November 21, 2019

Comments from Academics, Scientists and Clinicians on Proposed High-Priority Substance Designation Under the Toxic Substances Control Act (TSCA)

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These comments are submitted on behalf of the undersigned academics, scientists, and clinicians. We declare collectively that we have no direct or indirect financial or fiduciary interest in any chemical or product that is the subject of these comments. The co-signers' institutional affiliations are included for identification purposes only and do not imply institutional endorsement or support.

We appreciate the opportunity to provide written comments on the proposed high-priority chemical designations, issued under EPA's Toxic Substances Control Act (TSCA), as amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act ("amended TSCA").[1] TSCA defines a high-priority chemical as "a chemical substance that the Administrator concludes, without consideration of costs or other nonrisk factors, may present an unreasonable risk of injury to health or the environment because of a potential hazard and a potential route of exposure under the conditions of use, including an unreasonable risk to a potentially exposed or susceptible subpopulation."[2] All of the chemicals EPA has proposed for high priority designation meet this definition.

Based on EPA's prioritization process, high-priority chemicals, upon final designation, will immediately move into the risk evaluation process. For the risk evaluation, both TSCA[3] and EPA's regulation[4] require adequate information to make a determination of whether or not a chemical poses an unreasonable risk. The regulation also requires the evaluation of "relevant" potential human and environmental hazards.[5] We have previously commented on inadequacies in EPA's risk evaluation process, as have EPA's Science Advisory Committee on Chemicals (SACC) peer reviewers.[6, 7]

We have previously commented that we agree with EPA's "low bar" to designate a chemical as high-priority, as it is consistent with modern science based decision-making, where decisions reflect the extent to which we can be confident that desirable effects of an intervention outweigh its undesirable

[1] 84 FR 44300
[2] 15 USC §2605
[3] 15 USC §2601 (b)(1)
[4] 40 CFR § 702.41 (b)
[5] 40 CFR § 702.41 (d)(3)
[6] US EPA. (2019). Toxic Substances Control Act (TSCA) Science Advisory Committee on Chemicals Review of Risk Evaluation for 1, 4 Dioxane; SACC July 2019 Meeting Minutes and Final Report Docket. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063
[7] US EPA. (2019). Toxic Substances Control Act (TSCA) Science Advisory Committee on Chemicals Review of Risk Evaluation for 1-Bromopropane; Comment submitted by Swati Rayasam, Science Associate, Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco et al. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0053

effects for an individual.[8] However, we have concerns around the methodology with regard to consistency and transparency. We also recommended that any approach EPA uses for prioritization and onward should consider hazard over exposure, as hazards are intrinsic chemical properties while exposures can change over time.[9] At this stage, it is critical for EPA to obtain all reasonably available[10] information for high-priority candidates needed to complete comprehensive, scientifically accurate risk evaluations, assessing all conditions of use throughout lifecycle including disposal. In a recent decision by the U.S. Court of Appeals for the Ninth Circuit on challenges to the risk evaluation rule, the court ruled that EPA's exclusion of legacy activities was a violation of the plain language of TSCA, finding its rationale for the exclusion "without merit." [11] Therefore, EPA must revise its approach to TSCA risk evaluations to account for chemicals' uses and exposures per the court's decision.

Further, all relevant health hazards must be evaluated. Certain health hazards are specifically designated in TSCA, indicating that Congress expressly recognized these types of health effects as an unreasonable risk, and envisioned that EPA should assess them: "cancer/ carcinogenesis, mutagenesis/ gene mutation, teratogenesis, behavioral disorders, and birth defects."[12] Because adequate information is critical for decision-making on the high-priority chemicals, it is imperative that EPA determine the completeness of the database on the 20 high-priority chemicals, and quickly move forward to fill identified data gaps.

Our comments address the following main points:

EPA's Prioritization Process:

1. **EPA's approach for identifying, evaluating and summarizing data on human health hazards for the first 20 chemicals designated as high-priority substances are ad hoc, non-transparent, inconsistent with the Agency's mandate, and likely to have resulted in a biased evidence base.**

EPA's Risk Evaluation Process:

1. **Before beginning the risk evaluation process for the first 20 high-priority chemicals designated as high-priority substances, EPA must address the comments from the Science Advisory Committee on Chemicals (SACC) on the Draft Risk Evaluations for1,4-Dioxane and Cyclic Aliphatic Bromide Cluster (HBCD) through changes to its systematic review process and implement such changes for future TSCA risk evaluations.**

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[8] US EPA. (2017). Procedures for Prioritization of Chemicals for Risk Evaluation under the Toxic Substances Control Act; Comment submitted by J. Lam et al. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2016-0636-0071

[9] US EPA. (2018). Approaches for Identifying Potential Candidates for Prioritization for Risk Evaluation Under Amended TSCA; Comment submitted by Veena Singla, PhD, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF) et al. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2017-0586-0077

[10] 15 USC §2625 (k) requires the Administrator to consider all reasonably available information in the prioritization process; EPA's prioritization rule states: "Reasonably available information means information that EPA possesses or can reasonably generate, obtain and synthesize for use, considering the deadlines specified in 15 U.S.C. 2605(b) for prioritization and risk evaluation. Information that meets such terms is reasonably available information whether or not the information is confidential business information that is protected from public disclosure under 15 U.S.C. 2613." The preamble to the rule notes, "EPA agrees that it makes sense to view information that can be obtained through testing as 'reasonably available'…" 82 FR 33753

[11] *Safer Chemicals, Healthy Families v USEPA* (2019). No. 17-72260 (9th Cir. Nov. 14, 2019). Pg. 53. *"EPA's contention that TSCA can reasonably be read to refer to the future use of a product, and disposals associated with such use, only when the product will also be manufactured in the future for that use—and not when the product is no longer manufactured for the relevant use—is without merit. TSCA's "conditions of use" definition plainly addresses conditions of use of chemical substances that will be used or disposed of in the future, regardless of whether the substances are still manufactured for the particular use."*

[12] 15 USC §2603 (b)(2)(A); 15 USC §2603 (e); 15 USC §2605 (b)(2)(D)

2. **EPA should use a cumulative approach assessing all common adverse health outcomes for the risk evaluations of phthalates and chlorinated solvents.**
3. **EPA should proceed immediately with developing the information needed to fill data gaps on the flame retardants TPP, TCEP, and TBBPA.**

We appreciate the opportunity to provide public input. Please do not hesitate to contact us with any questions regarding these comments.

Sincerely,

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DETAILED COMMENTS

EPA's Prioritization Process

1. **EPA's approach for identifying, evaluating and summarizing data on human health hazards for the first 20 chemicals designated as high-priority substances are ad hoc, non-transparent, inconsistent with the Agency's mandate, and likely to have resulted in a biased evidence base.**

While we agree that the evidence EPA has presented for each chemical meets the definition of high priority in the statute, there are major scientific issues with EPA's approach that will affect the accuracy of the risk evaluations moving forward, and will affect the designation of future high priority chemicals. EPA must address these issues by responding to previous public comments and updating the document 'A Working Approach for Identifying Potential Candidate Chemicals for Prioritization' accordingly.

'A Working Approach for Identifying Potential Candidate Chemicals for Prioritization' states:

> "*TSCA requires that EPA use information in a manner consistent with the best available science and that EPA base decisions on the weight of the scientific evidence.* ***Through the prioritization and risk evaluation process, EPA plans to use a step-wise approach that is consistent with the TSCA science standards****. When gathering information to support the priority designation,* ***EPA plans to integrate elements of quality in the data eligibility criteria*** *during the screening process."* [13] (emphasis added)

There are two major scientific problems with EPA's approach to designation of high-priority chemicals, that are similar to methodological problems we commented on previously in designation of low priority chemicals.[14] First, EPA has not used an approach 'that is consistent with the TSCA science standards' or with currently accepted validated methods to systematically search, evaluate and synthesize data to inform the conclusions on human health hazards. Second, EPA has again changed its criteria for evaluating data quality. The greatest concern is that the 'elements of quality' used during the screening

[13] US EPA (2018). A Working Approach for Identifying Potential Candidate Chemicals for Prioritization September. Pp 13. Available: https://www.epa.gov/sites/production/files/201809/documents/preprioritization_white_paper_9272018.pdf
[14] Proposed Low-Priority Substance Designation Under the Toxic Substances Control Act (TSCA); Comment submitted by Veena Singla, PhD, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF) et al. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0106-0007

process to assess the eligibility of data, which have not been peer-reviewed, are not reported in any of the proposed designation documents, with no information about the development process or rationale for the new criteria. EPA's high-priority methods are ad hoc, non-transparent and inconsistent with the Agency's mandate.

TSCA science standards

As stated in 'A Working Approach for Identifying Potential Candidate Chemicals for Prioritization' EPA is required to use an approach 'that is consistent with the TSCA science standards', utilizing a weight-of-scientific-evidence approach **'through the prioritization and risk evaluation process.'** We have previously commented that EPA has codified a definition of "weight of the scientific evidence" in its risk evaluation rule as 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.'' [15,16]

Therefore, EPA has repeatedly failed to adhere to this requirement by failing to '*use a pre-established protocol*' or reporting the methods and processes used to select and evaluate the evidence in designating the first 20 chemicals as high-priority substances for upcoming risk evaluations in sufficient detail. 'Proposed High-Priority Substance Designations Under the Toxic Substances Control Act (TSCA)' states:

"EPA developed a document for each substance to identify the information, analysis and basis used to support the proposed designations as a High-Priority Substance for risk evaluation… Also included in each document is an explanation of the approach used by EPA to conduct the review" [17]

However, there is little information or 'explanation of the approach used by EPA to conduct the review' in any of proposed substance designations. For example, in the Proposed Designation of 1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-Hexamethylcyclopenta[γ]-2-Benzopyran (HHCB; CASRN 1222-05-5) EPA's explanation of its method to identify human health endpoints is limited to a few sentences:

"EPA considered reasonably available information from peer-reviewed assessments and databases to identify potential human health and environmental hazards for HHCB … EPA identified potential human health and environmental hazards based on a review of the reasonably available information for HHCB … EPA identified potential human health and environmental hazards based on a review of the reasonably

[15] US EPA (2019). Proposed Low-Priority Substance Designation Under the Toxic Substances Control Act (TSCA); Comment submitted by Veena Singla, PhD, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF) et al. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0106-0007

[16] 40 CFR 702.33

[17] US EPA (2019). Proposed High-Priority Substance Designations Under the Toxic Substances Control Act (TSCA). Pp 44302. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0446-0008

available information for HHCB. In addition, EPA received comments with references to studies identifying potential human health and environmental concerns." [18]

The lack of consistency with EPAs mandate to use an 'approach that is consistent with the TSCA science standards' and lack of transparency with its approach, is deeply concerning. These first 20 high-priority chemicals will set a precedent for how future evaluations will be conducted by EPA. Therefore, if in future evaluations chemicals are classified 'low-priority' and the methods and processes are reported as opaquely as they have been for these first 20 chemicals, there will be insufficient evidence to validate the decisions that have been made and hazardous chemicals may not go through the necessary risk evaluation process. Therefore, EPA **must be consistent** with its approach in designating chemicals as 'high-priority' and implement validated systematic review methods to assess chemical hazards.

Data Quality Criteria

EPA states in 'A Working Approach for Identifying Potential Candidate Chemicals for Prioritization':

"The initial emphasis will be the exclusion of unacceptable data sources based on data quality criteria outlined in the Application for Systematic Review in TSCA Risk Evaluations EPA document. Specifically, these criteria identify serious flaws that would make the information unreliable to use for risk evaluation purposes. This increases the efficiency of EPA's systematic review efforts by excluding unacceptable data sources early in the process for those chemical substances that may enter risk evaluation through a high-priority designation."[19]

We have previously commented to EPA and in a peer-reviewed commentary on the scientific flaws in the TSCA systematic review method and its approach to evaluating the quality of the included data that may lead to the exclusion of a study, due to one 'serious flaw.'[20,21,22] However, it is even more concerning that EPA has now been 'excluding unacceptable data sources' that will not be considered in its high-priority risk evaluations using an ad hoc method that has not been peer-reviewed or without documenting the evaluation process in any of the proposed substance documents. Therefore, the process that EPA has used to assess the quality of the data raises serious concerns for: 1) the future risk evaluations of the 20 chemicals already designated as high-priority substances, as evidence has now been removed from the evidence base without any justification; and 2) any future designations, as future 'high-priority' chemicals may be downgraded to 'low-priority' if studies are excluded based on "serious flaws that would make the information unreliable to use for risk evaluation purposes" without any reporting of the evaluation process.

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[18] US EPA (2019) Proposed Designation of 1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-Hexamethylcyclopenta[γ]-2-Benzopyran (HHCB; CASRN 1222-05-5) as a High-Priority Substance for Risk Evaluation. Pp 14. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0430-0010.

[19] US EPA (2018). A Working Approach for Identifying Potential Candidate Chemicals for Prioritization September. Pp 13-14. Available: https://www.epa.gov/sites/production/files/201809/documents/preprioritization_white_paper_9272018.pdf

[20] EPA (2018) Application of Systematic Review in TSCA Risk Evaluations.

[21] US EPA (2018) Problem Formulations for the Risk Evaluations to be Conducted for the First Ten Chemical Substances under the Toxic Substances Control Act, and Application of Systematic Review in TSCA Risk Evaluations; Notice of Availability, Comment submitted by Veena Singla, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco et al. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0210-0107

[22] Singla, V. I., Sutton, P. M., & Woodruff, T. J. (2019). The Environmental Protection Agency Toxic Substances Control Act Systematic Review Method May Curtail Science Used to Inform Policies, With Profound Implications for Public Health. *American Journal of Public Health*, *109*(7), 982–984. doi:10.2105/AJPH.2019.305068

We therefore once again recommend EPA use either of two previously validated methods, the Navigation Guide[23] or the Office of Health Assessment and Translation,[24] to assess the quality of the evidence. We also strongly recommend that EPA present the criteria used to assess the 'data quality' and all data evaluations that have been conducted to assess the first 20 chemicals designated as high-priority substances. EPA must clearly report any data that have been excluded from the future risk evaluation process due to 'serious flaws' and detail their justifications.

Formaldehyde IRIS Assessment

In EPA's proposed designation for formaldehyde document, [25] despite previously stating that the formaldehyde IRIS assessment will inform the prioritization process, the Agency fails to reference the stalled IRIS assessment even once, citing the 1989 IRIS assessment and the 2011 NRC review.[26]

EPA must **immediately** release the recently updated IRIS assessment for public comment and NAS review so that the TSCA office can directly utilize the extensive work already done by NAS and IRIS scientists. The NAS' most recent review of the IRIS program's implementation of systematic review found it to be robust.[27] Additionally, a 2019 report from the Government Accountability Office raised concerns about potential political interference through EPA leadership's unexplained directive to halt the formaldehyde assessment.[28]

EPA's Risk Evaluation Process:

1. **Before beginning the risk evaluation process for the first 20 high-priority chemicals designated as high-priority substances, EPA must address the comments from the Science Advisory Committee on Chemicals (SACC) on the Draft Risk Evaluations for1,4-Dioxane and Cyclic Aliphatic Bromide Cluster (HBCD) through changes to its systematic review process and implement such changes for future TSCA risk evaluations.**

The Science Advisory Committee on Chemicals (SACC) has made several recommendations on how EPA needs to improve the TSCA Systematic review process following its evaluation of 1,4-dioxane and Cyclic Aliphatic Bromide Cluster (HBCD). We have previously commented on recommendations made to EPA

[23] Woodruff TJ, Sutton P. The Navigation Guide systematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. Environ Health Perspect. 2014;122(10):1007-1014.
[24] National Toxicology Program (NTP). Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration. Research Triangle Park, NC: National Toxicology Program; 2015.
[25] US EPA. (2019). Formaldehyde; TSCA Review; Proposed Designation of Formaldehyde (CASRN 50-00-0) as a High-Priority Substance for Risk Evaluation. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0438-0013
[26] US EPA. (2019). Reaching Another TSCA milestone, EPA Identifies 40 Chemicals to Prioritize for Risk Evaluation Available: https://www.epa.gov/newsreleases/reaching-another-tsca-milestone-epa-identifies-40-chemicals-prioritize-risk-evaluation
[27] National Academies of Sciences, Engineering, and Medicine. 2018. *Progress Toward Transforming the Integrated Risk Information System (IRIS) Program: A 2018 Evaluation*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25086.
[28] US GAO (2019) Chemical Assessments: Status of EPA's Efforts to Produce Assessments and Implement the Toxic Substances Control Act. Available: https://www.gao.gov/assets/700/697212.pdf

by the SACC following its evaluation of the Draft Risk Pigment Violet 29 (PV29)[29,30] that echo the recommendations made once again here. Below, we highlight the SACC's recommendations on EPA's systematic review process that must be addressed before it commences the risk evaluations of the high-priority chemicals:

Recommendation 1. *"Document how all the information was gathered and evaluated for possible use. This includes how previous chemical assessments, such as those done by EPA, were selected that formed the basis of the systematic review for this Evaluation."* [31]

Recommendation 4. *"Be more descriptive and transparent in how sources were identified and evaluated."* [32]

In the SACC review of 1,4-dioxane the committee "did not find the systematic review to be a transparent and objective method for gathering the relevant scientific information, scoring its quality, and integrating the information," while they concluded that "EPA should document how all the information was gathered and evaluated for possible use." [33] EPA's July 2017 risk evaluation framework rule defines systematic review as a comprehensive, consistent and transparent process to "identify and evaluate each stream of evidence" and "to integrate evidence as necessary and appropriate based on strengths, limitations, and relevance."[34] Therefore, the current methods being employed by EPA using the TSCA systematic review process are not consistent with this definition and have mostly likely resulted in biased reviews and therefore unreliable risk evaluations.

We again strongly recommend that EPA use one of the existing empirically based systematic review methodologies for its TSCA risk evaluations, including the Navigation Guide[35] and the Office of Health Assessment and Translation (OHAT)[36] to improve the objectivity and transparency of the review process in order to minimize bias. These methods have been peer-reviewed, validated and recommended for use in chemical evaluations by the National Academies of Science (NAS),[37] while the Navigation Guide methodology is currently being utilized by the World Health Organization to assess the global burden of work-related injury and disease.[38] The SACC committee for 1,4-dioxane and HBCD stated clearly:

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[29] US EPA (2019) Draft Risk Evaluation for 1-Bromopropane. Comment submitted by Swati Rayasam, Science Associate, Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco et al. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0053

[30] US EPA (2019) Peer Review of the Draft Risk Evaluation for Pigment Violet 29 (PV29). Available: https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2018-0604 D=EPA-HQ-OPPT-2018-0604

[31] US EPA (2019) SACC July 2019 Meeting Minutes and Final Report Docket. Pp 37 Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063.

[32] US EPA (2019) SACC July 2019 Meeting Minutes and Final Report Docket. Pp 38 Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063.

[33] US EPA (2019) SACC July 2019 Meeting Minutes and Final Report Docket. Pp 31. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063

[34] 40 C.F.R. 704.33.

[35] Woodruff TJ, Sutton P. The Navigation Guide systematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. Environ Health Perspect. 2014;122(10):1007-1014.

[36] National Toxicology Program (NTP). Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration. Research Triangle Park, NC: National Toxicology Program; 2015.

[37] The National Academies of Sciences. *Application of Systematic Review Methods in an Overall Strategy for Evaluating Low-Dose Toxicity from Endocrine Active Chemicals.* Washington, D.C.: National Academies Press; 2017.

[38] Mandrioli, D., Schlünssen, V., Ádám, B., Cohen, R. A., Colosio, C., Chen, W., … Scheepers, P. T. J. (2018, October 1). WHO/ILO work-related burden of disease and injury: Protocol for systematic reviews of occupational exposure to dusts and/or fibres and of the effect of occupational exposure to dusts and/or fibres on pneumoconiosis. Environment International, Vol. 119, pp. 174–185. https://doi.org/10.1016/j.envint.2018.06.005

Recommendation 5. *"Follow best practices in the field and simplify the data quality criteria".*[39]

Recommendation 6. *"Do not be overly stringent and exclude studies based on a single criterion".*[40]

We have commented previously that EPA needs to assess the studies that are used in its regulatory decision making with transparent and scientifically accepted methods.[41,42,43] As the SACC committee highlights, the current use of weighted quality scores lacks both empirical validation or statistical justification and is not considered 'best practice' for evaluating the internal validity or risk of bias of a study.[44,45,46] Further, as the SACC highlight, EPA is also excluding 'studies based on a single criterion.' In its review of the Draft Risk Evaluation of C.I. Pigment Violet 29 the SACC committee also commented on how the use of this current weighted scoring system may lead to the exclusion of a study, due to one 'fatal flaw'.[47] Further, such methods are not consistent with the EPA's 2017 regulation that requires all relevant science to be considered while accounting for "strengths and limitations. Therefore, we again recommend the use of the validated methods of the Navigation Guide[48] or the Office of Health Assessment and Translation,[49] which are not 'overly stringent and exclude studies based on a single criterion' to assess the quality of the evidence before making final determinations on a chemicals hazards.

Recommendation 14. *"Continue with the EPA plan to submit its process for review to the National Academy of Sciences for review".*[50]

This recommendation is consistent with the previous recommendation made by the SACC committee responsible for the review of Draft Risk Evaluation of C.I. Pigment Violet 29, who stated that EPA "As

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[39] US EPA (2019) SACC July 2019 Meeting Minutes and Final Report Docket. Pp 38. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063

[40] US EPA (2019) SACC July 2019 Meeting Minutes and Final Report Docket. Pp 38. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063.

[41] EPA (2018) Application of Systematic Review in TSCA Risk Evaluations.

[42] US EPA (2018) Problem Formulations for the Risk Evaluations to be Conducted for the First Ten Chemical Substances under the Toxic Substances Control Act, and Application of Systematic Review in TSCA Risk Evaluations; Notice of Availability, Comment submitted by Veena Singla, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco et al. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0210-0107

[43] Singla, V. I., Sutton, P. M., & Woodruff, T. J. (2019). The Environmental Protection Agency Toxic Substances Control Act Systematic Review Method May Curtail Science Used to Inform Policies, With Profound Implications for Public Health. *American Journal of Public Health*, *109*(7), 982–984. doi:10.2105/AJPH.2019.305068

[44] Juni P, Witschi A, Bloch R, Egger M. The hazards of scoring the quality of clinical trials for meta-analysis. *Jama.* 1999;282(11):1054-1060

[45] Higgins J, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions. Chichester: The Cochrane Collaboration and Wiley-Blackwell; 2008.

[46] Herbison P, Hay-Smith J, Gillespie WJ. Adjustment of meta-analyses on the basis of quality scores should be abandoned. J Clin Epidemiol. *2006 Dec; 59(12):1249-56.*

[47] US EPA (2019) Peer Review of the Draft Risk Evaluation for Pigment Violet 29 (PV29). Page 26. Available: https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2018-0604 D=EPA-HQ-OPPT-2018-0604

[48] Woodruff TJ, Sutton P. The Navigation Guide systematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. Environ Health Perspect. 2014;122(10):1007-1014.

[49] National Toxicology Program (NTP). Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration. Research Triangle Park, NC: National Toxicology Program; 2015.

[50] US EPA (2019) SACC July 2019 Meeting Minutes and Final Report Docket. Pp 38. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063.

soon as practical have NAS conduct a peer review of the TSCA SR protocol".[51] Further, in its review of Cyclic Aliphatic Bromide Cluster (HBCD) the SACC "Members viewed the EPA methodology as still subject to amendment and/or replacement by an alternative approach and encourage EPA to seek additional review of their SR procedure." [52]

We strongly endorse the recommendations from these three separate committees and urge EPA to have its current TSCA systematic review method assessed by the NAS prior to conducting the risk evaluations for the first 20 chemicals designated as high-priority substances and implement any recommendations given to them before any future TSCA risk evaluations. Alternatively, we recommend that EPA save valuable time and resources and use one of two existing empirically based systematic review methodologies, including the Navigation Guide[53] and the Office of Health Assessment and Translation (OHAT)[54] for its TSCA risk evaluations. The implementation of these methods would allow EPA to use a method that is line with each of the recommendations made by the SACC to improve the TSCA systematic method.

We also recommend that EPA should use existing Integrated Risk Information System (IRIS) assessments as the foundation for its risk evaluations as there are existing IRIS assessments for 14 of the 20 high priority candidate chemicals designated as high-priority substances.[55] EPA should request IRIS to update and incorporate new evidence where needed. [56] This approach, that EPA should build on existing high-quality reviews to incorporate new studies and then use this updated systematic review as a basis for its assessment, has also been endorsed by the NAS in 2017.[57]

2. EPA should use a cumulative approach assessing all common adverse health outcomes for the risk evaluations of phthalates and chlorinated solvents.

Phthalates

The National Research Council (NRC) specifically recommended "that a cumulative risk assessment be conducted for phthalates and that the assessment include other antiandrogens."[58] The NRC found that because people are exposed simultaneously to multiple phthalates, and phthalates can contribute to

[51] US EPA (2019) Peer Review of the Draft Risk Evaluation for Pigment Violet 29 (PV29). Page 28. Available: https://www.regulations.gov/docket?D=EPA-HQ-OPPT-2018-0604 D=EPA-HQ-OPPT-2018-0604

[52] US EPA (2019) SACC July 2019 Meeting Minutes and Final Report Docket. Pp 85. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0238-0063.

[53] Woodruff TJ, Sutton P. The Navigation Guide systematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. Environ Health Perspect. 2014;122(10):1007-1014.

[54] National Toxicology Program (NTP). Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration. Research Triangle Park, NC: National Toxicology Program; 2015.

[55] While we support the use of the IRIS assessments as the foundation for 14 of the 20 current 20 high priority candidate chemicals designated as high-priority substances, we also recognize that the IRIS systematic review process requires further methodological development to ensure it is in line with other empirically based systematic review methodologies including the the Navigation Guide and the Office of Health Assessment and Translation (OHAT).

[56] US EPA (2019). Initiation of Prioritization Under the Toxic Substances Control Act (TSCA). Comment submitted by Veena Singla, PhD, Associate Director, Science and Policy, Program on Reproductive Health and the Environment, University of California, San Francisco (UCSF) et al. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0131-0010

[57] The National Academies of Sciences. *Application of Systematic Review Methods in an Overall Strategy for Evaluating Low-Dose Toxicity from Endocrine Active Chemicals.* Washington, D.C.: National Academies Press; 2017.

[58] Id. pg 7

common adverse health outcomes, the scientifically appropriate approach is a cumulative risk assessment.[59]

As there are 5 phthalates listed in EPA's high-priority list, moving forward to the risk evaluation process, EPA should assess DIBP, DCHP, DEHP, BBP, and DBP together as the high-priority dossiers indicate that these chemicals share many common human health hazards such as reproductive toxicity, developmental toxicity, and systemic toxicity (Appendix A).[60] As outlined in our previous comments, if EPA decides to proceed with the manufacturer-requested risk evaluations of DIDP and DINP, these two phthalates should also be considered in a cumulative assessment with the 5 phthalates EPA listed as high-priority.[61,62]

For its evaluations, EPA should draw on relevant reviews and publications, such as the Consumer Product Safety Commission's Chronic Hazard Advisory Panel (CHAP) on phthalates.[63] Previous cumulative assessments of phthalates by the NRC and the CHAP focused on one particular health outcome- effects on the development of the male reproductive system due to anti-androgenicity- but the NRC cautioned that while this is the most extensively studied endpoint, "The committee's suggestions should not be interpreted to imply that other health effects are not important or that nonchemical stressors should be ignored."[64] Likewise, the CHAP acknowledged concerns for other health effects, including cancer and neurodevelopmental toxicity, but did not quantify cumulative risks for these endpoints due to lack of data.[65]

Therefore, the NRC and CHAP risk findings on particular phthalates are not comprehensive; no cumulative assessment was conducted for other relevant health endpoints. In particular, since the NRC and CHAP reports, additional evidence on phthalates' neurodevelopmental toxicity has emerged

[59] National Research Council (U.S.), & Committee on the Health Risks of Phthalates. (2008). *Phthalates and cumulative risk assessment: the task ahead*. Retrieved from http://site.ebrary.com/id/10274055

[60] 84 FR 44300

[61] US EPA. (2019). Di-isodecyl Phthalate (DIDP); Manufacturer Request for Risk Evaluation Under the Toxic Substances Control Act (TSCA); Comment submitted by Veena Singla et al., Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco (UCSF). Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0435-0008

[62] US EPA. (2019). Di-isononyl Phthalate (DINP); Manufacturer Request for Risk Evaluation Under the Toxic Substances Control Act (TSCA); Comment submitted by Veena Singla et al., Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco (UCSF). Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0436-0009

[63] Gennings, C., Hauser, R., Koch, H. M., Kortenkamp, A., Lioy, P. J., Mirkes, P. E., & Schwetz, B. A. (2014). *Report to the U.S. Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives*. Retrieved from U.S. Consumer Product Safety Commission website: http://www.cpsc.gov/PageFiles/169902/CHAP-REPORT-With-Appendices.pdf

[64] National Research Council (U.S.), & Committee on the Health Risks of Phthalates. (2008). *Phthalates and cumulative risk assessment: the task ahead*. Retrieved from http://site.ebrary.com/id/10274055. Pg. 4

[65] Gennings, C., Hauser, R., Koch, H. M., Kortenkamp, A., Lioy, P. J., Mirkes, P. E., & Schwetz, B. A. (2014). *Report to the U.S. Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives*. Retrieved from U.S. Consumer Product Safety Commission website: http://www.cpsc.gov/PageFiles/169902/CHAP-REPORT-With-Appendices.pdf pg. 13; pg. 29-33

indicating that prenatal and early life exposures are associated with a variety of adverse outcomes including lower IQ and problems with attention, hyperactivity and poorer social communication. [66,67]

Regarding what health endpoints should be included in a cumulative assessment, the NRC committee found "…that the focus in cumulative risk assessment should be on the health outcomes and not on the pathways that lead to them, whether defined as mechanisms of action or as modes of action. Multiple pathways can lead to a common outcome, and a focus on only a specific pathway can lead to too narrow an approach in conducting a cumulative risk assessment. **Accordingly, the chemicals that should be considered for cumulative risk assessment should be ones that cause the same health outcomes or the same types of health outcomes…**(emphasis added)"[68] This indicates that any phthalates that can contribute to an adverse health outcome (such as neurodevelopmental toxicity) should be grouped together.

To identify the relevant health endpoints for cumulative assessment, EPA should conduct a systematic literature review using an established, peer-reviewed method such as the National Toxicology Program's OHAT or the Navigation Guide. [69,70] The TSCA systematic review method should not be used, as it is not peer-reviewed or validated, and EPA's SACC has raised serious concerns about it.[71]

At a minimum the health endpoints in the cumulative evaluation should include those already identified by the NRC and the CHAP, those raising concern in recent studies, as well as those which are common outcomes as per EPA's high-priority dossiers (Appendix A):

- Reproductive Toxicity
- Male reproductive system
- Developmental toxicity
- Neurodevelopmental toxicity
- Other developmental toxicity (ie, skeletal malformations,[72] immune toxicity, fertility)
- Cancer
- Genetic Toxicity

[66] US EPA. (2019). Di-isodecyl Phthalate (DIDP); Manufacturer Request for Risk Evaluation Under the Toxic Substances Control Act (TSCA); Comment submitted by Veena Singla et al., Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco (UCSF), Appendix A. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0435-0008

[67] US EPA. (2019). Di-isononyl Phthalate (DINP); Manufacturer Request for Risk Evaluation Under the Toxic Substances Control Act (TSCA); Comment submitted by Veena Singla et al., Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco (UCSF), Appendix A. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0436-0009

[68] National Research Council (U.S.), & Committee on the Health Risks of Phthalates. (2008). *Phthalates and cumulative risk assessment: the task ahead*. Retrieved from http://site.ebrary.com/id/10274055. Pg. 4

[69] National Toxicology Program (2015) Handbook for Conducting a Literature-Based Health Assessment Using OHAT Approach for Systematic Review and Evidence Integration. In: U.S. Department of Health and Human Services, editor.: Office of Health Assessment and Translation, Division of National Toxicology Program, National Institute of Environmental Health Sciences.

[70] Woodruff TJ, Sutton P (2014) The Navigation Guide sytematic review methodology: a rigorous and transparent method for translating environmental health science into better health outcomes. Environmental Health Perspectives. 122(10):A283.

[71] SACC (2019) A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding: Peer Review for EPA Draft Risk Evaluation of C.I. Pigment Violet 29

[72] Gennings, C., Hauser, R., Koch, H. M., Kortenkamp, A., Lioy, P. J., Mirkes, P. E., & Schwetz, B. A. (2014). *Report to the U.S. Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives*. pg. 8. Retrieved from U.S. Consumer Product Safety Commission website: http://www.cpsc.gov/PageFiles/169902/CHAP-REPORT-With-Appendices.pdf

- Toxicokinetic/Systemic toxicity (ie, liver, kidney effects)[73]

Chlorinated Solvents

Similarly, for chlorinated solvents, EPA designates 7 as high-priority and as stated for phthalates above, EPA should conduct a cumulative evaluation of these 7 chemicals, as they share many common human health hazard outcomes such as (Appendix A):

- Acute and Repeated Dose Toxicity
- Irritation
- Neurotoxicity
- Genetic Toxicity
- Carcinogenicity, and
- Systemic Toxicity

The NAS defines cumulative risk broadly to mean the risk posed by multiple chemicals and other stressors that cause varied health effects and to which people are exposed by multiple pathways and exposure routes and for varied durations.[74] Cumulative risk is critical for susceptible and more highly exposed sub-populations, who face greater chemical exposures (more chemicals, higher levels, and higher frequency) as well as non-chemical stressors.[75] The NAS found that "Where single-chemical risk assessments might yield the verdict 'absence of risk,' dose addition might yield the opposite conclusion."[76] Additionally, effects of toxic chemicals can be compounded by non-chemical stressors such as socio-economic status.

Therefore, moving forward EPA should conduct a cumulative risk assessment for phthalates, chlorinated solvents and, for all chemicals, it is critical that EPA incorporate information on non-chemical stressors in this cumulative assessment to ensure that the most vulnerable populations, including those living in poverty, are accounted for in the evaluation of risk.

3. EPA should proceed immediately with developing the information needed to fill data gaps on the flame retardants TPP, TCEP, and TBBPA.

In March 2017[77] and April 2017[78], EPA responded to TSCA section 21 petitions that requested testing on the flame retardants TBBPA and TCEP (included in the chlorinated phosphate esters cluster, CPEs). In its response, EPA identified data, model development and other critical types of information needed to characterize hazard and exposure for these chemicals.[79] EPA should proceed immediately with the

[73] Id. pg. 8

[74] National Research Council (U.S.), & Committee on the Health Risks of Phthalates. (2008). *Phthalates and cumulative risk assessment: the task ahead*. Pg. 4 Retrieved from http://site.ebrary.com/id/10274055

[75] Solomon, G. M., Morello-Frosch, R., Zeise, L., & Faust, J. B. (2016). Cumulative Environmental Impacts: Science and Policy to Protect Communities. *Annual Review of Public Health*, *37*(1), 83–96. https://doi.org/10.1146/annurev-publhealth-032315-021807

[76] National Research Council (U.S.), & Committee on the Health Risks of Phthalates. (2008). *Phthalates and cumulative risk assessment: the task ahead*. Pg. 8 Retrieved from http://site.ebrary.com/id/10274055

[77] 82 FR 14171

[78] 82 FR 17601

[79] US EPA. (2019). Initiation of Prioritization Under the Toxic Substances Control Act (TSCA); Comment submitted by Veena Singla, Associate Director, Science and Policy, Program on Reproductive Health and the Environment Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco et al. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0131-0010

scientific work, section 4 test orders, section 8 rules, and/ or other activities needed to fill data gaps and generate adequate information for risk evaluation of TPP, TCEP, and TBBPA.

Inhalation, dermal and oral exposure pathways are all significant sources of exposure for both TCEP and TBBPA and all three pathways must be included in the risk evaluations. Despite being designated as high-priority, these data gaps have persisted (see Appendix A). EPA indicated that there was a data gap for respiratory sensitization as a hazard endpoint for TCEP and TPP, and that based on the data referenced in the prioritization process, respiratory sensitization was not reported hazard endpoint for TBBPA. (Appendix A) Similarly, EPA found that based on the data gathered in the prioritization process for all three flame retardants, dermal sensitization was not a reported hazard endpoint. (Appendix A) Lastly, EPA cited no studies for TPP's carcinogenicity endpoint, but the Agency failed to reference a report conducted by US EPA DfE classifying TPP as having moderate carcinogenicity potential.[80] It is unclear what EPA's data gathering process was for the prioritization process and how it arrived at this final set of references (see Point 1; Prioritization Process).

EPA indicated that it was not required to "provide information on other life-cycle phases such as distribution or chemical end-of-life after use in products (i.e., disposal). While EPA may be aware of additional uses, CDR submitters are not required to provide information on chemical uses that are not regulated under TSCA." [81] However, the Ninth Circuit has now held that EPA's interpretation violates the plain language of TSCA, therefore the Agency must address all ongoing uses of legacy products and associated disposal activities.[82]

Moving forward, EPA should collect data on recycling and disposal facilities (including incineration) compliant with this recent ruling on legacy uses. It should also quantify risk associated with related worker and community exposures, such as: number and location of facilities, types and volumes of products processed, and recycling and/or disposal methods employed at each; and assessment of whether data collected at recycling and disposal facilities in other countries are comparable to data collected in the U.S. EPA also needs to assess the sufficiency of available data on incineration byproducts, including brominated/ chlorinated dioxins, furans and polycyclic aromatic hydrocarbons. If any of these data are not adequate, EPA should use its authorities to generate the needed data.

[80] US EPA (2015). Flame retardants used in flexible polyurethane foam: An alternatives assessment update. U.S. Environmental Protection Agency. Retrieved from https://www.epa.gov/sites/production/files/2015-08/documents/ffr_final.pdf

[81] US EPA. (2019). Phosphoric acid, triphenyl ester (TPP); TSCA Review; Proposed Designation of Triphenyl Phosphate (CASRN 115-86-6) as a High-Priority Substance for Risk Evaluation. Available: https://www.regulations.gov/document?D=EPA-HQ-OPPT-2018-0458-0010

[82] *Safer Chemicals, Healthy Families v USEPA* (2019). No. 17-72260 (9th Cir. Nov. 14, 2019). Pg. 53. *"EPA's contention that TSCA can reasonably be read to refer to the future use of a product, and disposals associated with such use, only when the product will also be manufactured in the future for that use—and not when the product is no longer manufactured for the relevant use—is without merit. TSCA's "conditions of use" definition plainly addresses conditions of use of chemical substances that will be used or disposed of in the future, regardless of whether the substances are still manufactured for the particular use."*

Appendix A. Potential Human Health Hazards (transcribed for clarity from the respective high priority dossiers)

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1. Formaldehyde

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X	X	ATSDR (1999); ATSDR (2014); CalEPA (2014); ECHA (2019); Environment Canada (2000); NICNAS (2006); OECD (2002); U.S. EPA (2008a)
Repeated Dose Toxicity	X	X	ATSDR (1999); CalEPA (2014); ECHA (2019); Environment Canada (2000); NICNAS (2006); NTP (2010); OECD (2002)
Genetic Toxicity	X	X	ATSDR (1999); ATSDR (2010); ATSDR (2014); IARC (2012); NRC (2011); NTP (2010)
Reproductive Toxicity	X		ATSDR (1999); ATSDR (2010); CalEPA (2014); ECHA (2019); Environment Canada (2000); WHO (2002); NICNAS (2006); NTP (2010); OECD (2002)
Developmental Toxicity	X		ATSDR (1999); ATSDR (2010); CalEPA (2014); ECHA (2019); Environment Canada (2000); WHO (2002); NICNAS (2006); NTP (2010); OECD (2002)
Toxicokinetic	X		ATSDR (1999); ECHA (2019); Environment Canada (2000); IARC (2012); NICNAS (2006); NTP (2010); U.S. EPA (2008a)
Irritation/Corrosion	X	X	ATSDR (1999); ATSDR (2010); ATSDR (2014); CalEPA (2014); CPSC (2016); ECHA (2019); Environment Canada (2000); IARC (2012); WHO (2002); NRC (2011); NICNAS (2006); NTP (2010); OECD (2002); U.S. EPA (2008a)
Dermal Sensitization	X	X	ATSDR (1999); ECHA (2019); Environment Canada (2000); IARC (2012); NICNAS (2006); NTP (2010); OECD (2002); U.S. EPA (2008a)
Respiratory Sensitization	X	X	ATSDR (1999); CalEPA (2014); CPSC (2016); ECHA (2019); Environment Canada (2000); WHO (2002); NTP (2010)
Carcinogenicity	X	X	ATSDR (1999); ATSDR (2010); ATSDR (2016);; CalEPA (2011) CPSC (2016); ECHA (2019); Environment Canada (2000); IARC (2012); WHO (2002); NRC (2011); NICNAS (2006); NTP (2016); OECD (2002); U.S. EPA (1989); U.S. EPA (2008a); U.S. EPA (2014)
Immunotoxicity	X		ATSDR (2014); Environment Canada (2000); WHO (2002); NRC (2011); NTP (2010)
Neurotoxicity	X		ATSDR (1999); CPSC (2016); CalEPA (2014); NTP (2010)
Epidemiological Studies or Biomonitoring Studies	X		ATSDR (1999); Environment Canada (2000); NICNAS (2006); NTP (2010)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

2. 1,1,2-Trichloroethane

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X	X	OECD (2000); ATSDR (1989)
Repeated Dose Toxicity	X	X	U.S. EPA (2011); ATSDR (2010); CalEPA (2006); OECD (2000); IARC (1999); ATSDR (1989); U.S. EPA (1987); NCI (1978)
Genetic Toxicity	X	X	OECD (2003); OECD (2000); IARC (1999); ATSDR (1989); U.S. EPA (1987)
Reproductive Toxicity	X		ATSDR (1989)
Developmental Toxicity	X		U.S. EPA (2011); OECD (2000); ATSDR (1989)
Toxicokinetic	X	X	OECD (2000); IARC (1999); ATSDR (1989)
Irritation/Corrosion	X	X	CalEPA (2006); OECD (2000); ATSDR (1989)
Dermal Sensitization			
Respiratory Sensitization			
Carcinogenicity	X	X	U.S. EPA (2011); ATSDR (2010); CalEPA (2006); OECD (2000); IARC (1999); ATSDR (1989); U.S. EPA (1987); NCI (1978)
Immunotoxicology	X	X	U.S. EPA (2011); ATSDR (1989)
Neurotoxicity	X	X	CalEPA (2006); OECD (2000); ATSDR (1989)
Epidemiological Studies or Biomonitoring Studies	X	X	ATSDR (2010)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

3. 1,1-Dichloroethane

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X	X	ATSDR (2015), NICNAS (2015), OEHHA (2003)
Repeated Dose Toxicity	X	X	ATSDR (2015), U.S. EPA (2006), NICNAS (2015), OEHHA (2003)
Genetic Toxicity	X	X	ATSDR (2015), NICNAS (2015), OEHHA (2003)
Reproductive Toxicity			
Developmental Toxicity	X	X	ATSDR (2015), NICNAS (2015), OEHHA (2003)
Toxicokinetic	X		ATSDR (2015), NICNAS (2015), OEHHA (2003)
Irritation/Corrosion	X	X	NICNAS (2015)
Dermal Sensitization	X		NICNAS (2015)
Respiratory Sensitization			
Carcinogenicity	X	X	ATSDR (2015), U.S. EPA (1990), U.S. EPA (2006), NICNAS (2015), OEHHA (1992) OEHHA (2003), OEHHA (2011),
Immunotoxicity			
Neurotoxicity	X	X	ATSDR (2015), NICNAS (2015), OEHHA (2003)
Epidemiological Studies or Biomonitoring Studies	X		ATSDR (2015)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

4. 1,2-Dichloroethane

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X	X	NICNAS (2013), U.S. EPA (2010), OECD (2002), ATSDR (2001), RIVM (2001), EnvCanada (1994)
Repeated Dose Toxicity	X	X	NICNAS (2013), U.S. EPA (2010), OECD (2002), ATSDR (2001), RIVM (2001), IARC (1999), EnvCanada (1994), NTP (1991), U.S. EPA (1987), NCI (1978)
Genetic Toxicity	X	X	NICNAS (2013), OECD (2002), RIVM (2001), ATSDR (2001), IARC (1999), NTP (1991)
Reproductive Toxicity	X		NICNAS (2013), U.S. EPA (2010), OECD (2002), ATSDR (2001)
Developmental Toxicity	X		NICNAS (2013), U.S. EPA (2010), OECD (2002), ATSDR (2001)
Toxicokinetic	X	X	NICNAS (2013), U.S. EPA (2010), OECD (2002), ATSDR (2001), RIVM (2001), CalEPA (2005), EnvCanada (1994)
Irritation/Corrosion	X	X	NICNAS (2013), U.S. EPA (2010), OECD (2002)
Dermal Sensitization	X		NICNAS (2013)
Respiratory Sensitization			
Carcinogenicity	X	X	NICNAS (2013), U.S. EPA (2010), OECD (2002), ATSDR (2001), RIVM (2001), IARC (1999), U.S. EPA (1987), NCI (1978)
Immunotoxicology	X	X	OECD (2002), ATSDR (2001), EnvCanada (1994), NTP (1991)
Neurotoxicity	X	X	NICNAS (2013), U.S. EPA (2010), OECD (2002), ATSDR (2001), CalEPA (2005), EnvCanada (1994)
Epidemiological Studies or Biomonitoring Studies	X	X	U.S. EPA (2010), CalEPA (2005), ATSDR (2001), IARC (1999)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

5. 1,2-Dichloropropane

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X	X	NICNAS (2017), U.S. EPA (2016b), OECD (2006), CalEPA (1999), ATSDR (1989)
Repeated Dose Toxicity	X	X	IARC (2017), NICNAS (2017), U.S. EPA (2016b), OECD (2006), CalEPA (1999), U.S. EPA (1991), ATSDR (1989), NTP (1986)
Genetic Toxicity	X	X	IARC (2017), NICNAS (2017), U.S. EPA (2016b), OECD (2006), CalEPA (1999), ATSDR (1989)
Reproductive Toxicity	X	X	NICNAS (2017), U.S. EPA (2016b), OECD (2006), CalEPA (1999), ATSDR (1989)
Developmental Toxicity	X	X	NICNAS (2017), U.S. EPA (2016b), OECD (2006), CalEPA (1999), U.S. EPA (1991), ATSDR (1989)
Toxicokinetic	X	X	NICNAS (2017), U.S. EPA (2016b), OECD (2006), CalEPA (1999), U.S. EPA (1991), ATSDR (1989)
Irritation/Corrosion	X	X	NICNAS (2017), OECD (2006), CalEPA (1999), ATSDR (1989)
Dermal Sensitization	X	X	IARC (2017), NICNAS (2017), U.S. EPA (2016b), ATSDR (1989)
Respiratory Sensitization			
Carcinogenicity	X	X	IARC (2017), NICNAS (2017), U.S. EPA (2016b), OECD (2006), CalEPA (1999), ATSDR (1989)
Immunotoxicology			
Neurotoxicity	X	X	IARC (2017), NICNAS (2017), U.S. EPA (2016b), ATSDR (1989)
Epidemiological Studies or Biomonitoring Studies	X	X	IARC (2017), NICNAS (2017), U.S. EPA (2016b), OECD (2006), CalEPA (1999), ATSDR (1989)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

6. *o*-Dichlorobenzene

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X	X	EPA (2009); Cal EPA (2009), ATSDR (2006); RIVM (2001); OECD (2001); NICNAS (2001); IARC (1999)
Repeated Dose Toxicity	X	X	EPA (2009); ATSDR (2006); RIVM (2001); OECD (2001); NICNAS (2001); IARC (1999)
Genetic Toxicity	X		EPA (2009); ATSDR (2006); OECD (2001); NICNAS (2001)
Reproductive Toxicity	X	X	EPA (2009); ATSDR (2006)
Developmental Toxicity	X		EPA (2009); OECD (2001); NICNAS (2001); IARC (1999)
Toxicokinetic	X		EPA (2009); ATSDR (2006); OECD (2001); NICNAS (2001)
Irritation/Corrosion	X	X	EPA (2009); ATSDR (2006); OECD (2001); NICNAS (2001)
Respiratory Sensitization			
Dermal Sensitization	X	X	OECD (2001); NICNAS (2001)
Carcinogenicity	X		EPA (2009); Cal EPA (2009); ATSDR (2006); RIVM (2001); NICNAS (2001); IARC (1999)
Neurotoxicity	X	X	ATSDR (2006)
Immunotoxicity	X	X	RIVM (2001); OECD (2001); NICNAS (2001)
Epidemiological Studies or Biomonitoring Studies	X	X	ATSDR (2006)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

7. *p*-Dichlorobenzene

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X	X	ATSDR (2006), ECHA (2004), NICNAS (2000), CalEPA (1997)
Repeated Dose Toxicity	X	X	ATSDR (2006), NTP (1987), ECHA (2004), RIVM (2001), NICNAS (2000), CalEPA (1997), U.S. EPA (1994)
Genetic Toxicity	X		ATSDR (2006), ECHA (2004), OECD (2003), RIVM (2001), NICNAS (2000), IARC (1999), RIVM (1991), U.S. EPA (1994), NTP (1987)
Reproduction Toxicity	X		ATSDR (2006), ECHA (2004), IARC (1999), U.S. EPA (1994)
Developmental Toxicity	X	X	ATSDR (2006), IARC (1999), RIVM (1991)
Toxicokinetic	X	X	ATSDR (2006), ECHA (2004), NICNAS (2000)
Irritation/Corrosion	X	X	ATSDR (2006), ECHA (2004), NICNAS (2000), CalEPA (1997), RIVM (1991)
Dermal Sensitization	X		ECHA (2004), NICNAS (2000), U.S. EPA (1994)
Respiratory Sensitization	X		CalEPA (2009), ECHA (2004), NICNAS (2000), U.S. EPA (1994)
Carcinogenicity	X	X	NTP (2016), U.S. EPA (2014), ATSDR (2006), ECHA (2004), OECD (2003), NICNAS (2000), IARC (1999), U.S. EPA (1994), NTP (1987)
Immunotoxicity			
Neurotoxicity	X	X	ATSDR (2006), ECHA (2004), CalEPA (2008), NICNAS (2000), CalEPA (1997), U.S. EPA (1994), NTP (1987)
Epidemiological Studies or Biomonitoring Studies	X	X	ATSDR (2006), ECHA (2004), NICNAS (2000), IARC (1999), CalEPA (1997), NTP (1987)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

8. *trans*-1,2-Dichloroethylene

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X	X	U.S. EPA (2015), U.S. EPA (2008), NTP (2002), ATSDR (1996)
Repeated Dose Toxicity	X	X	U.S. EPA (2015), U.S. EPA (2010b), U.S. EPA (2010a), U.S. EPA (2008), NTP (2002), RIVM (2001), ATSDR (1996)
Genetic Toxicity	X	X	U.S. EPA (2008), U.S. EPA (2010a), U.S. EPA (2010b), NTP (2002), RIVM (2001), ATSDR (1996)
Reproductive Toxicity			
Developmental Toxicity			
Toxicokinetic	X	X	U.S. EPA (2010b), RIVM (2001), ATSDR (1996)
Irritation/Corrosion	X	X	U.S. EPA (2008), RIVM (2001), ATSDR (1996)
Dermal Sensitization			
Respiratory Sensitization			
Carcinogenicity			
Immunotoxicity	X	X	U.S. EPA (2010a), U.S. EPA (2010b), ATSDR (1996)
Neurotoxicity			
Epidemiological Studies or Biomonitoring Studies			

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

9. 4,4'-(1-Methylethylidene)bis[2, 6-dibromophenol] (TBBPA)

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X		U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014), Environment Canada (2013), ECB (2006), NICNAS (2001), IPCS (1995)
Repeated Dose Toxicity	X	X	U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014), Environment Canada (2013), ECB (2006), EFSA (2005), NICNAS (2001), IPCS (1995)
Genetic Toxicity	X		IARC (2018), U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014), Environment Canada (2013), ECB (2006), NICNAS (2001), IPCS (1995)
Reproductive Toxicity	X		U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014), Environment Canada (2013), ECB (2006), EFSA (2005)
Developmental Toxicity	X	X	U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014), Environment Canada (2013), ECB (2006), NICNAS (2001), IPCS (1995)
Toxicokinetic	X	X	IARC (2018), U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014), Environment Canada (2013), ECB (2006), NICNAS (2001), IPCS (1995)
Irritation/Corrosion	X	X	U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014), Environment Canada (2013), ECB (2006), NICNAS (2001), IPCS (1995)
Dermal Sensitization	X		U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014), Environment Canada (2013), ECB (2006), NICNAS (2001), IPCS (1995)
Respiratory Sensitization	X		U.S. EPA (2015a), Environment Canada (2013), ECB (2006)
Carcinogenicity	X	X	IARC (2018), U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014)
Immunotoxicity	X	X	U.S. EPA (2015c), NTP (2014), Environment Canada (2013)
Neurotoxicity	X	X	IARC (2018), U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014), Environment Canada (2013), ECB (2006), EFSA (2005)
Epidemiological Studies or Biomonitoring Studies	X	X	IARC (2018), U.S. EPA (2015a), U.S. EPA (2015c), NTP (2014), Environment Canada (2013), ECB (2006), IPCS (1995)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

10. Triphenyl Phosphate

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X		EPA (2015); UK (2009); OECD (2002)
Repeated Dose Toxicity	X	X	EPA (2015); UK (2009); OECD (2002)
Genetic Toxicity	X		EPA (2015); UK (2009); OECD (2002)
Reproductive Toxicity	X		EPA (2015); UK (2009); OECD (2002)
Developmental Toxicity	X	X	EPA (2015); UK (2009); OECD (2002)
Toxicokinetic			
Irritation/Corrosion	X	X	EPA (2015); UK (2009); OECD (2002)
Dermal Sensitization	X		EPA (2015); UK (2009); OECD (2002)
Respiratory Sensitization			
Carcinogenicity			
Immunotoxicity	X		EPA (2015); UK (2009); OECD (2002)
Neurotoxicity	X		EPA (2015); UK (2009); OECD (2002)
Epidemiological Studies or Biomonitoring Studies	X	X	EPA (2015)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

11. Tris(2-chloroethyl) Phosphate

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X	X	ECHA (2018a), ECHA (2018b), U.S. EPA (2015a), U.S. EPA (2015b), CPSC (2015), CPSC (2013), U.S. EPA (2009), EC (2009), IPCS (1998), NTP (1991)
Repeated Dose Toxicity	X	X	NICNAS (2016), U.S. EPA (2015a), U.S. EPA (2015b), CPSC (2015), CPSC (2013), U.S. EPA (2009), EnvCanada (2009), EC (2009), IPCS (1998)
Genetic Toxicity	X	X	ECHA (2018b), NICNAS (2016), U.S. EPA (2015b), CPSC (2013), U.S. EPA (2009), EnvCanada (2009), EC (2009), IARC (1999), IPCS (1998), NTP (1991)
Reproductive Toxicity	X	X	ECHA (2018a), NICNAS (2016), U.S. EPA (2015a), U.S. EPA (2015b), CPSC (2013), U.S. EPA (2009), EnvCanada (2009), EC (2009), IPCS (1998)
Developmental Toxicity	X	X	U.S. EPA (2015a), U.S. EPA (2015b), CPSC (2013), U.S. EPA (2009), EnvCanada (2009), EC (2009)
Toxicokinetic	X	X	ECHA (2018a), U.S. EPA (2015a), U.S. EPA (2015b), CPSC (2015), CPSC (2013), EC (2009), IPCS (1998)
Irritation/Corrosion	X		ECHA (2018b), U.S. EPA (2015b), CPSC (2013), EC (2009), IPCS (1998)
Dermal Sensitization	X		U.S. EPA (2015b), EC (2009)
Respiratory Sensitization			
Carcinogenicity	X	X	ECHA (2018a), NICNAS (2016), U.S. EPA (2015a), U.S. EPA (2015b), CPSC (2013), U.S. EPA (2009), EnvCanada (2009), EC (2009), IARC (1999), IPCS (1998), NTP (1991)
Immunotoxicity			
Neurotoxicity	X	X	ECHA (2018a), U.S. EPA (2015a), U.S. EPA (2015b), CPSC (2013), EnvCanada (2009), IARC (1999), IPCS (1998)
Epidemiological Studies or Biomonitoring Studies	X	X	U.S. EPA (2015a), NICNAS (2016), U.S. EPA (2015b), CPSC (2015), IPCS (1998)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

12. Butyl Benzyl Phthalate

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X		NICNAS (2015), NICNAS (2008), ECB (2007), NTP (2003), RIVM (2001), Environment Canada (2000)
Repeated Dose Toxicity	X	X	NICNAS (2015), CPSC (2014), CPSC (2010), NICNAS (2008), ECB (2007), RIVM (2001), IRIS (1989)
Genetic Toxicity	X	X	NICNAS (2015), OEHHA (2013), NICNAS (2008), ECB (2007), NTP (2003), U.S. EPA (2002), RIVM (2001), Environment Canada (2000), IARC (1999), NTP (1997), IRIS (1989)
Reproductive Toxicity	X	X	UNEP (2016), CPSC (2014), CPSC (2010), ECHA (2010), NICNAS (2008), ECB (2007), NTP (2003), RIVM (2001), IRIS (1989)
Developmental Toxicity	X	X	UNEP (2016), CPSC (2014), OEHHA (2013), OEHHA (1986), CPSC (2010), NICNAS (2008), ECB (2007), NTP (2003), Environment Canada (2000), IARC (1999)
Toxicokinetic	X	X	NICNAS (2015), OEHHA (1986), CPSC (2010), NICNAS (2008); NTP (2003), U.S. EPA (2002), RIVM (2001), Environment Canada (2000), IARC (1999)
Irritation/ Corrosion	X		NICNAS (2008), ECB (2007), NTP (2003), Environment Canada (2000)
Dermal Sensitization	X		NICNAS (2015), NICNAS (2008), ECB (2007), NTP (2003)
Respiratory Sensitization	X	X	UNEP (2016)
Carcinogenicity	X	X	NICNAS (2015), OEHHA (2013), Lowell Center (2011), CPSC (2010), NICNAS (2008), ECB (2007), U.S. EPA (2002), RIVM (2001), Environment Canada (2000), IARC (1999), NTP (1997), IRIS (1989)
Immunotoxicity			
Neurotoxicity	X		ECB (2007), Environment Canada (2000)
Epidemiological Studies or Biomonitoring Studies	X	X	CPSC (2017), UNEP (2016), NICNAS (2015), CSPC (2015), OEHHA (2013), ECHA (2010), OEHHA (1986), ECB (2007), NTP (2003)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

13. Di-Ethylhexyl Phthalate

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X		CPSC (2010), NICNAS (2010), ECB (2008), NICNAS (2008), ATSDR (2002), RIVM (2001), OEHHA (1997), NICNAS (2013)
Repeated Dose Toxicity	X	X	CPSC (2010), NICNAS (2010), ECB (2008), NICNAS (2008), NTP-CERHR (2006), ATSDR (2002), RIVM (2001), OEHHA (1997), NTP (1982), NICNAS (2013)
Genetic Toxicity	X		IARC (2013), CPSC (2010), NICNAS (2010), ECB (2008), NICNAS (2008), ATSDR (2002), OEHHA (2002), RIVM (2001), OEHHA (1997), U.S. EPA (1987), NTP (1982), NICNAS (2013)
Reproductive Toxicity	X	X	UNEP (2016), FDA (2012), CPSC (2010), NICNAS (2010), ECB (2008), NICNAS (2008), NTP-CERHR (2006), OEHHA (2005), ATSDR (2002), RIVM (2001), OEHHA (1997), NICNAS (2013)
Developmental Toxicity	X	X	CPSC (2014), FDA (2012), CPSC (2010), NICNAS (2010), ECB (2008), NICNAS (2008), NTP-CERHR (2006), OEHHA (2005), ATSDR (2002), RIVM (2001), OEHHA (1997), NICNAS (2013)
Toxicokinetics	X	X	IARC (2013), CPSC (2010), NICNAS (2010), ECB (2008), NICNAS (2008), NTP-CERHR (2006), OEHHA (2005), ATSDR (2002), OEHHA (2002), RIVM (2001), OEHHA (1997), NTP (1982), FDA (2004), NICNAS (2013)
Irritation/Corrosion	X		CPSC (2010), NICNAS (2010), ECB (2008), NICNAS (2008), ATSDR (2002), OEHHA (1997), NICNAS (2013)
Dermal Sensitization	X		CPSC (2010), NICNAS (2010), ECB (2008), NICNAS (2008), ATSDR (2002), NICNAS (2013)
Respiratory Sensitization			
Carcinogenicity	X	X	NTP (2016), CPSC (2014), IARC (2013), CPSC (2010), NICNAS (2010), ECB (2008), NICNAS (2008), NTP-CERHR 2006, ATSDR (2002), OEHHA (2002), RIVM (2001), OEHHA (1997), U.S. EPA (1987), NTP (1982), OEHHA (2011), NICNAS (2013)
Immunotoxicity			
Neurotoxicity	X	X	CPSC (2010), ATSDR (2002)
Epidemiological Studies or Biomonitoring Studies	X	X	NTP (2016), CPSC (2014), IARC (2013), CPSC (2010), ECHA (2010), NICNAS (2010), ECB (2008), NICNAS (2008), NTP- CERHR (2006), OEHHA (2005), ATSDR (2002), OEHHA (1997), U.S. EPA (1987), NTP (1982)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

14. Di-isobutyl Phthalate

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X		NICNAS (2008a); NICNAS (2016); CPSC (2011); NICNAS (2008b)
Repeated Dose Toxicity	X	X	NICNAS (2008a); NICNAS (2016); CPSC (2011); NICNAS (2008b)
Genetic Toxicity	X		NICNAS (2008a); NICNAS (2016); NICNAS (2008b)
Reproductive Toxicity	X	X	NICNAS (2008a); NICNAS (2016); CPSC (2011); CPSC (2014); NICNAS (2008b)
Developmental Toxicity	X	X	NICNAS (2008a); NICNAS (2016); CPSC (2011); CPSC (2014); NICNAS (2008b)
Toxicokinetic	X		NICNAS (2008a); CPSC (2011); CPSC (2014)
Irritation/Corrosion	X		NICNAS (2008a); NICNAS (2016); CPSC (2011); NICNAS (2008b)
Dermal Sensitization	X		NICNAS (2008a); NICNAS (2016); CPSC (2011); NICNAS (2008b)
Respiratory Sensitization	X		CPSC (2011)
Carcinogenicity	X		NICNAS (2008a); NICNAS (2016); CPSC (2011); NICNAS (2008b)
Immunotoxicity			
Neurotoxicity	X		CPSC (2011); CPSC (2014)
Epidemiological Studies or Biomonitoring Studies	X		CPSC (2014)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

15. Dibutyl Phthalate

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X	X	Environment Canada (1994), NTP (2000), RIVM (2001), ATSDR (2001); NICNAS (2008), CPSC (2010), NICNAS (2013), NICNAS (2016)
Repeated Dose Toxicity	X	X	U.S. EPA (1987), Environment Canada (1994), NTP (1995), NTP (2000), ATSDR (2001), ECB (2004), NICNAS (2008), CPSC (2010), NICNAS (2013), NICNAS (2016)
Genetic Toxicity	X	X	U.S. EPA (1987), Environment Canada (1994), NTP (1995), NTP (2000), ATSDR (2001), RIVM (2001), NICNAS (2008), CPSC (2010), NICNAS (2013), NICNAS (2016)
Reproductive Toxicity	X	X	U.S. EPA (1987), Environment Canada (1994), NTP (1995), NTP (2000), ATSDR (2001), ECB (2004), OEHHA (2007), NICNAS (2008), CPSC (2010), FDA (2012); NICNAS (2013), CPSC (2014), NICNAS (2016)
Developmental Toxicity	X	X	Environment Canada (1994), NTP (1995), NTP (2000), ATSDR (2001), OEHHA (2007), NICNAS (2008), CPSC (2010), FDA (2012); FDA (2014); NICNAS (2013), CPSC (2014), NICNAS (2016)
Toxicokinetic	X	X	NTP (1995), NTP (2000), ATSDR (2001), RIVM (2001), NICNAS (2008), CPSC (2010), NICNAS (2013), NICNAS (2016)
Irritation/Corrosion	X	X	NTP (2000), NICNAS (2008), NICNAS (2013), NICNAS (2016)
Dermal Sensitization	X	X	ATSDR (2001), ECB (2004), NICNAS (2008), CPSC (2010), NICNAS (2013), NICNAS (2016)
Respiratory Sensitization	X	X	ATSDR (2001), NICNAS (2008), CPSC (2010)
Carcinogenicity	X		NTP (1995)
Immunotoxicity			
Neurotoxicity	X	X	NTP (2000), ATSDR (2001), NICNAS (2013)
Epidemiological Studies or Biomonitoring Studies	X	X	Environment Canada (1994), ATSDR (2001), OEHHA (2007), CPSC (2010), NICNAS (2013), CPSC (2014), CPSC (2017)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.

16. Dicyclohexyl Phthalate

Human Health Hazards	Tested for Specific Effect	Effect Observed	Recommendation basis
Acute Toxicity	X		CPSC (2010), NICNAS (2016)
Repeated Dose Toxicity	X	X	CPSC (2010), NICNAS (2016)
Genetic Toxicity	X	X	CPSC (2010), NICNAS (2016)
Reproductive Toxicity	X	X	CPSC (2010), CPSC (2014), ECHA (2019), NICNAS (2016)
Developmental Toxicity	X	X	CPSC (2010), CPSC (2014), ECHA (2019), NICNAS (2016)
Toxicokinetic	X	X	CPSC (2010), NICNAS (2016)
Irritation/Corrosion	X	X	CPSC (2010), NICNAS (2016)
Dermal Sensitization	X		CPSC (2010), NICNAS (2016)
Respiratory Sensitization	X		CPSC (2010)
Carcinogenicity			CPSC (2010), NICNAS (2016)
Immunotoxicity			CPSC (2010)
Neurotoxicity			CPSC (2010)
Epidemiological Studies or Biomonitoring Studies	X	X	CPSC (2010)

Note: The "X" in the "Effect Observed" column indicates when a hazard effect was reported by one or more of the referenced studies. Blank rows indicate when information was not identified during EPA's review of reasonably available information to support the proposed designation.