February 28, 2023

Comments on the Request for Nominations for a Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer Requested Phthalate

Comments submitted via regulations.gov to the docket ID EPA-HQ-OPPT-2022-0918-0005

The following comments are being submitted by the University of California, San Francisco (UCSF) Program on Reproductive Health and the Environment (PRHE). We have no direct or indirect financial or fiduciary interest in the manufacture or sale of any chemical that would be the subject of the deliberations of this Committee.

We appreciate the opportunity to support qualified candidates to serve as members of the Science Advisory Committee on Chemicals (SACC), pursuant to section 2625(o) of the Frank R. Lautenberg Chemical Safety for the 21st Century Act. This panel will "provide independent advice and expert consultation, at the request of the Administrator, with respect to the scientific and technical aspects of issues relating to the implementation of this title" and will include "representatives of such science, government, labor, public health, public interest, animal protection, industry, and other groups as the Administrator determines to be advisable, including representatives that have specific scientific expertise in the relationship of chemical exposures to women, children, and other potentially exposed or susceptible subpopulations." We submit these comments on the candidates for selection as *ad hoc* participants on the SACC responsible for reviewing *EPA's Draft Proposed Principles of Cumulative Risk Assessment under the Toxic Substances Control Act* and *Draft Proposed Approach for Cumulative Risk Assessment of High-Priority Phthalates and a Manufacturer-Requested Phthalate.*

We encourage EPA to consider the following when finalizing nominations:

- **The role of reviewers and the SACC in supporting the mission of EPA in protecting human health and the environment**. EPA has a professional and legal duty to select committee members who will provide credible and independent scientific analysis and advice free from financial conflicts of interest (COI) or a strong bias toward the perspective of regulated industries that may have a vested interest in minimizing EPA's regulation of hazardous materials and products. It has been established that there is an association between financial COI and recommendations from clinical guidelines and expert reviews which favor the interests of the industry providing financial support[1,2]. It is likely then that allowing committee members on the SACC with financial ties to regulated chemical companies would risk biasing the SACC's recommendations towards the industry interests. Of further concern, is the potential "megaphone effect" that multiple SACC members with financial conflicts of interest are likely to bring as their influence and recommendations will be in the same direction, thus creating a systemic bias.[3]

[1] Nejstgaard CH, Bero L, Hróbjartsson A, et al. Association between conflicts of interest and favourable recommendations in clinical guidelines, advisory committee reports, opinion pieces, and narrative reviews: systematic review. BMJ2020;371:m4234.pmid:33298430

[2] Coyne DW. Influence of industry on renal guideline development. Clin J Am Soc Nephrol2007;2:3-7, discussion 13-4. doi:10.2215/CJN.02170606 pmid:17699377

[3] Ralston R, Hil SE, da Silva Gomes F, Collin J. Towards preventing and managing conflict of interest in nutrition policy? an analysis of submissions to a consultation on a draft WHO tool. Int J Health Policy Manag2021;10:255-65.pmid:32610752

- **The need for transparent and effective financial disclosure policies that are strictly enforced.** There are several candidates whose biographical profiles do not appear to have disclosed publicly their financial relationships with industries, some of which have a particular interest in the topic of this committee. While this information can be found in some published papers, not all funding arrangements can be tracked. Disclosure and COI policies play an essential role in protecting EPA and committee work products from the possibility of biased scientific conclusions and must be strictly enforced and routinely addressed to ensure the quality of SACC reviews and other work products.

  Further, although previously, disclosing COI was seen as sufficient to manage committee members' interests research has shown paradoxically, that those members who disclose COI provide more biased advice due the belief that they have adequately warned recipients of the information they have provided or to compensate for the fact that their advice will be disregarded[4,5]. Systematic reviews have established that that disclosed financial conflicts are associated with research outcomes biased towards the sponsor and therefore demonstrates why disclosure is not a solution to reducing bias in guideline committees[6].

- **The need for representation from directly impacted, susceptible, vulnerable, and/or highly exposed populations**. We urge the Agency to not only seek representatives that have *specific scientific expertise* in the relationship of chemical exposures to workers, women, children, and other potentially exposed or susceptible subpopulations, but to incorporate a broader and more inclusive definition to capture representation from individuals with diverse knowledge sources that represent unique perspectives to these critical issues. EPA has historically encouraged "citizen science" only to then erect expertise barriers that can prevent those with lived expertise regarding impacted communities but perhaps without certain advanced degrees (i.e., holding a postgraduate degree) from taking part in critical discussions. There are many examples of successful implementation of such approaches, which have demonstrated that incorporating knowledge resources outside of traditional academic and science fields can greatly enrich the research and policy process.[7]

In summary, our comments address the following main points:

1. **Support for the nominations of 9 individuals to the SACC; and**
2. **EPA should strive to eliminate or manage financial conflicts of interest and appearance of a loss of impartiality from selected committee members.**

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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[4] Loewenstein G, Sah S, Cain DM. The unintended consequences of conflict of interest disclosure. JAMA2012;307:669-70. doi:10.1001/jama.2012.154. pmid:22337676

[5] Romain PL. Conflicts of interest in research: looking out for number one means keeping the primary interest front and center. Curr Rev Musculoskelet Med. 2015 Jun;8(2):122-7. doi: 10.1007/s12178-015-9270-2. PMID: 25851417; PMCID: PMC4596167.

[6] Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. Cochrane Database Syst Rev2017;2:MR000033.pmid:28207928

[7] Anderson, B.E., Naujokas, M.F. and Suk, W.A., 2015. Interweaving knowledge resources to address complex environmental health challenges. *Environmental health perspectives*, 123(11):1095-1099.

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DETAILED COMMENTS

1. **Support for the nominations of 9 individuals to the SACC**

During the first 10 risk evaluations, EPA did not conduct cumulative risk assessments, preventing consideration of how chemical exposure risks may be amplified by co-exposures to other chemicals contributing to common adverse outcomes or to nonchemical stressors, such as poverty, food insecurity, racism and discrimination, and exacerbating the risk of adverse outcomes from chemical

exposures.[8] For EPA to meet the statutory mandate to use the "best available science" when considering cumulative risk and meet the environmental and racial justice goals of the Biden Administration and this current EPA[9,10,11,12] , it is integral that the Agency select candidates for the SACC who are unbiased and free of financial conflicts of interest, and have relevant experience including having worked with impacted communities experiencing the burden of cumulative exposures to multiple chemical and nonchemical stressors, and most importantly, be qualified to review the Cumulative Risk Guidance. There are several nominees we support due to the depth of their expertise in phthalates and cumulative risk assessment among their other professional qualifications, their experience providing guidance to EPA on the implementation of amended TSCA, and their experience working with directly affected communities:

a. El'gin Avila

i. Mr. Avila, who we nominated, has already been recognized by the TSCA program in its endeavors to improve occupational exposure consideration under TSCA. His background in occupational and environmental health and experience with workers and communities burdened by cumulative exposures will support the SACC's endeavors to better measure and address inaccessibility of information on chemical hazards and their mitigation. Additionally, he has experience using an equity- and/or justice- lens to create comprehensive and holistic solutions to address environmental health science and technical issues.

b. Joseph Braun

i. With regard to EPA's statutory requirement (under the "best available science") to focus on methodological rigor and its prioritization of PESS, specifically children, Dr. Braun's research explicitly focuses on applying advanced biostatistical techniques to phthalates and other toxic chemicals in order to quantify the health effects of chemical mixtures and identify periods of heightened susceptibility.

c. Antonia Calafat

i. Noting that EPA was in search of a scientist specializing in mixtures, Dr. Calafat is chemist at the Centers for Disease Control and Prevention (CDC), leading their biomonitoring programs and explicitly focusing on the impacts of combined exposures to phthalates and other harmful chemicals.

d. Stephanie Engel

i. Dr. Engel's work focuses on the use of exposure biomarkers to assess neurodevelopmental toxicity from phthalates and other complex exposure mixtures. Additionally, the primary population focus of her research is on the impacts of chemical exposures on children's health outcomes and adverse reproductive/pregnancy outcomes.

e. Mary Fox

i. Dr. Fox's research specifically focuses on developing and refining cumulative risk assessment methods which will be the subject of consideration for this SACC.

f. Kembra Howdeshell

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[8] Toxic Substances Control Act (TSCA) Implementation: How the Amended Law Has Failed to Protect Vulnerable Populations from Toxic Chemicals in the United States. Environ Sci Technol. 2022 09 06; 56(17):11969-11982. Rayasam SDG, Koman PD, Axelrad DA, Woodruff TJ, Chartres N.

[9] U.S. Executive Office of the President. Presidential Memorandum, Modernizing Regulatory Review, § 2(b)(i) , 2021.

[10] U.S. Executive Office of the President, Executive Order on Tackling the Climate Crisis at Home and Abroad § 219 , 2021

[11] U.S. Executive Office of the President. Justice40 – A Whole-of-Government Initiative. Available: https://www.whitehouse.gov/environmentaljustice/justice40/

[12] U.S. Executive Office of the President. Executive Order 13985 On Advancing Racial Equity and Support for Underserved Communities Through the Federal Government, FR 2021-01753, 2021.

i. The work that Dr. Howdeshell has done with the National Institute of Environmental Health Sciences (NIEHS) Division of Translational Toxicology, has been integral to the work of authoritative bodies such as the National Academy of Sciences (NAS), whose used her research into the dose-additive effects of multiple phthalate exposures in their 2008 review of the Cumulative Effects of Phthalate Esters in Risk Assessment.

g. Devon Payne-Sturges

i. Dr. Payne-Sturges is one of the premier researchers in environmental health on developing our understanding of cumulative exposures and publishing methodologies to better estimate cumulative risk focusing on the inclusion of non-chemical stressors. In addition to this, she has connections with organizations on the ground, such as Asian Pacific Environmental Network, who help inform her research regarding the complexities of cumulative exposure.

h. Shirlee Tan

i. Dr. Tan has served for the past few years on EPA's Children's Health Protection Advisory Committee (CHPAC) and is the incoming chair, bringing an opportunity to link the work of these two critical bodies. In addition to her experience in developing regulatory assays for phthalates and other chemicals, Dr. Tan's work at King County puts her in direct contact with communities experiencing the impact of cumulative exposures to chemicals, allowing her to ground her analysis in real-world impacts and feasibility.

i. Ami Zota

i. Dr. Zota is a researcher with a lengthy history in deepening public health's understanding of cumulative chemical exposures and health disparities within environmental justice communities, including from phthalate exposures. In addition to this, she has connections with organizations on the ground, such as Black Women for Wellness, who help inform her research regarding the complexities of cumulative exposure.

2. **EPA should strive to eliminate or manage financial conflicts of interest and appearance of a loss of impartiality from selected committee members.**

It has been demonstrated across multiple areas of research, including chemicals, that even when controlling for methodological biases, studies sponsored by industry or that have an author with a financial conflict of interest are more likely to have results that favor the sponsor's products than studies with no industry sponsorship or author conflict of interest.[13,14,15,16] The influence of financial ties on research can be traced to a variety of types of biases, and this conflict of interest needs to be distinguished from non-financial interests in the research.[17] Industry sponsorship and authors with a conflict of interest can bias research through various mechanisms, including how they design and conduct a study, selectively report the results, code events, analyze the study data, spin conclusions, as well as frame the questions that are asked. Additionally, conflicts of interest among committee

[13] Odierna DH, Forsyth SR, White J, et al. The cycle of bias in health research: a framework and toolbox for critical appraisal training. Account Res. 2013;20(2):127-41. 11

[14] Fabbri A, Lai A, Grundy Q, et al. The Influence of Industry Sponsorship on the Research Agenda: A Scoping Review. Am J Public Health. 2018;108(11):e9-e16. 12

[15] Psaty BM, Prentice RL. Minimizing bias in randomized trials: the importance of blinding. JAMA. 2010;304(7):793-4. 13

[16] Psaty BM, Kronmal RA. Reporting mortality findings in trials of rofecoxib for Alzheimer disease or cognitive impairment: a case study based on documents from rofecoxib litigation. JAMA. 2008;299(15):1813-7.

[17] Bero LA, Grundy Q. Why Having a (Nonfinancial) Interest Is Not a Conflict of Interest. PLoS Biol. 2016 Dec 21;14(12):e2001221. doi: 10.1371/journal.pbio.2001221. PMID: 28002462; PMCID: PMC5176169.

members are increasingly recognized as contributing to bias in guideline recommendations[18,19,20].Several factors influence the extent to which committee members are likely to influence guidelines and recommendations, including the relevance of the topic to the committee members interest and type and magnitude of the relationship comprising the conflict[21].

It has been established that there is an association between financial COI and recommendations from clinical guidelines and expert reviews, meaning that recommendations that are made by those with a COI, favor the interests of the industry providing support[22,23]. It is likely then that allowing committee members on the SACC with financial ties to any of the regulated chemical companies would risk the biasing the recommendations they make towards industry interests. Of further concern, is the potential "megaphone effect" that multiple conflicted SACC members are likely bring as their influence and recommendations will be in the same direction, thus creating a systemic bias.

Therefore, individuals who serve on EPA advisory committees with financial relationships with companies that can benefit from the recommendations of the advisory committee should be excluded from the committee.[24,25,26,27] EPA must use predetermined criteria to evaluate and respond to the risk of bias from the interests of prospective SACC members[28]. (See a modified version of Table 1 below)

[18] Blake P, Durão S, Naude CE, Bero L. An analysis of methods used to synthesize evidence and grade recommendations in food-based dietary guidelines.

[19] Tabatabavakili S, Khan R, Scaffidi MA, Gimpaya N, Lightfoot D, Grover SC. Financial conflicts of interest in clinical practice guidelines: a systematic review. Mayo Clin Proc Innov Qual Outcomes2021;5:466-75. Doi:10.1016/j.mayocpiqo.2020.09.016 pmid:33997642

[20] Brems JH, Davis AE, Clayton EW. Analysis of conflict of interest policies among organizations producing clinical practice guidelines. PLoS One2021;16:e0249267. doi:10.1371/journal.pone.0249267 pmid:33930893

[21] Parker L, Bero L. Managing risk from conflicts of interest in guideline development committees BMJ 2022; 379 :e072252 doi:10.1136/bmj-2022-072252

[22] Nejstgaard CH, Bero L, Hróbjartsson A, et al. Association between conflicts of interest and favourable recommendations in clinical guidelines, advisory committee reports, opinion pieces, and narrative reviews: systematic review. BMJ2020;371:m4234.pmid:33298430

[23] Coyne DW. Influence of industry on renal guideline development. Clin J Am Soc Nephrol2007;2:3-7, discussion 13-4. doi:10.2215/CJN.02170606 pmid:17699377

[24] Bero L, Anglemyer A, Vesterinen H, Krauth D. The relationship between study sponsorship, risks of bias, and research outcomes in atrazine exposure studies conducted in non-human animals: Systematic review and meta-analysis. Environment International. 2016;92-93:597-604

[25] Yank V, Rennie D, Bero LA. Financial ties and concordance between results and conclusions in meta-analyses: Retrospective cohort study. British Medical Journal. 2007;335(7631):1202-5.

[26] Mandrioli D, Kearns CE, Bero LA. Relationship between Research Outcomes and Risk of Bias, Study Sponsorship, and Author Financial Conflicts of Interest in Reviews of the Effects of Artificially Sweetened Beverages on Weight Outcomes: A Systematic Review of Reviews. PLoS One. 2016;11(9):e0162198.

[27] Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. The Cochrane database of systematic reviews. 2017;2:MR000033-MR.

[28] Parker L, Bero L. Managing risk from conflicts of interest in guideline development committees BMJ 2022; 379 :e072252 doi:10.1136/bmj-2022-072252

Table 1. Risk management model for conflicts of interest in EPA SACC members. Adapted from Parker L, Bero L. Managing risk from conflicts of interest in guideline development committees BMJ 2022; 379 doi: https://doi.org/10.1136/bmj-2022-072252

Level of risk	Type of interest	Example	Examples of entity generating secondary interest	Suggested management
High risk	Financial link* with large national or multinational chemical corporation or position of control or decision making within such a corporation	Applicant, partner, or child is one of the following: A company employee Paid adviser or consultant Recipient of speaker fees Owner of financial holdings in the company (e.g., shares, patents, royalties) Recipient of research grant money from company Recipient of monetary gift (e.g., to cover conference travel, accommodation, registration) Managerial or advisory position, including unpaid (e.g., director, trustee, member of advisory board)	Large international chemical product manufacturers (e.g., Unilever, Procter & Gamble, , 3M) Chemical companies providing raw material used in large scale manufacturing and processing (e.g., Monsanto, DuPont, BASF, Bayer, Dow Chemical, Syngenta) Trade organizations and other groups that represent chemical company interests (e.g., American Chemistry Council, Treated Wood Council, Fertilizer Institute, Arsenic Science Task Force)	Reject committee membership until 3-5 years have passed since eliminating conflict(s) of interest (e.g., by divesting financial links, resigning from position, or rejecting speaker fees)
	Position of control or decision making over small industry company	Applicant, partner, or child is owner of small company	Local manufacturers such as boutique personal care product maker, small business, Small scale manufacturing business	
Medium risk	Financial link* with chemical industry, with no decision making or control over corporation	Applicant, partner, or child is a small chemical company employee	Local manufacturers such as boutique personal care product maker, small business, Small scale manufacturing business	Individual cannot chair and may have only restricted participation in guideline committee until 3-5 years have passed since eliminating conflict(s) of interest
	Financial link* with government-chemical industry partnership	Applicant, partner, or child receives grant funding for research from formal partnership between government department	Grant from government health department-multinational chemical company partnership to study health effects	

Level of risk	Type of interest	Example	Examples of entity generating secondary interest	Suggested management
		and multinational chemical company		
	Personal financial gain from chemical related work	Applicant, partner, or child is paid for self-employed work related to chemicals (e.g., book, consulting)	Not applicable	
Low risk	Professional interests of prospective member	Author of empirical studies, systematic reviews (where the research and researchers are not funded by industry or other chemical sector business) Recipient of research grant from non-industry sources (e.g., government) Member of previous guidelines committee Key opinion leader—e.g., author of opinion based articles, advocacy (not funded by industry or other chemical sector business) Member of a professional society that is not industry funded Working as a health professional in a public health/environmental health/medical related field (e.g., toxicologist, medical doctor)	Not applicable	Full participation
Minimal or no risk	Personal experiences, values, or lifestyle habits of prospective member	Political and economic views Spiritual or religious affiliation Cultural practices, upbringing, ethnicity Professional and personal experiences Lifestyle habits and preferences, including	Not applicable	Full participation

Level of risk	Type of interest	Example	Examples of entity generating secondary interest	Suggested management
		dietary patterns Health problems, including dietary allergies and intolerances and those with recommended dietary restrictions Social relationships, including professional interest group membership, friendly or hostile connections with others		

For example, any SACC member that has financial tie with a chemical company (a company employee, paid adviser or consultant, recipient of speaker fees, owner of financial holdings in the company (e.g., shares, patents, royalties), recipient of research grant money from company, recipient of monetary gift (e.g., to cover conference travel, accommodation, registration), managerial or advisory position, including unpaid) or position of control or decision making within such a chemical corporation, EPA should reject committee membership until 3-5 years have passed since eliminating conflict(s) of interest.

In the Federal Register notice for this panel, the selection criteria for panel membership "is based on the function of the Committee and the expertise needed to address the Agency's charge to the Committee … Other factors considered during the selection process include availability of the prospective candidate to fully participate in the Committee's reviews, **absence of any conflicts of interest or appearance of loss of impartiality, independence with respect to the matters under review, and lack of bias**. **Although financial conflicts of interest, the appearance of loss of impartiality, lack of independence, and bias may result in non-selection**, the absence of such concerns does not assure that a candidate will be selected to serve on the SACC."[29] (emphasis ours)

Federal ethics regulations require EPA to "[a]ssure that the interests and affiliations of advisory committee members are reviewed for conformance with applicable conflict of interest statutes".[30] Therefore, before finalizing the selection of individual advisory members the vetting process of conflicts of interest should include: publicly identifying and disclosing any conflicts that include financial ties with industry; determining whether a conflict of interest exists with the committee member; and finally implementing the necessary procedures to manage any conflicts of interest. Policies around declarations of financial conflicts of interest apply to entities who have a possibility of financial gain from the outcome of the SACC's activities, as such, consulting or working in support of community organizations or NGOs should not be interpreted as a financial conflict of interest. We have made these comments and more in our recommendations to EPA regarding conflicts of interest in our recent publication in

[29] US EPA. (2022). Requests for Nominations: Cumulative Risk Assessment; Science Advisory Committee on Chemicals, ad hoc Expert Reviewers; Public Meeting. Available: https://www.regulations.gov/document/EPA-HQ-OPPT-2022-0918-0001

[30] 41 C.F.R. § 102-3.105(h)

Environmental Health.[31] We encourage EPA to ensure the composition of the SACC cumulative risk panel cover a wide breadth of knowledge and experience from various relevant sectors who do not have a financial COI.

Regarding financial conflicts of interest, we have concerns about the following nominees:

1. Michael Bartels

As stated in his profile, Dr. Bartels has a history of consulting with and working for industries and trade associations with a particular financial interest in the outcome of the SACC's activities, such as Dow Chemical which manufactures two chemicals that may be evaluated using the Cumulative Risk Guidance (formaldehyde and 1,2-dichloropropane) and releases three others (1,3-butadiene, 1,2-dichloroethane, and 1,1,2-trichloroethane)[32], Corteva which releases formaldehyde[33], and the American Chemical Council, which represents a number of industries that have financial interests in the chemicals regulated under TSCA, including phthalates. In addition to that he has also been affiliated with the International Life Sciences Institute (ILSI) which is funded by myriad groups such as Monsanto, Bayer CropScience, Dow, Coca-Cola, Unilever, and the tobacco industry among others.[34,35,36] His expertise and work in toxicokinetics and biomonitoring, and the expertise he would offer to the SACC, is almost exclusively funded by or in collaboration with industries such as Dow Chemical[37,38,39,40], the American Chemistry

[31] Woodruff TJ, Rayasam SDG, Axelrad DA, Koman PD, Chartres N, Bennett DH, Birnbaum LS, Brown P, Carignan CC, Cooper C, Cranor CF, Diamond ML, Franjevic S, Gartner EC, Hattis D, Hauser R, Heiger-Bernays W, Joglekar R, Lam J, Levy JI, MacRoy PM, Maffini MV, Marquez EC, Morello-Frosch R, Nachman KE, Nielsen GH, Oksas C, Abrahamsson DP, Patisaul HB, Patton S, Robinson JF, Rodgers KM, Rossi MS, Rudel RA, Sass JB, Sathyanarayana S, Schettler T, Shaffer RM, Shamasunder B, Shepard PM, Shrader-Frechette K, Solomon GM, Subra WA, Vandenberg LN, Varshavsky JR, White RF, Zarker K, Zeise L. A science-based agenda for health-protective chemical assessments and decisions: overview and consensus statement. Environ Health. 2023 Jan 12;21(Suppl 1):132. doi: 10.1186/s12940-022-00930-3. PMID: 36635734; PMCID: PMC9835243.

[32] Zhongyu (June) Yan, Michael Bartels, Bhaskar Gollapudi, Jeffrey Driver, Matthew Himmelstein, Sean Gehen, Daland Juberg, Ian van Wesenbeeck, Claire Terry & Reza Rasoulpour (2020) Weight of evidence analysis of the tumorigenic potential of 1,3-dichloropropene supports a threshold-based risk assessment, Critical Reviews in Toxicology, 50:10, 836-860, DOI: 10.1080/10408444.2020.1845119

[33] Zhongyu (June) Yan, Michael Bartels, Bhaskar Gollapudi, Jeffrey Driver, Matthew Himmelstein, Sean Gehen, Daland Juberg, Ian van Wesenbeeck, Claire Terry & Reza Rasoulpour (2020) Weight of evidence analysis of the tumorigenic potential of 1,3-dichloropropene supports a threshold-based risk assessment, Critical Reviews in Toxicology, 50:10, 836-860, DOI: 10.1080/10408444.2020.1845119

[34] Jacobs, A. (2019, September 16). *A shadowy industry group shapes food policy around the world*. The New York Times. Retrieved August 4, 2022, from https://www.nytimes.com/2019/09/16/health/ilsi-food-policy-india-brazil-china.html

[35] Steele, S., Ruskin, G., & Stuckler, D. (2020). Pushing partnerships: Corporate influence on research and policy via the International Life Sciences Institute. *Public Health Nutrition*, *23*(11), 2032–2040. https://doi.org/10.1017/s1368980019005184

[36] UCSF Industry Documents Library. (2022). Query – author: International Life Sciences Institute. Available: https://www.industrydocuments.ucsf.edu/results/#q=author%3A(INTL%20LIFE%20SCIENCES%20INST)&h=%7B%22hideDuplicates%22%3Atrue%2C%22hideFolders%22%3Atrue%7D&cache=true&count=508

[37] Troutman, J. A., Rick, D. L., Stuard, S. B., Fisher, J., & Bartels, M. J. (2015). Development of a physiologically-based pharmacokinetic model of 2-phenoxyethanol and its metabolite phenoxyacetic acid in rats and humans to address toxicokinetic uncertainty in risk assessment. Regulatory Toxicology and Pharmacology, 73(2), 530–543. https://doi.org/10.1016/j.yrtph.2015.07.012

[38] Smith, J. N., Hinderliter, P. M., Timchalk, C., Bartels, M. J., & Poet, T. S. (2014). A human life-stage physiologically based pharmacokinetic and pharmacodynamic model for chlorpyrifos: Development and validation. Regulatory Toxicology and Pharmacology, 69(3), 580–597. https://doi.org/10.1016/j.yrtph.2013.10.005

[39] Poet, T. S., Timchalk, C., Bartels, M. J., Smith, J. N., McDougal, R., Juberg, D. R., & Price, P. S. (2017). Use of a probabilistic PBPK/PD model to calculate data derived extrapolation factors for chlorpyrifos. Regulatory Toxicology and Pharmacology, 86, 59–73. https://doi.org/10.1016/j.yrtph.2017.02.014

[40] Poet, T. S., Timchalk, C., Hotchkiss, J. A., & Bartels, M. J. (2014). Chlorpyrifos PBPK/PD model for multiple routes of exposure. Xenobiotica, 44(10), 868–881. https://doi.org/10.3109/00498254.2014.918295

Council[41,42,43], or a combination of the two[44]. Therefore, given EPA's goal to convene a SACC without conflicts of interest or appearance of loss of impartiality, independence with respect to the matters under review, lack of bias, and lack of financial conflicts of interest, Dr. Bartels should be excluded from consideration.

2. James Bruckner

While not stated in Dr. Bruckner's profile, his work looking at the impacts of pyrethroid pesticides has historically been financially supported by industry groups and trade organizations such as the Consumer Specialty Products Association (CSPA, now known as the Household and Commercial Products Association), a consortium of 18 chemical companies (including BASF, Clorox, and Dow) that engage in the manufacture, formulation, distribution and sale of products grossing in more than $100 billion annually in the United States[45]. In 2012 Dr. Bruckner received nearly $900K from the CSPA to assess potential neurotoxic risks posed by pyrethroid insecticides to infants and children[46].

His research has been primarily funded by another industry group, the Council for the Advancement of Pyrethroid Human Risk Assessment (CAPHRA), whose members include BASF, which manufactures several chemicals that may be the subject of any potential cumulative risk guidance. [47,48] CAPHRA spearheaded a campaign to support eliminating the 3x safety factor on synthetic pyrethroids for children under 6 years of age[49] allowing children's exposure rates to these widely used chemicals (and particularly vulnerable children in farmworking communities) to increase, despite EPA's own manual on pesticide poisoning indicating there was "Little or no research has been done on the neurodevelopmental effects of other common agents, such as pyrethroids commonly used in households and agriculture."[50]

Since Dr. Bruckner's 2012 award from CSPA, he has authored fifteen papers according to PubMed.[51] Of these fifteen publications, twelve have been directly funded by CAPHRA (with no funding statements for two of them and ATSDR funding for one publication). In his profile for the SACC, Dr. Bruckner has failed

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[41] Corley, R. A., Saghir, S. A., Bartels, M. J., Hansen, S. C., Creim, J., McMartin, K. E., & Snellings, W. M. (2011). Extension of a PBPK model for ethylene glycol and glycolic acid to include the competitive formation and clearance of metabolites associated with kidney toxicity in rats and humans. Toxicology and Applied Pharmacology, 250(3), 229–244. https://doi.org/10.1016/j.taap.2010.10.011

[42] Price, P. S., Schnelle, K. D., Cleveland, C. B., Bartels, M. J., Hinderliter, P. M., Timchalk, C., & Poet, T. S. (2011). Application of a source-to-outcome model for the assessment of health impacts from dietary exposures to insecticide residues. Regulatory Toxicology and Pharmacology, 61(1), 23–31. https://doi.org/10.1016/j.yrtph.2011.05.009

[43] R. A. Corley, M. J. Bartels, E. W. Carney, K. K. Weitz, J. J. Soelberg, R. A. Gies, K. D. Thrall, Development of a Physiologically Based Pharmacokinetic Model for Ethylene Glycol and Its Metabolite, Glycolic Acid, in Rats and Humans, Toxicological Sciences, Volume 85, Issue 1, May 2005, Pages 476–490, https://doi.org/10.1093/toxsci/kfi119

[44] Hinderliter, P. M., Price, P. S., Bartels, M. J., Timchalk, C., & Poet, T. S. (2011). Development of a source-to-outcome model for dietary exposures to insecticide residues: An example using chlorpyrifos. Regulatory Toxicology and Pharmacology, 61(1), 82–92. https://doi.org/10.1016/j.yrtph.2011.06.004

[45] Environmental Expert. Companies: The Consumer Specialty Products Association (CSPA). Available: https://www.environmental-expert.com/companies/the-consumer-specialty-products-association-cspa-40169

[46] Roberson, S. 2012. Toxicologist awarded $898K for study of insecticide risks. Available: https://news.uga.edu/study-of-insecticide-risks/

[47] Mortuza, T. B., Edwards, G. L., White, C. A., Patel, V., Cummings, B. S., & Bruckner, J. V. (2018). Age dependency of blood-brain barrier penetration by cis- and trans-permethrin in the rat. Drug Metabolism and Disposition, 47(3), 234–237. https://doi.org/10.1124/dmd.118.084822

[48] Bruckner, J. V., Osmitiz, T. G., Anand, S., Minnema, D., Schmitt, W., Assaf, N., & Zastre, J. (2012). The influence of maturation on rat and human physiological processes involving protein and lipoprotein binding, gastrointestinal absorption, and blood brain permeability and transport of Pyrethroids. ACS Symposium Series, 55–64. https://doi.org/10.1021/bk-2012-1099.ch005

[49] Beyond Pesticides. (2019). EPA Proposes to Reduce Protections from Neurotoxic Pyrethroid Insecticides. Available: https://beyondpesticides.org/dailynewsblog/2019/11/epa-proposes-to-reduce-protections-from-neurotoxic-pyrethroid-insecticides/

[50] US EPA. (2013). Recognition and Management of Pesticide Poisionings (Sixth Editions). Available: https://www.epa.gov/sites/production/files/2015-01/documents/rmpp_6thed_final_lowresopt.pdf

[51] National Institutes of Medicine. PubMed Search: Bruckner, JV AND years:2012-2023. Available: https://pubmed.ncbi.nlm.nih.gov/?term=Bruckner%20JV&filter=years.2012-2023

to identify that his exclusive industry funding represents a financial conflict of interest in his work, with the majority of his research not having a conflict of interest statement or stating that there is no conflict of interested explicitly despite industry funding.

As Dr. Bruckner is primarily working for CAPHRA, his work in cumulative risk is likely a direct representation of CAPHRA's membership in the Cumulative and Aggregate Risk Evaluation System Next Generation (CARES NG)[52], with other member organizations such as

- Bayer
- BASF
- Dow
- Outdoor Residential Task Force (a consortium of 30+ agrochemical companies including BASF, Bayer, Dow, Syngenta, Valent, and Monsanto)
- Pyrethrin Joint Venture (a consortium of companies whose members include BASF)
- Pyrethroid Working Group (a pesticide industry alliance whose members include Syngenta, DuPont, and Bayer)
- Residential Exposure Joint Venture (a pesticide consortium including Syngenta, Valent, and BASF)
- Syngenta, and
- Valent

The work that CARES NG undertakes, which Dr. Bruckner is paid for, and its recommendations is directly informed by the manufacturers it represents reflecting a direct conflict of interest. Therefore, given EPA's goal to convene a SACC without conflicts of interest or appearance of loss of impartiality, independence with respect to the matters under review, lack of bias, and lack of financial conflicts of interest, Dr. Bruckner should be excluded from consideration.

3. Raymond David

As identified in his profile, Dr. David previously worked with BASF which manufactures several chemicals that may come under evaluation by the SACC (formaldehyde; 1,3-butadiene; phosphoric acid, triphenyl ester; phthalic anhydride, and trans-1,2-dichloroethylene) and chaired the toxicology research group for the American Chemistry Council's phthalate esters panel, representing a clear financial conflict of interest. He has published numerous papers downplaying phthalate risks[53,54], with either no reference to

[52] CARES NG. About. Available: https://caresng.org/about/

[53] David RM, Moore MR, Finney DC, Guest D. Reversibility of the chronic effects of di(2-ethylhexyl)phthalate. Toxicol Pathol. 2001 Jul-Aug;29(4):430-9. doi: 10.1080/01926230152500040. PMID: 11560248.

[54] Prospector Knoweldge Center. 2013. Phthalates: Softening Plastics and Making Vinyl Soft and Pliant. Available: https://knowledge.ulprospector.com/1987/phthalates-softening-plastics-making-vinyl-soft-pliant/

funding or funding from the American Chemistry Council[55,56,57,58], ILSI[59], or BASF[60,61,62,63] his employer. Combined with the financial conflict of interest due to Dr. David's funding and employment history, his publications advocate a particular position and approach to phthalates, it indicates an appearance of a loss of impartiality relevant to this panel and should thus be sufficient to exclude him from consideration.

4. Katy Goyak

Dr. Goyak is employed by ExxonMobil, which manufactures several chemicals that will come under the purview of this panel, such as di-isononyl phthalate, diisodecyl phthalate, 1,3-butadiene, and phthalic anhydride and releases two others formaldehyde, ethylene dibromide. As a part of her employment with Exxon, she attended joint agency and American Chemical Council meetings on various phthalates topics as an industry expert on toxicology and specifically the Manufacturer Requested Risk Assessment of di-isononyl phthalate and di-isodecyl phthalate that will come under review of this panel. Similar to our concerns with other nominees such as Dr. Bruckner, according to PubMed [64], Dr. Goyak has almost exclusively published research with and funded by industries with a vested financial interest in the outcome and does not represent a person with expertise to conduct an "independent scientific and technical peer review" and should be sufficient to exclude him from the panel.

5. Daniele Wikoff – ToxStrategies LLC

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[55] David RM. Exposure to phthalate esters. Environ Health Perspect. 2000 Oct;108(10):A440. doi: 10.1289/ehp.108-a440a. PMID: 11097555; PMCID: PMC1240143.

[56] David RM. Proposed Mode of Action for In Utero Effects of Some Phthalate Esters on the Developing Male Reproductive Tract. *Toxicologic Pathology*. 2006;34(3):209-219. doi:10.1080/01926230600642625

[57] Clark, K. E., David, R. M., Guinn, R., Kramarz, K. W., Lampi, M. A., & Staples, C. A. (2011). Modeling human exposure to phthalate esters: A comparison of indirect and biomonitoring estimation methods. Human and Ecological Risk Assessment: An International Journal, 17(4), 923–965. https://doi.org/10.1080/10807039.2011.588157

[58] Moses T. Bility, Jerry T. Thompson, Richard H. McKee, Raymond M. David, John H. Butala, John P. Vanden Heuvel, Jeffrey M. Peters, Activation of Mouse and Human Peroxisome Proliferator-Activated Receptors (PPARs) by Phthalate Monoesters, Toxicological Sciences, Volume 82, Issue 1, November 2004, Pages 170–182, https://doi.org/10.1093/toxsci/kfh253

[59] Klaunig JE, Babich MA, Baetcke KP, Cook JC, Corton JC, David RM, DeLuca JG, Lai DY, McKee RH, Peters JM, Roberts RA, Fenner-Crisp PA. PPARalpha agonist-induced rodent tumors: modes of action and human relevance. Crit Rev Toxicol. 2003;33(6):655-780. doi: 10.1080/713608372. PMID: 14727734.

[60] David RM, White RD, Larson MJ, Herman JK, Otter R. Toxicity of Hexamoll(®) DINCH(®) following intravenous administration. Toxicol Lett. 2015 Oct 14;238(2):100-9. doi: 10.1016/j.toxlet.2015.07.013. Epub 2015 Jul 26. PMID: 26211741.

[61] Langsch A, David RM, Schneider S, Sperber S, Haake V, Kamp H, Leibold E, Ravenzwaay BV, Otter R. Hexamoll® DINCH: Lack of in vivo evidence for obesogenic properties. Toxicol Lett. 2018 May 15;288:99-110. doi: 10.1016/j.toxlet.2018.02.008. Epub 2018 Feb 21. PMID: 29474903.

[62] Dumont LJ, Baker S, Dumont DF, Herschel L, Waters S, Calcagni K, Sandford C, Radwanski K, Min K, David RM, Otter R. Exploratory in vitro study of red blood cell storage containers formulated with an alternative plasticizer. Transfusion. 2012 Jul;52(7):1439-45. doi: 10.1111/j.1537-2995.2011.03506.x. Epub 2011 Dec 30. PMID: 22211692.

[63] David, R. Letter on 'A review of alternatives to di(2-ethylhexyl)phthalate-containing medical devices in the neonatal intensive care unit'. *J Perinatol* **32**, 393 (2012). https://doi.org/10.1038/jp.2011.169

[64] National Institutes of Medicine. PubMed Search: Goyak KO. Available: https://pubmed.ncbi.nlm.nih.gov/?term=Goyak%20KO&cauthor_id=35862579&page=2

Dr. Wikoff has previously consulted with corporate clients and published research funded by industries who she failed to declare as an association or potential conflict of interest, such as ExxonMobil, Dow Chemical and American Chemistry Council. [65,66,67]

In addition to these undeclared financial conflicts of interest the Dr. Wikoff would bring to the panel were she selected, we have commented extensively on our concerns with Dr. Wikoff's scientifically unsound systematic review methodologies which underestimate risk, particularly to children.

EPA's draft risk evaluation on Trichloroethylene is an evaluation which EPA's current administration has widely recognized as suffering from political interference[68,69], at the center of this interference was added information underestimating the risk of fetal cardiac defects, which relied heavily on an analysis focused on data quality reliability conducted by Dr. Wikoff. We discuss the myriad methodological issues with Dr. Wikoff's work and a study by Charles River Laboratories in our public comments to EPA, however we will reiterate the relevant points in brief below[70].

Dr. Wikoff's lack of consideration of mechanistic studies removes from its evidence base " *In vivo* animal studies in rats and chicks [which] have identified an association between TCE exposures and cardiac defects in the developing embryo and/or fetus (U.S. EPA, 2011e)" [71] and "provided strong and consistent supporting information for effects of TCE and metabolites on cardiac development and precursor effects." [72] This indicates that the study conclusions for Wikoff likely underestimates risk by excluding this key evidence stream. Additionally, in the TCE draft risk evaluation EPA indicates that this lack of mechanistic data may "explain the different overall conclusions between that study and this analysis," which seems to imply that the analysis for the draft risk evaluation showed a positive association between Trichloroethylene and fetal cardiac defects in comparison to Wikoff's negative association, which impacted the validity of the draft risk evaluation, represented internal inconsistencies within the evaluation and was used as a vehicle to disguise political interference as evidence-based methodologies.

During the nomination process we recognized that EPA was interested in and would benefit from having representation on the SACC from systematic review experts, as an organization with access to a number of experts in systematic review for environmental health, we nominated Dr. Juleen Lam who has independently led numerous projects to apply systematic review and evidence mapping approaches to

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[65] Grace A Chappell, Daniele S Wikoff, Chad M Thompson, Assessment of Mechanistic Data for Hexavalent Chromium-Induced Rodent Intestinal Cancer Using the Key Characteristics of Carcinogens, Toxicological Sciences, Volume 180, Issue 1, March 2021, Pages 38–50, https://doi.org/10.1093/toxsci/kfaa187 https://www.sciencedirect.com/science/article/pii/S0273230020302166#sec5

[66] Wikoff D, Lewis RJ, Erraguntla N, Franzen A, Foreman J. Facilitation of risk assessment with evidence-based methods - A framework for use of systematic mapping and systematic reviews in determining hazard, developing toxicity values, and characterizing uncertainty. Regul Toxicol Pharmacol. 2020 Dec;118:104790. doi: 10.1016/j.yrtph.2020.104790. Epub 2020 Oct 7. PMID: 33038430.

[67] Daniele S Wikoff, Jonathan D Urban, Caroline Ring, Janice Britt, Seneca Fitch, Robert Budinsky, Laurie C Haws, Development of a Range of Plausible Noncancer Toxicity Values for 2,3,7,8-Tetrachlorodibenzo-p-Dioxin Based on Effects on Sperm Count: Application of Systematic Review Methods and Quantitative Integration of Dose Response Using Meta-Regression, Toxicological Sciences, Volume 179, Issue 2, February 2021, Pages 162–182, https://doi.org/10.1093/toxsci/kfaa171

[68] Shogren, E. (2020). EPA scientists found a toxic chemical damages fetal hearts. The Trump White House rewrote their assessment. Available: https://revealnews.org/article/epa-scientists-found-a-toxic-chemical-damages-fetal-hearts-the-trump-white-house-rewrote-their-assessment/

[69] Hegsted, M. (2021). Freedhoff Says 'Political Interference' Compromised TSCA TCE Evaluation. Available: https://insideepa.com/daily-news/freedhoff-says-political-interference-compromised-tsca-tce-evaluation

[70] US EPA. (2020). Comment submitted by Swati Rayasam et al., Science Associate, Program on Reproductive Health and the Environment, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco (UCSF PRHE). Available: https://www.regulations.gov/comment/EPA-HQ-OPPT-2019-0500-0106

[71] US EPA. (2020). Trichloroethylene (CASRN 79-01-6); Draft Toxic Substances Control Act (TSCA) Risk Evaluation. Page 216. Available: EPA Document #740R18008

[72] US EPA. (2020). Trichloroethylene (CASRN 79-01-6); Draft Toxic Substances Control Act (TSCA) Risk Evaluation. Page 223. Available: EPA Document #740R18008

environmental health questions, and specifically to developmental and reproductive health outcomes that will be the subject of the SACC's review. We advise EPA to revisit Dr. Lam's nomination if it finds itself in need of systematic review expertise, as Dr. Wikoff's work has been directly linked to scientific integrity concerns that underestimate risk to a deeply vulnerable population, newborns.

6. Judy LaKind

Dr. LaKind has consulted for, and been funded by, several entities with financial conflicts of interest without publicly disclosing these ties in her profile. Particularly, her primary research and work around data quality on risk assessment and systematic review, as identified by her profile, has been almost exclusively funded by industries through contracts with her consulting firm LaKind Associates, LLC. For example, her systematic review of:

- Triclosan, used in toothpastes, was funded by Colgate-Palmolive[73];
- Ozone, a criteria air pollutant, was funded by the American Petroleum Institute, which was given an advance copy of the manuscript[74];
- Synthetic Organic Chemicals and Children's Neurodevelopmental Outcomes was funded by the American Chemistry Council who represents manufacturers[75]; and
- Phthalates, the subject of this SACC, and BPA were both funded by the European Chemical Industrial Council[76,77].

Additionally, Dr. LaKind's editorials or opinion pieces around her expertise in systematic review and chemical risk assessment has been funded by Corteva[78]. Similar to our concerns regarding Dr. Wikoff's candidacy and specific expertise in systematic review, we are concerned that both Dr. Wikoff and Dr. LaKind, two candidates with identified systematic review expertise, are almost entirely funded by industries with a financial interest in the outcome of this work. We again reiterate our recommendation for the consideration of Dr. Lam's candidacy as an unconflicted systematic review expert who was nominated.

7. Rita Schoeny

Similar to a number of other nominees we have concern with the fact that Dr. Schoeny has a long history of co-authoring publications funded by industries with financial interest in the outcome of the research. Dr. Shoeny has co-authored publications with the American Chemistry Council, 3M, Dow, DuPont, and ILSI, as well as been on publications that have received funding from entities who have a

[73] Goodman M, Naiman DQ, LaKind JS. Systematic review of the literature on triclosan and health outcomes in humans. Crit Rev Toxicol. 2018 Jan;48(1):1-51. doi: 10.1080/10408444.2017.1350138. Epub 2017 Jul 25. PMID: 28741979.

[74] LaKind JS, Burns CJ, Pottenger LH, Naiman DQ, Goodman JE, Marchitti SA. Does ozone inhalation cause adverse metabolic effects in humans? A systematic review. Crit Rev Toxicol. 2021 Jul;51(6):467-508. doi: 10.1080/10408444.2021.1965086. Epub 2021 Sep 27. PMID: 34569909.

[75] LaKind JS, Anthony LG, Goodman M. Review of reviews on exposures to synthetic organic chemicals and children's neurodevelopment: Methodological and interpretation challenges. J Toxicol Environ Health B Crit Rev. 2017;20(8):390-422. doi: 10.1080/10937404.2017.1370847. Epub 2017 Sep 27. PMID: 28952888.

[76] Lakind JS, Goodman M, Mattison DR. Bisphenol A and indicators of obesity, glucose metabolism/type 2 diabetes and cardiovascular disease: a systematic review of epidemiologic research. Crit Rev Toxicol. 2014 Feb;44(2):121-50. doi: 10.3109/10408444.2013.860075. Epub 2014 Jan 6. PMID: 24392816.

[77] Goodman M, Lakind JS, Mattison DR. Do phthalates act as obesogens in humans? A systematic review of the epidemiological literature. Crit Rev Toxicol. 2014 Feb;44(2):151-75. doi: 10.3109/10408444.2013.860076. Epub 2014 Jan 14. PMID: 24417397.

[78] LaKind, J. S., Naiman, J., & Burns, C. J. (2020). Translation of Exposure and Epidemiology for Risk Assessment: A Shifting Paradigm. International Journal of Environmental Research and Public Health, 17(12), 4220. MDPI AG. Retrieved from http://dx.doi.org/10.3390/ijerph17124220

direct financial interest in the outcome of the work[79,80,81,82,83,84]. Additionally, Dr. Schoeny was recently paid by the Arsenic Science Task Force, an industry consortium of trade associations and companies, such as the Treated Wood Council, the Fertilizer Institute, and the National Mining Association, to submit comments to EPA's Office of Research and Development on the Draft IRIS Handbook[85]. Considering that Dr. Schoeny's career at EPA was marked by close relationships with regulated industries and the consulting groups that support them, given EPA's goal to convene a SACC without conflicts of interest or appearance of loss of impartiality, independence with respect to the matters under review, lack of bias, and lack of financial conflicts of interest, Dr. Schoeny should be excluded from consideration.

[79] Simon TW, Simons SS Jr, Preston RJ, Boobis AR, Cohen SM, Doerrer NG, Fenner-Crisp PA, McMullin TS, McQueen CA, Rowlands JC; RISK21 Dose-Response Subteam. The use of mode of action information in risk assessment: quantitative key events/dose-response framework for modeling the dose-response for key events. Crit Rev Toxicol. 2014 Aug;44 Suppl 3:17-43. doi: 10.3109/10408444.2014.931925. PMID: 25070415.

[80] Pottenger LH, Andrews LS, Bachman AN, Boogaard PJ, Cadet J, Embry MR, Farmer PB, Himmelstein MW, Jarabek AM, Martin EA, Mauthe RJ, Persaud R, Preston RJ, Schoeny R, Skare J, Swenberg JA, Williams GM, Zeiger E, Zhang F, Kim JH. An organizational approach for the assessment of DNA adduct data in risk assessment: case studies for aflatoxin B1, tamoxifen and vinyl chloride. Crit Rev Toxicol. 2014 Apr;44(4):348-91. doi: 10.3109/10408444.2013.873768. Epub 2014 Feb 4. PMID: 24494825.

[81] Moore MM, Schoeny RS, Becker RA, White K, Pottenger LH. Development of an adverse outcome pathway for chemically induced hepatocellular carcinoma: case study of AFB1, a human carcinogen with a mutagenic mode of action. Crit Rev Toxicol. 2018 Apr;48(4):312-337. doi: 10.1080/10408444.2017.1423462. Epub 2018 Feb 12. PMID: 29431554.

[82] Kozal JS, Lynch HN, Klapacz J, Schoeny RS, Jean PA, Maier A. Mode of action assessment for propylene dichloride as a human carcinogen. Chem Biol Interact. 2023 Feb 6:110382. doi: 10.1016/j.cbi.2023.110382. Epub ahead of print. PMID: 36754223.

[83] Becker RA, Dellarco V, Seed J, Kronenberg JM, Meek B, Foreman J, Palermo C, Kirman C, Linkov I, Schoeny R, Dourson M, Pottenger LH, Manibusan MK. Quantitative weight of evidence to assess confidence in potential modes of action. Regul Toxicol Pharmacol. 2017 Jun;86:205-220. doi: 10.1016/j.yrtph.2017.02.017. Epub 2017 Feb 20. PMID: 28232103.

[84] Elcombe CR, Peffer RC, Wolf DC, Bailey J, Bars R, Bell D, Cattley RC, Ferguson SS, Geter D, Goetz A, Goodman JI, Hester S, Jacobs A, Omiecinski CJ, Schoeny R, Xie W, Lake BG. Mode of action and human relevance analysis for nuclear receptor-mediated liver toxicity: A case study with phenobarbital as a model constitutive androstane receptor (CAR) activator. Crit Rev Toxicol. 2014 Jan;44(1):64-82. doi: 10.3109/10408444.2013.835786. Epub 2013 Nov 4. PMID: 24180433; PMCID: PMC4019974.

[85] US EPA. (2022). Comment submitted by Rita Schoeny. Available: https://www.regulations.gov/comment/EPA-HQ-ORD-2018-0654-0004