

November 29, 2024

Comments on EPA’s Science Advisory Committee on Chemicals (SACC) Peer Review for 1,3-Butadiene; Request for Nominations

Comments submitted via regulations.gov to the docket ID EPA-HQ-OPPT-2024-4025-0003

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 these comments.

We appreciate the opportunity to support qualified candidates to serve as members of EPA’s Science Advisory Committee on Chemicals (“SACC”), pursuant to section 2625(o) of the Frank R. Lautenberg Chemical Safety for the 21st Century Act.¹ 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 Risk Evaluation of 1,3- Butadiene under the Toxic Substances Control Act (TSCA)* (hereafter referred to as the “1,3-butadiene SACC”).

There is an established association between financial conflicts of interest (COI) and recommendations from clinical guidelines and expert reviews that favors the interests of the industry providing financial support.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.

The role of the SACC is to support the mission of EPA in protecting human health and the environment. We, therefore, encourage EPA to consider the following when finalizing nominations for the 1,3-butadiene SACC: 1) the elimination of financial COI among nominated members; 2) the need for transparent and effective financial disclosure policies that are strictly enforced; and 3) the need for representation from directly impacted, susceptible, and/or highly exposed populations.

In summary, our comments address the following main points:

- 1. EPA should strive to eliminate financial conflicts of interest from nominated 1,3-butadiene SACC members.**
- 2. EPA should implement and strictly enforce transparent and effective financial disclosure policies.**
- 3. EPA should prioritize representation from directly impacted, susceptible and/or highly exposed populations on the 1,3-butadiene SACC.**
- 4. Support for the nomination of two individuals to the 1,3-butadiene SACC.**

¹ 15 U.S.C. § 2625(o).

² 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. *BMJ*2020;371:m4234.pmid:33298430;
Coyne DW. Influence of industry on renal guideline development. *Clin J Am Soc Nephrol*2007;2:3-7, discussion 13-4. doi:10.2215/CJN.02170606 pmid:17699377.

Thank you for the opportunity to provide nominations. Please let us know if we can provide any additional information or be of further help.

Sincerely,

Abena BakenRa, MPH
Science Associate, Science and Policy
Program on Reproductive Health and the Environment
University of California, San Francisco

Rashmi Joglekar, PhD
Associate Director, Science and Policy
Program on Reproductive Health and the Environment
University of California, San Francisco

Emily Lasher, MPH
Science Associate, Science and Policy
Program on Reproductive Health and the Environment
University of California, San Francisco

Jessica Trowbridge, PhD, MPH
Associate Research Scientist, Science and Policy
Program on Reproductive Health and the Environment
University of California, San Francisco

Nicholas Chartres, PhD
Senior Research Fellow
School of Pharmacy, Faculty of Medicine & Health
The University of Sydney

Tracey Woodruff, PhD, MPH
Professor and Director
Program on Reproductive Health and the Environment
University of California, San Francisco

DETAILED COMMENTS

1. EPA should eliminate financial conflicts of interest from nominated 1,3-butadiene SACC 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 (COI) are more likely to have results that favor the sponsor's products than studies with no industry sponsorship or author COI.³ The influence of financial ties on research can be

³ 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;

traced to a variety of types of biases, and this COI needs to be distinguished from non-financial interests, including personal beliefs and interests, theoretical approach, and desire for academic advancement in the research, as non-financial interests do not reflect the same systematic biases.⁴ Industry sponsorship and authors with a COI 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.

EPA has a professional and legal duty to select committee members who will provide credible and independent scientific analysis and advice free from financial 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. In the Federal Register notice for this panel, the selection criteria for panel membership include "the breadth of collective experience needed to address EPA's charge to the SACC, as well as ... Absence of financial conflicts of interest or the appearance of a loss of impartiality."⁵ (emphasis ours). In addition, 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".⁶

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, or those with certain affiliations should be recused when decisions that have financial implications for their profession are made.⁷ Of further concern is the potential "megaphone effect" that may occur when multiple SACC members with financial conflicts of interest align their influence and recommendations in the same direction, creating a systemic bias.⁸

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;

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

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.

⁴ 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; Bero L. Addressing bias and conflict of interest among biomedical researchers. *JAMA*. 2017;317(17):1723-1724. doi:10.1001/jama.2017.3854.

⁵ US EPA. (2024). 1,3-Butadiene; Draft Risk Evaluation Under the Toxic Substances Control Act (TSCA); Science Advisory Committee on Chemicals (SACC) Peer Review; Request for Nominations of ad hoc Peer Reviewers. Available: <https://www.regulations.gov/document/EPA-HQ-OPPT-2024-0425-0001>.

⁶ 41 C.F.R. § 102-3.105(h).

⁷ 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;

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.;

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.;

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.

⁸ 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 Manag* 2021;10:255-65.pmid:32610752.

Before finalizing the nomination of individual advisory members, EPA's vetting process of conflicts of interest must include: identifying and disclosing any conflicts that include financial ties with industry; determining whether a COI exists with the committee member; and finally implementing the necessary procedures to eliminate any COIs. Further, the committee chair must be free of any financial conflicts of interest.

2. EPA should implement and strictly enforce transparent and effective financial disclosure policies.

It is critical that EPA publicly disclose all financial relationships of nominees with regulated industries, particularly industries with a specific financial interest in the activities of the SACC. While some of this information can be found in published papers, not all funding arrangements can be identified through publications in the public domain. Disclosure and COI policies play an essential role in protecting EPA and SACC 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 disclosing COI was previously seen as sufficient to manage committee members' interests, research has shown that paradoxically, those members who disclose COI provide more biased advice due to 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.⁹ Systematic reviews have established that disclosed financial conflicts are associated with research outcomes biased towards the sponsor and therefore demonstrate why disclosure alone is not a solution to reducing bias in guideline committees.¹⁰ We therefore urge EPA to implement and strictly enforce transparent and effective financial disclosure policies for the 1,3-butadiene SACC. We want to emphasize that the burden of vetting COI should *not* fall on the public, but rather should be integrated into the initial evaluation and review of SACC nominations by the Agency.

3. EPA should prioritize representation from directly impacted, susceptible, and/or highly exposed populations on the 1,3-butadiene SACC.

When nominating members to the 1,3-butadiene SACC, EPA should both seek representatives that have *specific scientific expertise* in the relationship of chemical exposures to health effects in workers, women, children, and other potentially exposed or susceptible subpopulations, and incorporate a broader and more inclusive definition to capture representation from individuals with diverse knowledge sources that represent unique perspectives on 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 approaches that have demonstrated that incorporating knowledge resources outside of traditional academic and

⁹ Loewenstein G, Sah S, Cain DM. The unintended consequences of conflict of interest disclosure. *JAMA* 2012;307:669-70. doi:10.1001/jama.2012.154. pmid:22337676;

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.

¹⁰ Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. *Cochrane Database Syst Rev* 2017;2:MR000033. pmid:28207928.

science fields can greatly enrich the research and policy process.¹¹ As such, EPA should ensure that SACC nominees cover a wide breadth of knowledge and experience from various relevant sectors that do not have financial COI. We, therefore, urge EPA to prioritize representation from directly impacted, susceptible, and/or highly exposed populations on the 1,3-butadiene SACC.

4. Support for the nomination of two individuals to the 1,3-butadiene SACC.

We are pleased to support the following two candidates due to the depth of their expertise, their other professional qualifications, and their experience providing guidance to EPA on the implementation of amended TSCA. We believe these individuals are extremely well qualified, are not financially conflicted, and have considerable experience and expertise that would contribute valuable service to EPA.

a) Ms. Ruthann Rudel

- i. Ms. Rudel's distinguished 30-year career in toxicology and environmental health research makes her exceptionally qualified to serve as a peer reviewer on the 1,3-butadiene SACC. As Director of Research at Silent Spring Institute, she has led groundbreaking work on endocrine-disrupting chemicals, carcinogens, and their links to breast cancer risk. Her extensive experience in evaluating toxicity and risk assessment methodologies, combined with her service on prestigious advisory committees, positions her as an ideal candidate to contribute valuable perspectives during the peer review process.

b) Dr. Keeve Nachman

- i. Dr. Nachman's extensive 20-year career in environmental health and risk assessment, coupled with his leadership roles at Johns Hopkins University, makes him an ideal candidate to serve as a peer reviewer on the 1,3-butadiene SACC. His expertise spans a broad range of topics, from chemical risk evaluations to epidemiologic investigations, and his experience as an Associate Editor and Editorial Review Board member for prominent journals further demonstrates his capacity to critically evaluate scientific research. Dr. Nachman's in-depth knowledge of environmental exposures and regulatory policy will bring valuable insights to the peer review process.

¹¹ 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.