

October 23, 2026

Comments from Scientists and Academics to the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM).

Submitted online via Regulations.gov to FR Doc. 2026-19297

These comments are submitted on behalf of the undersigned scientists and academics. We declare that we have no direct or indirect financial or fiduciary interests in the subjects 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 to the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) in advance of the November 4-5 meeting.

Our comments address the following main points:

1. A rigorous, health-protective framework is needed to incorporate new approach methodologies (NAMs) into regulatory decision-making.
2. There is a need for a more balanced SACATM membership.

We urge the SACATM to recommend that federal agencies develop a consistent, transparent, systematic review-based framework for integrating data from NAMs with existing *in vivo* and epidemiologic evidence to inform health-protective regulatory decision-making. Without an established framework, flawed and underpowered NAMs can be used to weaken regulation of toxic chemicals and increase risk of adverse health outcomes, inconsistent with the mission and vision of the National Institute of Environmental Health Sciences (NIEHS).

We also encourage NIEHS to ensure that future SACATM membership is more balanced, with equal participation by industry representatives and individuals without financial conflicts of interest, including experts from academia, NGOs, and community groups.

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:

1. A rigorous, health-protective framework is needed to incorporate data from NAMs into regulatory decision-making.

Across federal agencies, there is an urgent need for a transparent, rigorous framework to incorporate data from NAMs alongside existing human and animal evidence to inform regulatory chemical hazard and risk assessments. Agencies like the U.S. Environmental Protection Agency (EPA) currently lack science-based frameworks for translating data from NAMs into regulatory decisions. Without one, NAMs could be used to prematurely exonerate chemicals for safety.

This concern is particularly important for complex outcomes such as neurodevelopmental harm, for which the science underlying NAMs is still evolving. EPA and other agencies should be cautious about relying exclusively on these methods to determine that a chemical poses no hazard or risk.

Recent EPA actions illustrate this concern. In its recent updated draft risk assessments of three organophosphate insecticides (acephate, malathion, and dimethoate), the Office of Pesticide Programs relied on flawed and underpowered NAMs data to propose eliminating a critical 10X safety factor required by the 1996 Food Quality Protection Act (FQPA).¹ That factor is intended to protect infants and children when there are uncertainties or data gaps regarding developmental neurotoxicity. In other words, EPA's decision relied on data from underpowered NAMs to claim *certainty* that these pesticides do not harm neurodevelopment, dismissing decades of epidemiologic and animal evidence showing that organophosphate pesticides are neurotoxic and harm neurodevelopment.² Removing this safeguard will weaken protections for children and increase the risk of adverse outcomes, including autism, ADHD, and lower IQ.

Negative findings from NAMs are increasingly being used by EPA in other offices and programs to discount evidence of harm and support conclusions of safety, even when animal and human evidence point in the opposite direction. Instead, NAMs should be evaluated as a line of evidence within a systematic review framework alongside all other evidence. Positive findings can contribute to hazard identification, but negative findings should not be treated as evidence of

¹ Project TENDR (2024). Comments on EPA's Proposed Interim Registration Decisions for Several Organophosphate Pesticides: Acephate, Malathion, Dimethoate. <https://www.regulations.gov/comment/EPA-HQ-OPP-2009-0059-0124>

² Bennett D, Bellinger DC, Birnbaum LS, et al. Project TENDR: Targeting Environmental Neuro-Developmental Risks The TENDR Consensus Statement. *Environ Health Perspect.* 2016;124(7):A118-A122. doi:10.1289/EHP358.; Bemanalizadeh M, Khoshhali M, Goli P, Abdollahpour I, Kelishadi R. Parental Occupational Exposure and Neurodevelopmental Disorders in Offspring: a Systematic Review and Meta-analysis. *Curr Environ Health Rep.* 2022;9(3):406-422. doi:10.1007/s40572-022-00356-6

safety. All evidence should be integrated together to support transparent and scientifically defensible decisions. *If there is sufficient existing data, protective action should not be delayed.*

2. There is a need for a more balanced SACATM membership.

The SACATM is a federally chartered advisory body, which is governed by the provisions of the Federal Advisory Committee Act (FACA). FACA imposes requirements on federal agencies when they establish or utilize any advisory committee, like the SACATM.³ For example, when an agency seeks to obtain such advice or recommendations, it must ensure the advisory committee: is "in the public interest;"⁴ is "fairly balanced in terms of points of view represented and the function to be performed;"⁵ and will not be "inappropriately influenced by . . . any special interest, but will instead be the result of the advisory committee's independent judgment."⁶

The ICCVAM Authorization Act requires the SACATM to include representatives from "the personal care, pharmaceutical, industrial chemicals, or agriculture industry." This creates a risk that committee recommendations will be biased or influenced by financial interests. The ICCVAM Authorization Act also notes the inclusion of "any corporation developing or marketing new or revised or alternative test methodologies." Inclusion of such corporations may also introduce bias, as they have a vested financial interest in demonstrating that their methods are effective and suitable for regulatory use.

This concern is well-supported by empirical research. Systematic reviews have found that financial conflicts of interest in scientific studies are associated with research outcomes biased towards the financial sponsor.⁷ 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.^{8,9,10,11}

³ 42 U.S.C. 2851-3(d)

⁴ Id. App. II, § 9(2).

⁵ Id. § 5(b)(2).

⁶ Id. § 5(b)(3).

⁷ Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. *Cochrane Database Syst Rev* 2017;2:MR000033.pmid:28207928

⁸ 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

⁹ 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

¹⁰ Psaty BM, Prentice RL. Minimizing bias in randomized trials: the importance of blinding. *JAMA.* 2010;304(7):793-4. 13

¹¹ 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.

Financial conflicts of interest among committee members are increasingly being recognized as significant contributors to bias in guideline recommendations.^{12,13,14} An association has been established between financial conflicts of interest among expert reviewers and clinical guideline recommendations that favor the interests of the industry providing support.^{15,16}

The SACATM’s current and historical composition does not appear to reflect the “fair balance” envisioned by FACA. Since 2015, more than 60% of committee members each year have had industry or consulting affiliations.

At a minimum, the SACATM should have equal representation from industry and individuals without financial conflicts of interest, including experts from academia, NGOs, and community groups.

¹² Blake P, Durao S, Naude CE, Bero L. An analysis of methods used to synthesize evidence and grade recommendations in food-based dietary guidelines. *Nutr Rev* 2018;76(4):290-300.

¹³ 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 Outcomes* 2021;5:466-75. Doi:10.1016/j.mayocpiqo.2020.09.016 pmid:33997642

¹⁴ Brems JH, Davis AE, Clayton EW. Analysis of conflict of interest policies among organizations producing clinical practice guidelines. *PLoS One* 2021;16:e0249267. doi:10.1371/journal.pone.0249267 pmid:33930893

¹⁵ 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

¹⁶ 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