Comment Submitted in Response to Cumulative Risk Assessment; Science Advisory on Chemicals Committee (SACC) Virtual Public Meeting; Notice of Availability and Request for Comment;
Docket EPA-HQ-OPPT-2022-0918; 88 Fed. Reg. 12354 (Feb. 27, 2023)

April 28, 2023

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Executive Summary

These comments reflect the views of several entities (the Coalition), including the Butyl Benzyl Phthalate Consortium, the Dibutyl Phthalate Consortium, the Di-ethylhexyl Phthalate Consortium, the Di-isobutyl Phthalate Consortium, and the North American Metals Council. The Coalition represents more than 30 entities, consisting of trade associations, chemical manufacturers, processors, and downstream users that are all key stakeholders for the U.S. Environmental Protection Agency's (EPA) actions under Section 6 of the Toxic Substances Control Act (TSCA). We appreciate the opportunity to review and comment on this important issue and provide recommendations below to improve EPA's development of cumulative risk assessments (CRA) under TSCA. A summary of our concerns with each of the draft documents is provided below. Thereafter, the Coalition provides more detailed comments in the sections that follow.

The Coalition notes that EPA should expand the list of source documents relied upon, including for example, the chemical categories document developed by EPA's New Chemicals Program over the past 20-plus years, in the *Draft Proposed Principles of Cumulative Risk Assessment (CRA) under TSCA*. EPA should coordinate with and/or investigate all recent evaluations, such as those conducted within the Integrated Risk Information System (IRIS) program or by the Agency for Toxic Substances and Disease Registry (ATSDR), on a chemical substance group. EPA should also provide a more transparent discussion of its intent to use its information-gathering authorities under TSCA and the timeframe within which EPA intends to use those authorities. The Coalition believes that EPA would be better positioned to complete risk evaluations and CRAs if, for example, it established an earlier point in the risk evaluation process for communicating data gaps and scientific issues, such as before prioritization, to designate chemical substances as high-priority substances, although the Coalition understands that this was not practicable given the timelines for the phthalate prioritizations. Further, the Coalition believes that EPA should provide, at a minimum, the types of data sets that it would consider as sufficiently robust for supporting dose additivity and other approaches it discusses in the draft principles document.

The Coalition's primary concern with the *Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the Toxic Substances Control Act* document is the timing of its release. EPA has yet to issue its draft risk evaluations on the individual phthalates, yet the draft CRA document includes numerous preliminary scientific conclusions. These may change based on the public comments and peer-review recommendations that EPA receives from the TSCA Science Advisory Committee on Chemicals (SACC) on the individual substance risk evaluations. For example, EPA's evaluation of study quality on a toxicological study on an individual phthalate should be identical in the risk evaluation and the CRA.

The Coalition believes that EPA's proposal to use the relative potency factor approach for dose additivity is premature, given that EPA does not describe sufficiently why this approach is more appropriate for a CRA than, for example, the hazard index (HI) approach.

Finally, the draft document appears to be pre-decisional, since EPA has not completed its systematic review of the available information, and as noted, has not received public comments or peer-review recommendations from the TSCA SACC on any of the phthalate risk evaluations.

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Introduction

These comments are submitted on the U.S. Environmental Protection Agency's (EPA) *Draft Proposed Principles of Cumulative Risk Assessment under the Toxic Substances Control Act* and its proposed approach for applying those principles to the evaluation of the cumulative risk posed by certain phthalate chemicals undergoing Toxic Substances Control Act (TSCA) Section 6 risk evaluation in a document entitled *Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the Toxic Substances Control Act*. The coalition of consortia (Coalition) that has contributed to the preparation of these comments represents more than 30 entities, consisting of trade associations, chemical manufacturers, processors, and downstream users that are all key stakeholders for EPA's actions under TSCA Section 6. Although separate and distinct, all of these consortia exist for the purpose of chemical advocacy that is premised on the common principle of sound science.

Commenting Entities

Butyl Benzyl Phthalate Consortium membership includes manufacturers and importers of butyl benzyl phthalate (BBP) and was formed to serve as a platform for its members to address potential data needs and to advocate for the use of sound science in the risk evaluation of BBP.

Dibutyl Phthalate Consortium membership includes manufacturers and importers of dibutyl phthalate (DBP) and was formed to serve as a platform for its members to address potential data needs and to advocate for the use of sound science in the risk evaluation of DBP.

Di-ethylhexyl Phthalate Consortium membership includes manufacturers and importers of di-ethylhexyl phthalate (DEHP) and was formed to provide its members a platform to address potential data needs and to advocate for the use of sound science in the risk evaluation of DEHP.

Di-isobutyl Phthalate Consortium is composed of manufacturers, importers, and downstream users of di-isobutyl phthalate (DIBP). The mission of the DIBP Consortium is to serve as a platform to address scientific, regulatory, and product stewardship issues concerning the health, safety, and/or environmental aspects of DIBP, and to advocate for the use of sound science in the risk evaluation of DIBP.

North American Metals Council (NAMC) provides a collective voice for North American metals producers and users on science, regulatory, and policy-based issues that are unique to metals and the various stages of their life cycles -- sourcing, production, engineering, use, recycling, and recovery. NAMC members include trade associations and individual companies.

I. Draft Proposed Principles of Cumulative Risk Assessment (CRA) under TSCA

A. EPA Should Expand the List of Existing Documents It Intends to Rely on for Its Proposed Principles of CRA under TSCA

Under Section 3 of the *Draft Proposed Principles of Cumulative Risk Assessment under the Toxic Substances Control Act* (Draft Proposed Principles Document), EPA provides a

list of authoritative documents that it relied upon when preparing the Draft Proposed Principles Document.[1] We urge EPA to consider the following additional source documents. First, EPA's Office of Pollution Prevention and Toxics (OPPT) developed the *TSCA New Chemicals Program (NCP) Chemical Categories*, which includes 56 chemical categories that OPPT established for "chemicals with shared chemical and toxicological properties …."[2] OPPT may find this document useful for existing chemical substances, as it proceeds with considering additional cumulative chemical groups.

Second, OPPT established "low" hazard benchmarks for chemical substances that it used for identifying low-priority substances under Section 6 of TSCA.[3] These benchmarks may aid OPPT with determining whether members of a cumulative chemical group and specific endpoints warrant evaluation as part of a CRA. This consideration is consistent with EPA's *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (Mixtures Guidance), which states "When certain toxic effects are known to occur, but at much higher exposure levels than those being assessed, then the HI [hazard index] for those effects may not need to be evaluated …."[4]

Finally, the Coalition recommends that OPPT include the *Framework for Metals Risk Assessment*,[5] since this document includes discussion on "Mixtures and Interactions," which is appropriate for evaluating metal complexes under TSCA Section 6 and as part of CRAs.[6] This

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1 EPA, *Draft Proposed Principles of Cumulative Risk Assessment under the Toxic Substances Control Act*, EPA-740-P-23-001, Office of Chemical Safety and Pollution Prevention (Feb. 2023), at 7, available at https://www.epa.gov/system/files/documents/2023-02/Draft%20Principles%20of%20CRA%20under%20TCSA_0.pdf.

2 EPA, *TSCA New Chemicals Program (NCP) Chemical Categories*, OPPT, at ii (last revised Aug. 2010), available at https://www.epa.gov/sites/default/files/2014-10/documents/ncp_chemical_categories_august_2010_version_0.pdf.

3 *See*, *e.g.*, EPA, *Supporting Information for Low-Priority Substance 1-Butanol, 3-Methoxy-, 1-Acetate (CASRN 4435-53-4) (3-Methoxybutyl Acetate) Final Designation*, OPPT (Feb. 20, 2020), at 11-13, available at https://downloads.regulations.gov/EPA-HQ-OPPT-2019-0106-0011/content.pdf.

4 EPA, *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures*, EPA/630/R-00/002, Risk Assessment Forum Technical Panel (Aug. 2000), at 86, available at https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=4486.

5 EPA, *Framework for Metals Risk Assessment*, EPA 120/R-07/001 (Mar. 2007), at 4-14 to 4-16, available at https://www.epa.gov/sites/default/files/2013-09/documents/metals-risk-assessment-final.pdf.

6 *See*, *e.g.*, TSCA § 6(b)(2)(E), 15 U.S.C. § 2605(b)(2)(E).

would be consistent with the TSCA Section 6(b)(2)(E) requirement that EPA consider the Framework for Metals Risk Assessment in its prioritization and risk evaluations for metals and metal compounds.

B. EPA Should Specify When It Will Use Its Authorities under TSCA to Gather Existing Data or Require the Development of New Data to Aid the Grouping of Chemical Substances for CRA under TSCA

Under Section 3.4 of the Draft Proposed Principles Document, EPA states that it intends to group existing chemical substances based on "toxicologic similarity" and "evidence of co-exposure over a relevant timeframe."[7] EPA provides further details on these considerations under Sections 3.4.1 and 3.4.2, respectively. Under Section 3.4.1, "Toxicologic Similarity," EPA provides the continuum of effects, as identified in the Mixtures Guidance, that it intends to use for identifying cumulative chemical groups (*e.g.*, identical toxicodynamics or shared syndrome).[8] We agree with EPA's intended approach.

We note, however, that even for groups of chemicals that are well studied by one route of exposure, such as phthalates and oral exposures, data gaps may lead to significant uncertainties in the individual risk evaluations and the CRA, such as the absence of route-specific data for chemical substances (*e.g.*, dermal and inhalation) during a critical window of exposure. OPPT has not, however, provided any information on approaches it may use for informing these data gaps, other than stating that it "may use [its authority under TSCA Section 4] to require the development of data to inform the toxicological similarity of a group of chemical substances undergoing risk evaluation in a CRA."[9] EPA's actions to date do not support this planned approach to addressing data gaps in a timely manner, as discussed below.

As an example, we note that OPPT issued the final scope documents on individual phthalates in August 2020.[10] On June 29, 2021, EPA issued a direct final rule under TSCA Section 8(d) requiring manufacturers (including importers) of the phthalates undergoing TSCA risk evaluation to "report certain lists and copies of unpublished health and safety studies to EPA" by September 27, 2021.[11] OPPT has only very recently had follow-up conversations with entities that provided this information more than a year and a half ago and only after repeated requests for these

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7 Draft Proposed Principles Document, *supra* note 1, at 9.

8 *Id*. at 10.

9 *Id*. at 14.

10 *See*, *e.g.*, EPA, *Final Scope of the Risk Evaluation for Di-ethylhexyl Phthalate (1,2-Benzenedicarboxylic acid, 1,2-bis(2-ethylhexyl) ester) CASRN 117-81-7*, EPA-740-R-20-017 (Aug. 2020), available at https://www.epa.gov/sites/default/files/2020-09/documents/casrn_117-81-7_di-ethylhexyl_phthalate_final_scope.pdf.

11 86 Fed. Reg. 34147, 34149 (June 29, 2021).

initial meetings. Therefore, we believe it would be helpful to provide a hierarchy of the information OPPT will use for informing data gaps for route-specific data or simply state that OPPT will use conservative default assumptions and route-to-route extrapolations in CRAs, as it did in other final risk evaluations on individual chemical substances when route-specific data were lacking.[12]

Under Section 3.4.2 "Co-exposure Considerations," EPA states that it will evaluate "whether exposure to multiple chemical substances occur at toxicologically significant concentrations and over relevant and/or overlapping timeframes (*e.g.*, during a critical window of development)."[13] EPA lists several data sources that may be relevant for this determination, including product formulation data, workplace monitoring, facility releases, and environmental monitoring.[14] We agree with EPA's intended approach for assessing co-exposures; we question, however, EPA's failure to inform the public how it intends to obtain data regarding co-exposures. For example, EPA states that it "may use its test order authority to obtain further information on product formulation, emission testing, and manufacturing process information to support evidence of co-exposure."[15] While that is one approach to data gathering, we note that several members of the above-listed consortia have approached EPA and inquired about data needs and have only had an opportunity to meet with EPA in the past few weeks.

We believe EPA could address the above issues regarding data gaps on toxicological similarity and co-exposures by providing a roadmap in the Draft Proposed Principles Document that outlines the timing for up-front approaches it intends to use prior to designating existing chemical substances as high-priority substances, which may also undergo CRA. For example, EPA could hold webinars on their findings from prioritization and the data gaps and scientific issues identified, similar to what EPA's IRIS now does at the early stages of preparing its draft assessment materials.[16]

As an example, IRIS held a Public Science Meeting on January 11, 2023, for its assessment plan and protocol for evaluating cancer risk from cobalt and cobalt compounds.[17] An important scientific issue that came up during this discussion was the solubility of these substances. IRIS noted that EPA's Office of Air and Radiation (OAR) nominated "water-soluble and water-

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12 *See*, *e.g.*, EPA, *Final Risk Evaluation for 1,4-Dioxane CASRN: 123-91-1*, EPA-740-R1-8007 (Dec. 2020), at 164, available at https://www.epa.gov/sites/default/files/2020-12/documents/1._risk_evaluation_for_14-dioxane_casrn_123-91-1.pdf.

13 Draft Proposed Principles Document, *supra* note 1, at 10-11.

14 *Id*. at 12-13.

15 *Id*. at 14.

16 *See*, *e.g.*, EPA, *IRIS Public Science Meeting, January 11, 2023*, IRIS, 68 slides, available at https://ordspub.epa.gov/ords/eims/eimscomm.getfile?p_download_id=546178.

17 *Id*.

insoluble cobalt compounds for an inhalation cancer assessment."[18] The *IRIS Assessment Plan and Protocol for Cobalt and Cobalt Compounds (Cancer, Inhalation)* states that its initial scoping identified cobalt sulfate and cobalt metal as representative water-soluble and water-insoluble compounds, respectively, which were the "best suited for dose-response analysis."[19] Members of the public had an opportunity to comment and noted that scientific studies[20] have shown that cobalt sulfate and cobalt metal are both reactive substances, because they are highly soluble in biological fluids versus compounds like tricobalt tetraoxide, which is poorly reactive and poorly soluble in biological fluids.[21]

This finding was supported by higher tiered (biologically relevant) *in vitro* and *in vivo* studies, demonstrating the difference in upregulation of key biological markers between the two groups of substances. It is unclear whether IRIS will consider this key piece of information (*i.e.*, biological solubility versus water solubility) in its assessment. If so, it will change not only the representative compounds evaluated, but also the dose metric used, that is, deposited dose for biosoluble cobalt compounds versus retained dose for bioinsoluble compounds.

Since cobalt and cobalt compounds, as well as other metals,[22] are listed on EPA's TSCA Work Plan for Chemical Assessments, this key scientific issue will arise during EPA's future risk evaluation activities on metal compounds and CRAs that it may perform on these substances. The IRIS process illustrates the importance of early engagement with the public to ensure that scientific issues and data gaps are transparently communicated.

We mention this specific example with cobalt because EPA has demonstrated that it will not consider retained dose as a dose metric for bioinsoluble compounds in its risk evaluations. For example, EPA chose to use the deposited dose as the dose metric in the risk

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18 *Id*. at slide 11.

19 *Id*. at slide 17.

20 *See*, *e.g.*, Verougstraete *et al*. (2022), "A Tiered Approach to Investigate the Inhalation Toxicity of Cobalt Substances. Tier 1: Bioaccessibility Testing." *Regul. Toxicol. Pharmacol.*, 129, 105124, available at https://doi.org/10.1016/j.yrtph.2022.105124.

21 *IRIS Public Science Meeting, January 11, 2023*, *supra* note 16, at slide 59.

22 EPA, TSCA Work Plan for Chemical Assessments: 2014 Update, OPPT (Oct. 2014), at 7, available at https://www.epa.gov/sites/default/files/2015-01/documents/tsca_work_plan_chemicals_2014_update-final.pdf.

evaluation for C.I. Pigment Violet 29,[23] a poorly soluble and poorly reactive particle, despite the best available science that supports using retained dose as the dose metric.[24]

For EPA's risk evaluation activities, it should communicate scientific issues and identified data gaps to the public before prioritization or at least before designating a chemical as a high-priority substance. This would give members of the public an opportunity to provide feedback to EPA; it would also allow EPA to communicate its intent on using its authorities under, for example, TSCA Sections 8(a), 8(d), and, if necessary, Section 4, to obtain timely information to support risk evaluations and CRAs. EPA's authority under these sections of TSCA is focused on obtaining "reasonably available information," as EPA defined these terms in the regulations titled *Procedures for Prioritization of Chemical Substances for Risk Evaluation* and *Procedures for Chemical Substance Risk Evaluations*.[25,26]

This approach would notify members of the regulated community about the need for evaluating their chemistries, identifying potential data gaps that EPA may seek to inform through unpublished data and/or testing, and foster early engagement with EPA on potential testing strategies. It would also ensure that EPA receives data in time to ensure its use in risk evaluations and CRAs. We note that data availability was recognized as a limitation in EPA's *Framework for Cumulative Risk Assessment*, which states "identification of critical information and research needs may be the primary result of many cumulative risk assessment endeavors."[27] The amended authorities under TSCA (*e.g.*, TSCA Section 4 order authority) can aid with advancing the generation of data to inform EPA's individual risk evaluations and CRAs and avoid default values, but only if EPA engages at the early stages of its intended TSCA Section 6 activities.

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23 EPA, *Risk Evaluation for C.I. Pigment Violet 29 (Anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,3,8,10(2H,9H)-tetrone) CASRN: 81-33-4*, 740-R-18-015 (Jan. 2021), at 67-68, available at https://www.epa.gov/sites/default/files/2021-01/documents/1_final_risk_evaluation_for_c.i._pigment_violet_29.pdf.

24 *See*, *e.g.*, 86 Fed.Reg. 15476, 15477 (Mar. 23, 2021).

25 40 C.F.R. § 702.3.

26 40 C.F.R. § 702.33.

27 EPA, *Framework for Cumulative Risk Assessment*, EPA/630/P-02/001F, Risk Assessment Forum (May 2003), at xii, available at https://www.epa.gov/sites/default/files/2014-11/documents/frmwrk_cum_risk_assmnt.pdf.

C. EPA Should Communicate the Minimum Types of Data It Will Require for Justifying Dose Additivity Approaches

Under Section 3.5 of the Draft Proposed Principles Document, EPA proposes using the default assumption of dose additivity for cumulative chemical groups.[28] We agree with this approach, noting that the data requirements generally increase from basic HI methods, to relative potency factor (RPF) methods, to interactive HI methods.

EPA does not, however, provide any information on, for example, the minimum types of data that it would require to support the use of one of these approaches over another. EPA acknowledges that "Deciding, …, which chemical substances to include in a cumulative chemical group that subsequently would be evaluated using dose additive models is an important element of a CRA."[29]

We agree with this statement, and we expect that EPA will engage with the stakeholder community on its intended use of its information-gathering authorities under TSCA in forming chemical groups and determining what communication of dose additivity approach should be used in each case.

D. EPA Should Consider All of Its Information-Gathering Authorities under TSCA and the Appropriate Time to Use These Authorities

Under Section 3.6 of the Draft Proposed Principles Document, EPA discusses its approaches for addressing data gaps, yet limits the discussion to authorities under TSCA Section 4. We encourage EPA to expand this section to include its information-gathering authorities under TSCA Sections 8(a), 8(d), and 11.

We encourage EPA to provide information on the timing of its intent to use these authorities. We urge this because EPA's use of its authority under TSCA Section 4, to date, has not been as efficient as it could be in generating data for a variety of reasons. EPA issued the test orders a year or more (*i.e.*, January 2021 through August 2022)[30] after it had designated the subject chemical substances as high-priority substances (*i.e.*, December 30, 2019)[31] and started the three-

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28 Draft Proposed Principles Document, *supra* note 1, at 14.

29 *Id*.

30 EPA, *List of Chemicals Subject to Section 4 Test Orders*, Assessing and Managing Chemicals under TSCA (last updated Jan. 4, 2023), available at https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/list-chemicals-subject-section-4-test-orders.

31 84 Fed. Reg. 71924 (Dec. 30, 2019).

to three-and-a-half-year statutory timeline for completing the risk evaluations.[32] Testing has been delayed by a variety of scientific and, in some cases, legal issues -- issues that could perhaps be resolved by engaging with stakeholders in advance to identify data needs. We recognize EPA has made progress in this regard, and we are appreciative of EPA's efforts.

E. EPA Should Consider Refinements When Default Screening Approaches Suggest Unreasonable Risk

Under Section 3.7 of the Draft Proposed Principles Document, EPA summarized CRA refinement considerations and stated "refinements are typically made when lower tier cumulative assessments that rely on highly conservative assumptions do not demonstrate an adequate margin of exposure (MOE)."[33] We agree with this approach but note that it is inconsistent with EPA's past practices. For example, EPA retained its default conservative assumptions in the final *Risk Evaluation for n-Methylpyrrolidone (2-Pyrrolidoninone, 1-Methyl- (NMP)*, despite receiving extensive information from the Semiconductor Industry Association on its workplace controls, information that EPA concluded was "high quality" data.[34]

We question whether EPA will make refinements to its CRAs, if it is unwilling to make refinements to individual risk evaluations. Further, Section 3.7 includes a discussion of the World Health Organization (WHO)/International Program on Chemical Safety (IPCS) framework that states "Tier 0 hazard assessments may group chemical substances based on a conservative assumption of dose addition with limited evidence of toxicological similarity (*e.g.*, predictive hazard tools might be used to group chemical substances based on similar target organ) …."[35]

In comparison, EPA stated under Section 3.4.1 that it "is unlikely to conduct CRAs under TSCA when the reasonably available information is limited to an effect on the same target organ as this approach may introduce too much uncertainty to risk estimates."[36] We recommend for clarity that EPA limit its discussion on CRA refinement considerations to those that it intends to use.

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32 TSCA § 6(b)(4)(G), 15 U.S.C. § 2605(b)(4)(G).

33 Draft Proposed Principles Document, *supra* note 1, at 14.

34 *See*, *e.g.*, Cardno ChemRisk, *Review of TSCA Section 6 Risk Evaluation of the Conditions of Use of NMP in the Semiconductor Industry* (May 24, 2021), available at https://www.epa.gov/sites/default/files/2021-06/documents/final-chemrisk-review-nmp.pdf.

35 Draft Proposed Principles Document, *supra* note 1, at 14.

36 *Id*. at 10.

II. Draft Proposed Approach for CRA of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the TSCA

A. EPA Should Reconsider the Timing for Proposing a CRA Approach for Phthalates

The timeline for EPA to complete the final risk evaluations on the phthalates designated as high-priority substances under TSCA and on the phthalates for manufacturer-requested risk evaluations is approximately **June 2023**. As of the date of these comments, EPA has not issued a single draft risk evaluation on a phthalate. EPA's intent on conducting a CRA on phthalates now appears to be ill-timed because the underlying science from the support documents for the CRA (*i.e.*, the individual phthalate risk evaluations) has not undergone public comment or peer review by the TSCA SACC, yet EPA has made preliminary "weight of evidence" conclusions on the science to support a CRA on phthalates. EPA may instead wish to consider a CRA on phthalates after the draft risk evaluations have been proposed and EPA has received comments from the public and the SACC.

The Coalition also notes that the conditions of use (COU) for phthalate substances have been changing over the past five to ten years. While the COUs that EPA identified during the risk evaluation scoping process may have been relevant at that time, the market and COUs continue to evolve. EPA should verify its previous view of the COUs before using risk evaluation scope documents to identify where co-exposures may exist. It is likely some COUs have been phased out, and assuming certain COUs continue would lead to a mischaracterization of potential co-exposures in the evaluation of cumulative risk.

B. EPA Should Evaluate Phthalates Using the HI and RPF Approaches

EPA stated that it is "proposing to use an RPF approach for the phthalate CRA conducted in support of TSCA section 6 risk evaluations."[37] EPA acknowledged that the National Research Council (NRC) "concluded that RPFs cannot be recommended for phthalates …."[38] EPA noted, however, that "the science has evolved since the NRC made their recommendation against the use of RPFs."[39] The Coalition has two concerns with EPA's proposal for using only an RPF approach. First, EPA has not completed its systematic review of the available information on

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37 EPA, *Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate under the Toxic Substances Control Act* (Draft Proposed Approach for CRA on Phthalates) (Feb. 2023), EPA-740-P-23-002, at 102, available at https://www.epa.gov/system/files/documents/2023-02/Draft%20Phthalate%20CRA%20Approach.pdf.

38 *Id*. at 101-102.

39 *Id*. at 102.

phthalates, as required for making its weight of scientific evidence determination.[40] Second, EPA acknowledged that a "source of uncertainty is [the] lack of inhalation and dermal studies [on phthalates] that include an exposure that covers the critical window of development."[41] These represent significant data gaps that EPA proposed using route-to-route extrapolation to fill.[42]

Given these uncertainties and EPA's intent on evaluating oral, inhalation, and dermal exposures, we recommend that EPA perform its CRA using the HI and RPF approaches. This will ensure that EPA documents the associated uncertainties with each approach. It will also ensure that the TSCA SACC has an opportunity to peer review both approaches and to make recommendations to EPA.

C. EPA Should Characterize Its Scientific Conclusions as Preliminary and Not as Apparent Conclusions of Law

The 2016 amendments to TSCA included specific scientific standards, including "weight of scientific evidence."[43] These terms were not defined under TSCA; rather, the amended text of TSCA simply stated that "The Administrator shall make decisions under sections 4, 5, and 6 based on the weight of the scientific evidence."[44] EPA subsequently defined these terms under 40 C.F.R. Section 702, Subpart B as:[45]

> [A] systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently, identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance.

In comparison, EPA states the following in the Draft Proposed Approach for CRA on Phthalates:[46]

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40 40 C.F.R. § 702.33.

41 Draft Proposed Approach for CRA on Phthalates, *supra* note 37, at 91.

42 *Id*.

43 TSCA § 26(i), U.S.C. 15 § 2625(i).

44 *Id*.

45 40 C.F.R. § 702.33.

46 Draft Proposed Approach for CRA on Phthalates, *supra* note 37, at 18.

> At the date of publication of this document, EPA has not yet completed all the expected systematic review or data quality evaluation for the individual high-priority and manufacturer-requested phthalates.

EPA acknowledges that it has not yet fulfilled the above legal requirement, it nonetheless used "weight of evidence" throughout the Draft Proposed Approach for CRA on Phthalates. For example, EPA states under Section 7, "Summary of Proposed Approach and Next Steps," that "Based on the weight of evidence, EPA proposes that DEHP, BBP, DBP, DIBP, DCHP, and DINP, but not DIDP, are toxicologically similar and induce effects on the developing male reproductive system consistent with phthalate syndrome."[47]

We question EPA's use of this terminology, given that "weight of evidence" and "weight of scientific evidence" are often used interchangeably. This gives the appearance that EPA has already made *final* conclusions on these points, when in fact, EPA's conclusions are *preliminary* conclusions based on the weight of evidence. EPA may wish to add a caveat to these statements, as they appear pre-decisional in the absence of EPA's application of a systematic review method consistent with the regulatory and statutory requirements under TSCA.

Conclusion

The Coalition supports EPA's intent to consider CRA as part of its TSCA Section 6 activities and agrees with EPA that CRA may represent the best available science for specific groups of chemical substances. The Coalition does, however, have concerns that EPA has yet to implement TSCA in a manner that is suited for efficiently completing risk evaluations and possibly CRAs within the statutory timeframes.

EPA could improve its processes by incorporating stakeholder outreach earlier in the process of screening and prioritizing chemical substances so that data gaps and scientific issues are communicated to the public earlier in the process. EPA has recently begun communication with three of the phthalate consortia to discuss data gaps and opportunities to close those gaps, and those consortia appreciate EPA's willingness to engage.

EPA should be more transparent in the types of data sets it considers relevant for different approaches it may use in assessing chemical substances as part of a CRA (*e.g.*, dose additivity approaches). The Coalition was pleased to see that EPA is considering alternative approaches to performing *in vivo* testing (*e.g.*, route-to-route extrapolation) and hopes that EPA will consider a tiered approach to reduce uncertainties, consistent with EPA's obligation to use the best available science and to minimize vertebrate testing.

The Coalition also encourages EPA to re-issue the draft CRA documents for another round of public comment, once EPA addresses the feedback it receives from the public and the SACC.

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47 *Id*. at 149.