg/day) in addition to control" was utilized, and that it "had a low sample size of 3 to 4 animals per group" (US EPA, 2024c, p. 60). Based on this, data from Clewell et al. (2009) was not included in the EPA meta-analysis[7].

Similar (serious) study quality concerns were identified in the reporting of DBP data from Gray et al., 2021. These authors report in Figure 2b the TPROD DBP data for 1, 10, 33, 50, 100, 300, and 750 mg/kg/d exposures as percent reduction from control values. Upon review of the supplemental information for the corresponding raw absolute values, blocks 69 and 70 are the only available DBP data and appear as 0, 300, 600, or 900 mg/kg/d dose levels. It is unclear why the raw data in the supplemental material do not represent that in the summary data of Figure 2b – that is, the data do not appear to support conclusions made, and are, at a minimum, conflicting and inconsistent. This lack of transparency in the generation of outcome data highlights potential serious issues with study quality and confidence in reporting. However, according to Table 2-1 of the Draft TSD, EPA has assigned a "high" rating to the DBP data. Similar issues with data presentation were noted for DCHP, BBP, and DEHP, which are also designated as "high" quality by EPA.

[7] It should be noted that, while important, study quality and/or limitations is not a documented exclusion criterion, further emphasizing the inconsistent data selection and lack of transparency in decision-making.

3 Charge Question 10 re: Use of BMD_{40} Values to Calculate RPFs

3.1 The use of BMD_{40} values to calculate RPFs is not consistent with best practices given the dose-response curves are not parallel; use of the BMD_{40} values as the basis for the RPFs leads to both over- and underestimation of risks.

As mentioned in the response to Charge Question 5f, and as shown in Figure 3, the log-slope of the best-fit models for each phthalate differs across phthalates. Consequently, the RPFs should be investigated at a range of potency estimates (i.e., different BMRs) (Dinse and Umbach 2012). Though EPA's basis for using the RPFs is based on an analysis that investigates the BMD_5, BMD_{10}, and BMD_{40} and shows these estimates to be similar, their analysis was done using models that are approximately linear in the response range (see Comment 1, response to Charge Question 5j) and are inherently approximately parallel. When the state-of-the-science BHM approach is applied (i.e., non-linear models are investigated), the RPFs from the best fit model (i.e., the Exponential-5) calculated from the three BMRs are shown to differ. That is, when using a modeling approach that actually allows for assessment of parallelism, it is demonstrated that the dose-response curves for phthalates evaluated are not parallel and thus selection of the BMD_{40} as the benchmark will not actually represent the underlying science appropriately, leading both to over- and under- estimation of risk.

In the MOE calculation (including all of Option 1 and the non-attributable exposures in Option 2), EPA's use of RPFs derived from BMD_{40}s with the index chemical PODs in the low dose region (i.e., DBP's BMD_5) is inappropriate. This misrepresents risk at human-relevant exposures, leading to overestimation and underestimation of risk. For example, BBP's POD relative to DBP's POD (in Table 2) is 121 mg/kg/day using the RPF_5, but it is 16 mg/kg/day based on the RPF_{40}. Consequently, using the RPF_{40} one overestimates risk.

Because of the lack of parallelism in a portion of the dose-response curves, RPFs should be developed with consideration for where curves are approximately parallel (versus from the region where they are not). For the phthalates herein, curves are most parallel in the lowest dose region, and thus EPA could consider using the lower BMRs (i.e., 5 or 10%) when calculating RPFs; this will better account for lack of parallelism that is observed in the range of the higher BMR (40%), as observed when the appropriate modeling approach is also applied. It is of note that in EPA's assessment, no BMD_5 or BMD_{10} values could even be determined with the use of Metaphor for DIBP (no BMD_5 only) and BBP – thus highlighting one of several critical deficiencies in the approach EPA applied.

If EPA does not consider the modeling aspects described herein, discussion on uncertainties related to EPA's modeling decisions – including corresponding relevance to human exposure – should be required. This should include uncertainties related to risk estimates derived from non-parallel dose-response curves that both over- and under-estimate risk in human relevant exposure ranges.

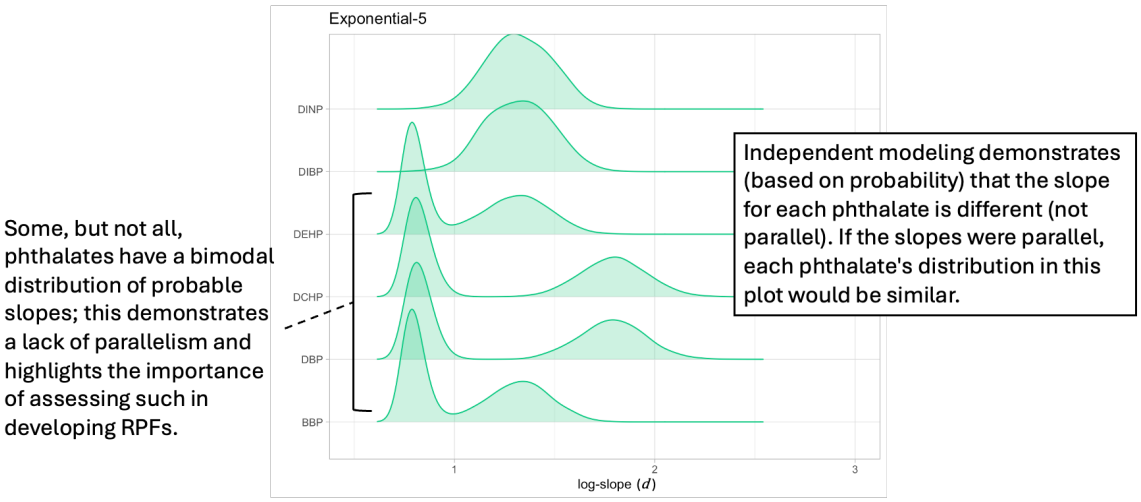

Figure 3: Posterior distributions of the log-slope term showing the differences between phthalate modeling of the dose-responses. *Here, the heterogeneity between the log-slope terms is evident as each phthalate's distribution is different*. For the log-slopes to be the same and the dose-responses parallel, the posterior distribution should be the same across all chemicals.

4 Charge Question 11 re: Strength and Uncertainties of Options 1 and 2 for Characterizing Cumulative Risk

4.1 Key sources of uncertainty in both Options 1 and 2 lie in the inherent limitations of the assumptions made in the individual phthalate and cumulative phthalate exposure assessments and of the meta-analysis modeling methodology used

EPA proposes two options for calculating MOEs and characterizing cumulative risk from exposure to phthalates under TSCA. Across both approaches, there are uncertainties and limitations that arise from assumptions made in exposure modeling and inherent limitations in the methods used for meta-analysis modeling of BMDs that were used to calculate RPFs. While appropriate as screening-level risk assessment options, both need refinement for use in informing cumulative risk in such a way that useful decisions can be made by risk managers.

4.2 Screening-level exposure estimates used as inputs for Options 1 and 2 are inappropriate for definitive risk determinations

In both Option 1 and Option 2, EPA relied upon screening-level exposure inputs to inform the risk conclusions. For example, use of bounding estimates ensures that potential high-end exposures are not missed, which is appropriate for initial screening. However, EPA's reliance on worst-case exposure assumptions (e.g., maximum concentrations, simultaneous dermal and inhalation exposure, highest-use scenarios) may yield unrealistic exposure values. The conservative nature of this approach allows for identification of low-risk scenarios (i.e., conditions of use (COUs) and OESs that do not present unreasonable risk), allowing EPA to focus resources on higher-priority scenarios. However, screening-level exposure estimates can only support screening-level cumulative risk estimates and are inadequate for definitive risk conclusions. While a screening-level CRA can be a valuable first step, regardless of whether Option 1 or Option 2 is progressed in the final risk evaluations, EPA should clarify when and how refined assessments will be pursued for regulatory decisions, ensuring that CRA evolves from a screening tool into a robust decision-support framework.

4.2.1 Occupational exposure is overestimated due to applying a screening-level approach that represents all exposures

In order to streamline the exposure assessment, EPA identified one OES as representative of one or more COUs, recognizing that other OESs in the same COU are likely to yield much lower exposures, if any. Furthermore, EPA applies the most conservative assumptions to one OES as representative of all activities in all COUs. This consolidation approach is likely to overestimate exposure across the value chain and result in potentially

greater overestimation in commercial settings given the small scale of the application. Specific examples of decisions that likely lead to overestimating exposure include:

- Selecting the highest reported concentrations measured in the workplace as representative of activities throughout the value chain.
- Using exposure scenario documentation (ESD) on the "Coating Application via Spray-Painting in the Automotive Refinishing Industry" model with conservative input parameters as representative of all potential exposures in five different COUs that include "Application of Adhesives and Sealants" and "Paints and Coatings", which include application scenarios, regardless of determinants of exposure.
- Using particulates not otherwise regulated (PNOR) model for all activities that can potentially generate aerosols, disregarding the effect of exposure determinants on the concentration of aerosols.
- Selecting the highest weight fraction of the phthalate as representative of the exposure for a scenario without verifying applicability.
- Disregarding the presence or use of administrative or engineering controls.
- Selecting of the reported exposures with the highest concentration as representative of the expected activities that occur within the COU and/or OES.

Assuming the highest potential exposure for each OES within each condition of use COU is a reasonable and protective screening-level approach, as it provides bounding estimates to identify potential risks. However, treating these maximum exposures as if they occur continuously for all individuals introduces compounded conservatism and may significantly overestimate actual exposures. EPA has acknowledged that while co-exposure to multiple phthalates in occupational settings is possible, it is unlikely or very limited in the manufacturing and formulation COUs.

Co-exposure may be more plausible during the use of formulations or articles containing varying concentrations of phthalates, but it is improbable that all phthalates would be present simultaneously. Therefore, using bounding estimates for each phthalate as representative of occupational exposure can lead to an overestimation of aggregate and cumulative exposures.

Related to overestimation of dermal exposure, EPA used default dermal loading metrics and default exposure duration in the workplace. Assuming the same dermal loading for activities associated with manufacture or transport or use of formulations without scaling for the concentration of the substance in the formulation will yield an even greater overestimation of exposures. This is the case of predicted exposures for COUs such as incorporation into adhesives and sealants, incorporation into paints and coatings, and incorporation into other formulations.

Additionally, as a conservative approach, EPA ignored the difference in absorption between rat and human skin, citing the potential facilitation of absorption due to the presence of other substances. The combination of these overly conservative assumptions is

likely to yield an estimate of exposure that is beyond a high-end and should serve as a bounding estimate of exposure, and therefore only be used for screening purposes.

4.2.2 Consumer exposure is overestimated by using bounding estimates to represent COUs as well as double-counting risk

Similar to occupational exposures, EPA used a conservative approach that is useful to screen out the pathways that present no unreasonable risk. The models used tend to yield conservative estimates, and the input parameters were selected to represent the highest potential for exposures. The combination of these two aspects can yield a bounding estimate (more than a high-end estimate of a plausible distribution of exposures). Additionally, when available, EPA selected the highest value between modeled and measured data, regardless of the fact that modeled results are recognized as conservative estimates.

EPA further overestimates consumer exposure by failing to consider that consumer exposure is likely to be already represented in NHANES data. NHANES biomonitoring data already reflects cumulative exposures in the general population, particularly for frequently used consumer products, as identified in the consumer exposure assessment. Therefore, adding biomonitoring data to modeled consumer exposure estimates for each COU may result in double-counting exposures. This could lead to inflated aggregate and cumulative exposure estimates and overly conservative risk characterizations.

Additionally, while biomonitoring data are valuable for understanding population-level exposures, the use of the 95th percentile for each phthalate further compounds conservatism. This approach assumes simultaneous exposure to the highest concentrations of all chemicals, which is highly unlikely in real-world scenarios. In fact, Qian et al (2015) reported the NHANES data suggest that high exposure to multiple phthalates is infrequent in the NHANES population. Furthermore, co-exposures among the phthalates change as a function of daily intake, even though co-exposure patterns seem to be consistent within age, ethnicity, and gender (Reyes and Price, 2017). While such bounding estimates may be appropriate for screening-level assessments, it is unclear how EPA intends to use these results in risk management decisions.

Application of cumulative risk assessment should result in better understanding of complex exposures and health risks with the potential to inform more effective controls and improved safety and health risk management overall (Fox et al. 2018). A conclusion of no unreasonable risk using such conservative estimates should provide confidence to the assessors that cumulative (or single chemical) exposure does not present unreasonable risk. However, an MOE<30 using such broad over-estimations of exposure should be an indication of additional refinement to be done at least at the exposure level.

4.2.3 Limitations in EPA's modeling equally impact reliability (or lack thereof) of Options 1 and 2; use of state-of-the-science modeling results in similar estimates from Options 1 and 2

Modeling choices determine the POD estimate, and unreliable modeling impacts the reliability of the POD approach. As shown in Table 2, the EPA approach fails to produce PODs for all phthalates at human-relevant exposure levels (e.g., BMD_5). When a BMD cannot be estimated, it is often a function of the dose-response model applied to the data. Consequently, EPA's modeling choices prevent the development of RPFs at human-relevant exposure levels, increasing uncertainty.

Option 2 attempts to remedy some of the flaws in Option 1 by estimating phthalate-specific PODs for the attributable portion of the analysis, while maintaining the non-attributable estimates using the CRA approach of Option 1 (i.e., RPF scaling). As the individual phthalate PODs are estimated at lower doses using a NOAEL or BMD_5, this approach is more relevant to human-relevant exposures. Option 2 is limited by the fact that not all phthalate-specific PODs are derived from the same endpoint (i.e., reduced fetal testicular testosterone), nor does this approach account for uncertainty in the POD when the NOAEL (rather than the BMD) is used. The inconsistencies in the methodology of Option 2 are difficult to predict in practice because the POD derivation depends much more heavily on the critical effect identified. The state of the science approach outlined above (see Comment 1, response to Charge Question 5f) shows how these issues impact estimates of the MOE.

As previously discussed in these comments, the uncertainties and limitations in the original 2017 NASEM analysis persist in the updated EPA analysis: namely, the inability to adequately account for heterogeneity and assess parallelism of the dose-response curves for fetal testicular testosterone between phthalates. This is because the RPFs used in the MOE calculations are estimated using non-standard dose-response functions that do not accurately model sigmoid-shaped responses. Consequently, RPFs using the BMD_{40} may not be properly health protective based on the current state-of-the-science (see response to charge question 5f for specifics).

To demonstrate the importance of using state-of-the-science derived $BMDL_5$ and RPF_5 values in both Option 1 and Option 2, the MOEs (for female workers of reproductive age in the Application of Paints and Coatings (solids) OES) calculated in EPA's CRA technical support document for DCHP and DEHP using the Metafor derived POD and RPF_{40} values were re-calculated according to the state-of-the-science BHM approach. A step-by-step comparison of the calculated MOEs for both Option 1 and Option 2 derived from the state-of-the-science method, and the EPA method are provided in Table 4. The MOEs between Options 1 and 2 are more consistent using the input from the state-of-the-science assessment versus the input from the EPA methodologies, the latter of which gives an approximately 2-fold difference between Option 1 and Option 2 (Table 5).

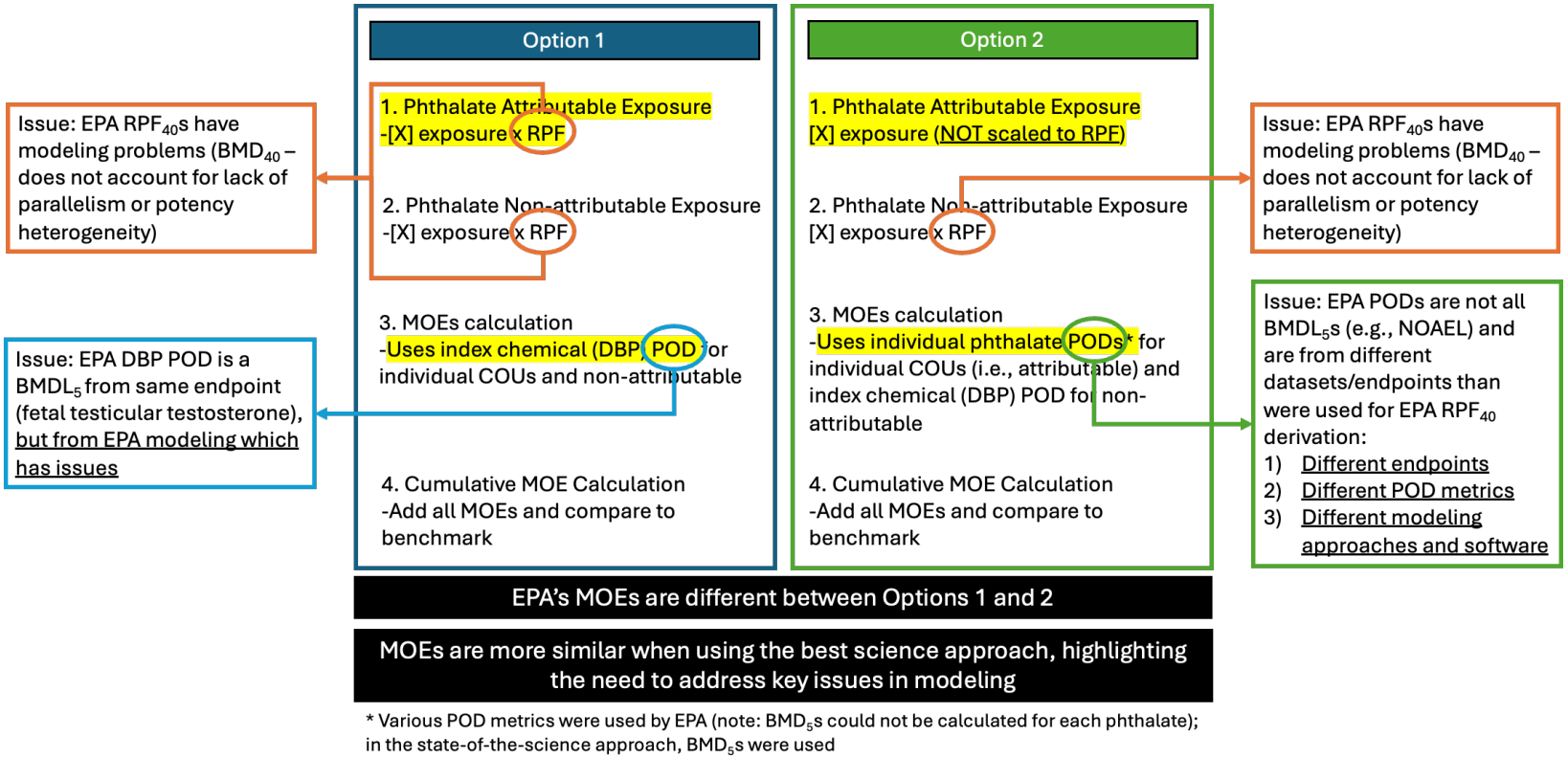

Figure 4: Comparison of key steps in EPA's Option 1 compared to Option 2. In both options, EPA uses RPF_{40s}; in Option 2, EPA relies on individual phthalate PODs of various types (e.g., $BMDL_5$, NOAEL/LOAEL) across various effects. In the state-of-the-science approach herein, the RPF_5 is used in both Options and in Option 2, $BMDL_5$ values for each phthalate are used.

Table 4: Step-by-step calculation of MOEs calculated using the state-of-the-science BHM approach compared to those given by the EPA TSD numerical examples (DCHP and DEHP). The BHM RPF_5 and EPA RPF_{40} values used in these calculations were previously reported in Table 3.

	BHM[D]		**EPA[D]**	
DCHP (for female workers of reproductive age in the Application of Paints and Coatings (solids) OES)				
	Option 1	*Option 2*	*Option 1*	*Option 2*
Attributable Exposures	**[DCHP] x RPF_5 = [DBP] equivalents** I: 38.7 ug/kg DCHP x 2.19 = 84.8 ug/kg DBP equivalents D: 2.07 ug/kg DCHP x 2.19 = 4.5 ug/kg DBP equivalents	**[DCHP]** I: 38.7 ug/kg DCHP D: 2.07 ug/kg DCHP	**[DCHP] x RPF_{40} = [DBP] equivalents** I: 38.7 ug/kg DCHP x 1.66 = 64.24 ug/kg DBP equivalents D: 2.07 ug/kg DCHP x 1.66 = 3.44 ug/kg DBP equivalents	**[DCHP]** I: 38.7 ug/kg DCHP D: 2.07 ug/kg DCHP
Non-Attributable Exposure	**Σ([phthalates] x RPF_5)** (4.28 ug/kg DEHP x 0.27) + (0.48 ug/kg DBP x 1) + (0.30 ug/kg BBP x 0.08) + (0.40 ug/kg DIBP x 0.15) + (3.40 ug/kg DINP x 0.10) = 2.06 ug/kg DBP equivalents	**Σ([phthalates] x RPF_5)** (4.28 ug/kg DEHP x 0.27) + (0.48 ug/kg DBP x 1) + (0.30 ug/kg BBP x 0.08) + (0.40 ug/kg DIBP x 0.15) + (3.40 ug/kg DINP x 0.10) = 2.06 ug/kg DBP equivalents	**Σ([phthalate] x RPF_{40})** (4.28 ug/kg DEHP x 0.84) + (0.48 ug/kg DBP x 1) = (0.30 ug/kg BBP x 0.52) x (0.40 ug/kg DIBP x 0.53) = (3.40 ug/kg DINP x 0.21) = 5.16 ug/kg DBP equivalents	**Σ([phthalate] x RPF_{40})** (4.28 ug/kg DEHP x 0.84) + (0.48 ug/kg DBP x 1) = (0.30 ug/kg BBP x 0.52) x (0.40 ug/kg DIBP x 0.53) = (3.40 ug/kg DINP x 0.21) = 5.16 ug/kg DBP equivalents
MOE Calculations	**MOE = DBP $BMDL_5$ / DBP equivalents [A]** MOE_{CNA} = 984 ug/kg / 2.06 ug/kg = 478 MOE_{COUI} = 984 ug/kg / 84.8 ug/kg = 11.6 MOE_{COUD} = 984 ug/kg / 4.5 ug/kg = 218	**MOE_{COU} = DCHP $BMDL_5$ / DCHP exposure [B]** MOE_{COUI} = 552 ug/kg / 38.7 ug/kg = 14.3 MOE_{COUD} = 552 ug/kg / 2.07 ug/kg = 267 **MOE_{CNA} = DBP $BMDL_5$ / DBP equivalents** 984 ug/kg / 2.06 ug/kg = 478	**MOE = DBP $BMDL_5$ / DBP equivalents** MOE_{CNA} = 2100 ug/kg / 5.16 ug/kg = 407 MOE_{COUI} = 2100 ug/kg / 64.2 ug/kg = 32.7 MOE_{COUD} = 2100 ug/kg / 3.44 ug/kg = 610	**MOE = DCHP NOAEL / DEHP exposure** MOE_{COUI} = 2400 ug/kg / 38.7 ug/kg = 62 MOE_{COUD} = 2400 ug/kg / 2.07 ug/kg = 1157 **MOE_{CNA} = DBP $BMDL_5$ / DBP equivalents** 2100 ug/kg / 5.16 ug/kg = 407
Cumulative MOE	**CumMOE = 1 / [(1/MOE_{CNA}) + (1/MOE_{COUI}) + (1/MOE_{COUD})]** 1/ [(1/478) + (1/11.6) + (1/218)] = 11	**CumMOE = 1 / [(1/MOE_{CNA}) + (1/MOE_{COUI}) + (1/MOE_{COUD})]** 1/ [(1/478) + (1/14.3) + (1/267)] = 13	**CumMOE = 1 / [(1/MOE_{CNA}) + (1/MOE_{COUI}) + (1/MOE_{COUD})]** 1/ [(1/407) + (1/32.7) + (1/610)] = 29	**CumMOE = 1 / [(1/MOE_{CNA}) + (1/MOE_{COUI}) + (1/MOE_{COUD})]** 1/ [(1/407) + (1/62) + (1/1157)] = 51
DEHP (for female workers of reproductive age in the Application of Paints and Coatings (solids) OES)				
	Option 1	*Option 2*	*Option 1*	*Option 2*

Attributable Exposures	**[DEHP] x RPF_5 = [DBP] equivalents** I: 46.9 ug/kg DEHP x 0.27 = 12.7 ug/kg DBP equivalents D: 2.36 ug/kg DEHP x 0.27 = 0.637 ug/kg DBP equivalents	**[DEHP]** I: 46.9 ug/kg DEHP D: 2.36 ug/kg DEHP	**DEHP] x RPF_{40} = [DBP] equivalents** [E] I: 46.9 ug/kg DEHP x 0.83 = 39.0 ug/kg DBP equivalents D: 2.36 ug/kg DEHP x 0.83 = 1.96 ug/kg DBP equivalents	**[DEHP]** I: 46.9 ug/kg DEHP D: 2.36 ug/kg DEHP
Non-Attributable Exposure	**Σ([phthalates] x RPF_5)** (4.28 ug/kg DEHP x 0.27) + (0.48 ug/kg DBP x 1) + (0.30 ug/kg BBP x 0.08) + (0.40 ug/kg DIBP x 0.15) + (3.40 ug/kg DINP x 0.10) = 2.06 ug/kg DBP equivalents	**Σ([phthalates] x RPF_5)** (4.28 ug/kg DEHP x 0.27) + (0.48 ug/kg DBP x 1) + (0.30 ug/kg BBP x 0.08) + (0.40 ug/kg DIBP x 0.15) + (3.40 ug/kg DINP x 0.10) = 2.06 ug/kg DBP equivalents	**Σ([phthalate] x RPF_{40})** (4.28 ug/kg DEHP x 0.84) + (0.48 ug/kg DBP x 1) = (0.30 ug/kg BBP x 0.52) x (0.40 ug/kg DIBP x 0.53) = (3.40 ug/kg DINP x 0.21) = 5.16 ug/kg DBP equivalents	**Σ([phthalate] x RPF_{40})** (4.28 ug/kg DEHP x 0.84) + (0.48 ug/kg DBP x 1) = (0.30 ug/kg BBP x 0.52) x (0.40 ug/kg DIBP x 0.53) = (3.40 ug/kg DINP x 0.21) = 5.16 ug/kg DBP equivalents
MOE Calculations	**MOE = DBP $BMDL_5$ / DBP equivalents** [A] MOE_{CNA} = 984 ug/kg / 2.06 ug/kg = 478 MOE_{COUI} = 984 ug/kg / 12.7 ug/kg = 77.5 MOE_{COUD} = 984 ug/kg / 0.637 ug/kg = 1544	**MOE = DEHP $BMDL_5$ / DEHP exposure** [C] MOE_{COUI} = 3260 ug/kg / 46.9 ug/kg = 69.5 MOE_{COUD} = 3260 ug/kg / 2.36 ug/kg = 1381 **MOE_{CNA} = DBP $BMDL_5$ / DBP equivalents** 984 ug/kg / 2.06 ug/kg = 478	**MOE = DBP $BMDL_5$ / DBP equivalents** MOE_{CNA} = 2100 ug/kg / 5.16 ug/kg = 407 MOE_{COUI} = 2100 ug/kg / 39.0 ug/kg = 54 MOE_{COUD} = 2100 ug/kg / 1.96 ug/kg = 1072	**MOE = DEHP NOAEL / DEHP exposure** MOE_{COUI} = 1100 ug/kg / 46.9 ug/kg = 23 MOE_{COUD} = 1100 ug/kg / 2.36 ug/kg = 466 **MOE_{CNA} = DBP $BMDL_5$ / DBP equivalents** 2100 ug/kg / 5.16 ug/kg = 407
Cumulative MOE	**CumMOE = 1 / [(1/MOE_{CNA}) + (1/MOE_{COUI}) + (1/MOE_{COUD})]** 1/ [(1/478) + (1/77.5) + (1/1544)] = 64	**CumMOE = 1 / [(1/MOE_{CNA}) + (1/MOE_{COUI}) + (1/MOE_{COUD})]** 1/ [(1/478) + (1/69.5) + (1/1381)] = 58	**CumMOE = 1 / [(1/MOE_{CNA}) + (1/MOE_{COUI}) + (1/MOE_{COUD})]** 1/ [(1/407) + (1/54) + (1/1072)] = 46	**CumMOE = 1 / [(1/MOE_{CNA}) + (1/MOE_{COUI}) + (1/MOE_{COUD})]** 1/ [(1/407) + (1/23) + (1/466)] = 21

Key: I – inhalation; D – dermal; COU – condition of use; RPF – relative potency factor; MOE – margin of exposure; BHM – Bayesian Hierarchical Modeling

[A] For BHM approach, DBP $BMDL_5$ = 4.1 mg/kg, which is equivalent to an HED of 0.984 mg/kg

[B] For BHM approach, DCHP $BMDL_5$ = 2.3 mg/kg, which is equivalent to an HED of 0.552 mg/kg

[C] For BHM approach, DCHP $BMDL_5$ = 13.6 mg/kg, which is equivalent to an HED of 3.26 mg/kg

[D] the $BMDL_5$ values for the BHM approach are not the same as the $BMDL_5$ values from EPA's approach, as previously shown in Table 2

[E] EPA uses an RPF_{40} of 0.83 in this calculation, although the RPF_{40} is 0.84

The key to understanding the differences between the BHM and EPA MOE estimates is first to recognize that the BHM's estimates (PODs and RPFs) are all based upon the BMD_5 using the same analysis. In the case of the BHM, by calculating the POD using fetal testosterone data, the POD used in Option 2 will be similar to the one produced using Option 1. As a consequence, the MOEs are comparable for the BHM method. However, EPA, by identifying the most sensitive endpoint for Option 2, bases its PODs on different data than it uses in the CRA, resulting in a risk assessment that is based on an amalgam of biological endpoints. Thus, for EPA, the Option 2 approach for DEHP results in an MOE ~2x lower than the MOE calculated from Option 1 (i.e., DEHP appears more potent using Option 2 than Option 1).

Table 5: Summary of MOEs calculated using the state-of-the-science BHM approach compared to those given by the EPA TSD numerical examples (DCHP and DEHP).

	BHM		***EPA***	
	Option 1	**Option 2**	**Option 1**	**Option 2**
DCHP	11	13	29	51
DEHP	64	58	46	21

Key: BHM – Bayesian Hierarchical Modeling

For DEHP, the POD 4.6 mg/kg/day is provided by EPA's DEHP risk assessment. In contrast, EPA's meta-analysis BMD estimates the POD to be 11 based upon the BMD_5, and the BHM approach's BMD_5 yields a value of 13.3 mg/kg/day. As a result, Options 1 and 2 have different MOEs, as calculated by EPA, due to the incongruity of the POD calculations. This is not the case with the BHM approach, as all estimates are derived from the same analysis with the same endpoint. *Using the BHM approach, the MOEs for Option 1 and Option 2 are qualitatively the same*

Notably, the options as presented by EPA in the Revised Draft TSD both in at least some aspect rely on the use of point estimate RPFs derived from the Metafor analysis with significant limitations and flaws (see Comments 1 and 3, in response to Charge Questions 5f and 10). Overall, Option 1 is more consistent with CRA practices and the current state-of-the-science than Option 2. However, when the BHM approach (which is more consistent with the state of the science) is used, the results from Option 1 and Option 2 are similar.

4.3 Additional limitations and uncertainties in the inputs and implications of the CRA neutral to the selection of Option 1 or 2

Beyond the limitations identified pertaining to the exposure assessment assumptions and the meta-analysis modeling methods that have direct impacts on both Options 1 and 2, there are several other key limitations and uncertainties not directly tied to either option that have pervasive impacts on the risk assessment. These include:

- Limited Human Data - Much of the RPF derivation relies on animal data, with limited human epidemiological confirmation for some endpoints.

- Assumption of Additivity - The RPF approach assumes dose additivity, which may not fully capture potential interactions (synergistic or antagonistic) among phthalates.
- Unclear Risk Management Implications - It is currently unclear how EPA intends to use the results of the CRA to inform risk management decisions, particularly given that the RPF approach does not identify which specific phthalate(s) are driving the cumulative risk. Without this information, it is difficult to design targeted and effective risk management measures.

5 Charge Question 12 re: Application of CRA in Individual Chemical Risk Evaluations

5.1 EPA should move beyond single-substance CRA integration and develop an integrated CRA risk communication tool to support informed risk management decisions.

EPA's effort to incorporate CRA into individual phthalate risk evaluations is commendable. However, it remains unclear how these multiple single-substance CRA assessments will inform risk management decisions or support refined assessments beyond the screening-level analyses conducted thus far for regulatory decisions.

TSCA is inherently structured around chemical-by-chemical evaluations, while CRA demands a cross-chemical, systems-level approach (US EPA, 2025a). This misalignment complicates the integration of CRA into TSCA's statutory framework and limits its utility when integrated into single-substance evaluations. For example, integrating CRA into phthalate single substance risk evaluations has led to contradictory outcomes—such as an increased number of COUs with MOEs below the benchmark MOE for DCHP, and a decreased number for DEHP. The non-intuitive nature of these inconsistencies makes them difficult to reconcile in a risk management context and may confuse decision-makers. Moreover, the current CRA approach does not clearly identify:

- Which chemicals contribute most significantly to cumulative risk[8], and
- Whether all assessed chemicals are reasonably expected to contribute to risk under specific COUs.

This understanding is essential for enabling risk managers to simulate changes (e.g., removing a chemical or reducing exposure) and evaluate how such actions would alter the overall risk profile.

To improve the utility of CRA in risk management decision-making, it is recommended that EPA develop a risk communication tool that:

- Integrates and interprets results from both single-substance risk evaluations and the CRA.
- Provides qualitative and/or quantitative summaries of risk, including key assumptions, limitations, variability, and uncertainties.

[8] ACC provided suggestions on approaches to this end in in its April 28, 2023 comments on EPA's Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates (EPA, 2023a) and a Manufacturer Requested Phthalate Under the Toxic Substances Control Act (Docket No. EPA-HQ-OPPT-2022-0918-006) and in its 2013 comments on EPA's request for information and citation on methods for cumulative risk assessment (submitted to Docket ID no. EPA-HQ-ORD-2013-0292).

- Clearly identifies the individual substances or COUs that contribute most significantly to the cumulative risk and whether potential concern arises from individual chemicals or combined exposures.
- Supports comparative analysis of risk management options.

Such a tool would enhance transparency and help translate complex CRA findings into actionable insights for risk managers. For example, in occupational settings, implementing controls for one substance during a specific activity (such as engineering or administrative controls) will also reduce exposures to other substances used in the same context. For example, controlling for the particular phthalate found to be the primary driver of risk in an OES, would concurrently reduce exposures to co-occurring phthalates, thereby improving efficiency and effectiveness while maintaining health-protective outcomes.

As EPA develops a phthalate CRA communication tool, it must remain mindful of the statutory constraints of TSCA, particularly regarding:

- The scope of risk evaluations, and
- The permissible actions following an "unreasonable risk" determination.

As noted in ACC's comments on EPA's CRA approach (April 28, 2023 Docket No. EPA-HQ-OPPT-2022-0918-006, and May 20, 2025 EPA-HQ-OPPT-2018-0504-0125), even if a cumulative risk evaluation supports an "unreasonable risk" determination of some kind, EPA may not impose risk management requirements through a TSCA Section 6(a) rule on any individual chemical substance included in the cumulative risk evaluation that is not the driver of the cumulative risk and the "unreasonable risk" determination based upon such evaluation. Notably the statute does not allow EPA to group chemicals for the purposes of a Section 6(a) rule, which could circumvent the mandate that risk management for any chemical substance must be imposed only "to the extent necessary."

Additionally, TSCA 6(g) requires an exemption be granted "for a specific condition of use of a chemical substance or mixture" upon certain findings by the Administrator (15 U.S.C. § 2605(g)). Such criteria for exemption will take on more expansive meaning where the cumulative risk evaluation that serves as the basis for the Section 6(a) risk management rulemaking is not specific to a particular phthalate and where the result of that risk assessment is not driven (or dictated) by the phthalate in question, but instead, is driven (or dictated) by other phthalates included as part of the cumulative risk assessment.

Finally, while screening-level CRA can be a valuable first step, EPA should clarify when and how refined assessments will be pursued for regulatory decisions, ensuring that CRA evolves from a screening tool into a robust decision-support framework.

5.2 Inconsistent organization and data summaries between pertinent documents impair critical evaluation of the individual phthalate assessments and the CRA.

For ease of interpretation and comparison of the results, it would be helpful for EPA to organize and present the results in a similar fashion across the various documents. Summarizing results in similar tables (format, organization, and content) will allow for a more efficient analysis of the results and comparison across the various approaches and substances. This could also prevent transcription or calculation errors.

For example, in the DCHP Risk Evaluation document there is no summary table for the reported MOEs for all COUs/OES in the body of the document, but it was reported in the risk calculator file; however, the MOEs estimated using the DBP-equivalents are reported in the Risk Evaluation document. On the other hand, the MOEs using both approaches are reported in the DEHP Risk Evaluation document, however, the order in which the COUs are reported is different.

6 Charge Questions 1 Re: Environmental Fate and Transport of DEHP

EPA states that it is seeking feedback on data and methods related to the environmental fate of DBP, DCHP, and DEHP; however, the only charge question directly related to fate and transport pertains to DCHP. Comments related to the fate and transport of DEHP are provided herein.

6.1 EPA utilized the incorrect model prediction for DEHP environmental distribution which overestimates the distribution of DEHP in water and soil

Level III Fugacity Model in EPI Suite™ is used to predict the behavior of phthalates in and between multiple environmental compartments (including air, water, soil and sediment) (U.S. EPA, 2024b). This information is important for understanding the environmental data and identifying the major compartments of phthalates distribution. However, selection of certain settings is needed when the physical and chemical properties of a substance exceed the applicability domain of the default **Molecular Connectivity Index** (MCI) settings.

In the draft Physical Chemistry, Fate, and Transport Assessment for Diethylhexyl Phthalate (DEHP) (U.S. EPA, 2024b: p. 24), EPA states that *"When primarily released to water, approximately 46 to 62 percent of DEHP will partition to sediment, with the remaining fraction remaining in the water compartment. Under an equal release scenario, DEHP is expected to predominantly partition into the soil compartment at approximately 57 to 60 percent, with the remaining fractions partitioning to water (21%) or sediment (18%)"*. These predictions are derived from Level III Fugacity Model with the default setting of MCI method, which overestimates the partitioning in water and under-estimates the partitioning in sediments.

The octanol-water partition coefficient (log Kow) for DEHP is 7.6 (EPA, 2024b, this value was used as input for EPI™ Suite). Regarding the applicability domain of MCI Method, the EPI Suite™ report (U.S. EPA, 2020: p.22) indicated "*When the Log Kow is > 7, the* default *MCI Method may be underestimating the mass of material in sediment and overestimating the mass of material in the water column (biota). Consider using the results of the default EQC model.*"

Therefore, consistent with the EPI Suite™ recommendation, the results from EQC method should be used to predict the distribution and partitioning of DEHP in the environment and identify the major environmental compartment, instead of the results from the MCI Method.

For example, when DEHP is released equally from air, water and soil, according to EQC methods, DEHP is expected to predominantly partition in sediments (65.8%) (U.S. EPA, 2020), instead of soil as indicated in the draft report (U.S. EPA, 2024b). This is aligned

with the physical-chemical properties of DEHP, namely low water solubility and high Kow (U.S. EPA, 2024b). Table 5 compares the results from EQC and MCI methods, showing that the MCI method largely underestimates the portioning of DEHP in sediment and overestimates the ones in water and soil.

The results calculated with EQC method was only presented for the equal emission scenario (equal release from soil, air and water) (U.S. EPA, 2020). Three other emission scenarios (100% soil release, 100% air release and 100% water release) will need to be recalculated with EQC method. Figure 5-1 (U.S. EPA, 2024b: p.24) needs to be updated.

Table 5: Comparison of predicted partitioning of DEHP from two Level III Fugacity Models: EQC and MCI

	Mass Amount (%) EQC	**Mass Amount (%) MCI**	**Half-Life (hr)**	**Emissions (kg/hr)**
Air	0.321	0.67	11.7	1000
Water Water Biota suspended sediment	3.75 (0.136) (0.272) (3.34)	17.2 (5.44) (10.8) (0.976)	360	1000
Soil	30.1	62.8	720	1000
Sediment	65.8	19.3	3.24e+003	0
	Persistence Time: 1.29e+003 h			

6.2 EPA should include WWTP removal efficiency for calculation of environmental media concentration estimates as "refinement" for each exposure evaluation.

When modeling the environmental media concentrations, EPA assumed all releases were directly discharged to surface waters without prior treatment, and that no releases were routed through publicly owned treatment works prior to release. EPA recognizes that this is a conservative assumption that results in no removal of DEHP prior to release to surface water. Considering high removal efficiency of DEHP in wastewater treatment plant (WWTP) based on both modelled prediction (94% removal) by STPWIN™ in EPI Suite™ (U.S. EPA, 2020: p.22) and measured data (>64% in U.S. POTW) listed by EPA (U.S. EPA, 2024b: p.32), EPA should add WWTP removal for DEHP environmental media concentration estimations as refinement.

WWTP removal is included in the modelled environmental media concentration evaluation for DCHP (U.S. EPA, 2024c) and DINP (U.S. EPA 2025e), but not for DEHP (U.S. EPA, 2025f) or DBP (U.S. EPA, 2025g).

The draft technical documents of "Environmental Media Concentrations and General Population and Environmental Exposure Assessment" for DIBP and BBP are not yet released by EPA.

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