FACT SHEET

EPA MUST RELY ON PROVEN SCIENCE:
MISUSE OF NEW APPROACH METHODOLOGIES (NAMS) WILL HARM WORKERS, COMMUNITIES, AND ECOSYSTEMS

The U.S. Environmental Protection Agency (EPA) is responsible for assessing the human and environmental health risks of new chemicals and then regulating these chemicals to protect people and wildlife. We rely on the EPA to provide accurate toxicity tests, especially for people in jobs such as manufacturing or farming that require close contact with chemical compounds.

In the last several years, pesticide and industrial chemical manufacturers have lobbied and worked closely with EPA to develop new approach methodologies (NAMs) for estimating the hazard and risks of chemicals to be regulated by EPA under its statutory authorities, including the Toxic Substances Control Act (TSCA) and the pesticide laws, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Food Quality Protection Act (FQPA).

These new NAMs, most of which are unproven, include many in vitro biochemical, molecular, and cell-based assays and computational models.[1] These tests frequently understate or incorrectly evaluate hazard and risk, with potentially harmful consequences for workers, families, wildlife and ecosystems.

Farm workers spraying pesticide over newly planted strawberries close to a fumigated field on a farm in California. If pesticide health hazards are underestimated workers will be put in harm's way.

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For decades, the EPA—along with other agencies and scientific bodies—has largely relied on rodent tests conducted in accordance with animal welfare rules to: identify health hazards; conduct risk determinations; assess chemicals for carcinogenicity, developmental and reproductive toxicity, neurotoxicity, immunotoxicity, and other serious and complex human health outcomes.

Over time, a comprehensive, peer-reviewed framework has been developed for using rodent studies to make judgments about the effects of chemicals on human health.[2] Following this framework, the EPA has used findings from rodent studies to justify significant reductions in exposure and risk for highly hazardous chemicals. As the agency notes in its NAMs Work Plan: "The scientific confidence associated with the traditional toxicity tests comes from the decades of experience in their development and application."[3]

The determinations of unreasonable risk in the EPA's first ten chemical-risk evaluations done in the last few years under the amended TSCA are based on findings of carcinogenicity, reproductive and developmental toxicity, neurotoxicity, and immune effects in rodent studies. Similarly, recent toxicity assessments on per- and polyfluoroalkyl substances (PFAS) have made extensive use of rodent data, as have chemical assessments issued by the EPA's Integrated Risk Information System (IRIS) on ethylene oxide, hexavalent chromium, methylene chloride, trichloroethylene, phthalates, and many other high-concern substances.

The 2016 amendments to TSCA direct the EPA to encourage the "use of scientifically valid test methods and strategies that reduce or replace the use of vertebrate animals," but TSCA requires such tests to "provide information of equivalent or better scientific quality and relevance that will support regulatory decisions under this title." Thus, before rodent testing can be reduced, the EPA must assure that the replacement test systems will "provide information of equivalent or better scientific quality" than rodent studies, and will "support regulatory decisions" under TSCA.

However, except for a limited number of NAMs that have been validated for acute toxicity endpoints, such as skin and eye irritation, which we support, most NAMs are not reliable for determining important health effects. According to the EPA's NAMs Work Plan, "While considerable progress is being made in developing NAMs, there are still scientific challenges and information gaps that limit a complete reliance on NAMs for Agency decisions related to the assessment of a chemical's potential risk to human health and the environment.[4]

In short, the NAMs cell-based tests and computational analysis do not replicate the complexity of living organisms, such as growth, reproductive health, and immune system functions in people and wildlife. This means that NAMs are highly likely to miss health effects such as cancer and birth defects, for which established rodent tests provide reliable and actionable data to support risk assessment and risk management.

Disregarding actionable information from rodent toxicity tests will stymie the EPA's ability to evaluate potential harm from the thousands of chemicals that currently lack adequate toxicity testing and will undercut health and environmental protections.

A soccer player practicing at Hartman Park in the Harrisburg/Manchester neighborhood beside the Valero Houston Refinery located on the Houston Ship Channel in Houston, Texas. People who live, work, play, or worship near facilities that release harmful emissions are often exposed to multiple, cumulative, and synergistic hazards that are completely unaddressed by NAMs. These fenceline and frontline communities deserve strong health protections based on proven science.

It is reasonable to use NAMs to flag concerns and possibly conduct further testing, but it is a misuse of NAMs to say that because a chemical showed no toxicity in these limited tests—which fail to replicate biological complexity—the chemical is safe. For example, the international Organisation for Economic Co-operation and Development (OECD) reviewed the NAMs that test for developmental neurotoxicity in November 2023. The OECD concluded that these NAMs had too many data gaps and limitations, and therefore a NAMs test result should not be interpreted as a lack of chemical hazard potential.[5] Similarly, the EPA's own Children's Health Protection Advisory Committee recommended that, "NAMs be used for screening purposes and to indicate a hazard or upgrade concern for a hazard, but conclusions about the absence of hazard cannot be drawn solely based on NAMs data.... [NAMs] should not be used to reduce default adjustment factors but could be used to add or increase such a factor."[6] In summary, scientists and global policy experts agree that it would be a misuse of NAMs to employ the test results to further weaken risk estimates or reduce health protections.

If the EPA misuses weak and unreliable toxicity test methods to approve chemicals or fails to regulate them without adequate testing, those suffering the greatest harm will be vulnerable populations, including pregnant people, farmworkers, fenceline and frontline communities and other environmental justice populations—often underserved and communities of color—who breathe, drink, and ingest toxic chemical pollution every day. The problems associated with using NAMs to estimate hazard will be compounded by the limitations inherent in the exposure estimations used in risk assessments, which often lead to underestimating the risks to vulnerable populations.

The EPA has acknowledged that "vibrant stakeholder engagement and partnerships are the backbone of" its environmental justice work.[7] Yet, discussions of NAMs development have been heavily skewed in favor of a small number of organizations promoting NAMs, most prominently the chemical industry.[8] In contrast, the EPA has dismissed serious concerns raised by academic researchers and government scientists; public interest groups, including wildlife and environmental groups, consumer advocates, farmworker representatives, and environmental justice organizations; a recent report from the U.S. National Academies of Sciences, Engineering, and Medicine; the OECD; and the EPA's Children's Health Protection Advisory Committee.[9]

To ensure robust protection of the environment and human health going forward, the EPA should:

- Ensure that NAMs will not be used to downgrade a chemical hazard evaluation. Given the limited nature of these tests, a showing of no impact or no result doesn't mean that a chemical is safe.
- Establish a peer-reviewed framework that meets scientific best practices to assess whether NAMs provide adequate and reliable data for chemical hazard assessments and achieve the same or greater level of health protection as rodent studies, as TSCA requires.
- Continue to rely on rodent tests conducted in accordance with animal-welfare-protection rules where needed to fill critical data gaps on the potential hazards of new and existing substances and to protect human health, including when directing chemical manufacturers to research the risks of their products.
- Conduct meaningful outreach to susceptible communities, whose interests in enhanced protection against chemical exposure will be directly impacted by NAMs and who deserve a strong voice in how agencies use these tests to address chemical risks.

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In addition, our groups have long advocated that the EPA take prudent, scientifically sound steps to reduce the need for chemical testing, consistent with the Louisville Charter for Safer Chemicals.[10] These include:

- Regulate related chemicals as classes rather than individually.
- Use established methods—including uncertainty factors and read-across and category-based approaches—to fill data gaps.
- Reduce known or suspected toxicants by promoting the elimination of unnecessary chemicals and supporting the development and use of safer substitutes.
- Make better use of existing data, including from epidemiologic studies, academic research, medical case reports, workplace incident reports, and spill and release information.

As stated in a letter to the EPA from 38 scientists, environmental justice groups, and farmworker advocates, "The ultimate usefulness of new NAMs assays resides in their potential ability to be protective of the health of workers, communities, and ecosystems."[11] NAMs should not be misused in ways that could understate chemical risks or that reduce, prevent, or delay needed health protections.

ENDNOTES

1 As used here, the term NAMs refers only to these newer NAMs and not to older and more established practices—such as "read across" and "quantitative structure-activity relationship"—that have long been used to evaluate and regulate chemicals.

2 EPA, Office of Research and Development, *ORD Staff Handbook for Developing IRIS Assessments*, 2022, https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=356370; EPA, Risk Assessment Forum, *Guidelines for Carcinogen Risk Assessment*, 2005, https://www.epa.gov/risk/guidelines-carcinogen-risk-assessment.

3 EPA, Office of Research and Development, Office of Chemical Safety and Pollution Prevention, "Section III. Establish Scientific Confidence in NAMs and Demonstrate Application to Regulatory Decisions," in *New Approach Methods Work Plan*, December 2021, 12, https://www.epa.gov/system/files/documents/2021-11/nams-work-plan_11_15_21_508-tagged.pdf.

4 EPA, "Section IV. Develop NAMs to Address Scientific Challenges and Fill Important Information Gaps," in *New Approach Methods Work Plan*, 16. https://www.epa.gov/system/files/documents/2021-11/nams-work-plan_11_15_21_508-tagged.pdf

5 OECD, Environment Directorate, *Initial Recommendations on Evaluation of Data From the Developmental Neurotoxicity (DNT) In-Vitro Testing Battery*, Series on Testing and Assessment no. 377, November 3, 2023, https://one.oecd.org/document/ENV/CBC/MONO(2023)13/en/pdf.

6 Children's Health Protection Advisory Committee, letter to EPA acting administrator Jane Nishida, "Protecting Children's Health Under Amended TSCA: Chemical Prioritization," January 26, 2021, 9, https://www.regulations.gov/document/EPA-HQ-OA-2022-0574-0011.

7 EPA, *EJ 2020 Action Agenda*, October 2016, 10, https://www.epa.gov/sites/default/files/2016-05/documents/052216_ej_2020_strategic_plan_final_0.pdf.

8 Gina M. Hilton et al., "A New Paradigm for Regulatory Sciences," *Regulatory Toxicology and Pharmacology* 145 (December 2023), https://doi.org/10.1016/j.yrtph.2023.105524; Douglas C. Wolf et al., "Transforming the Evaluation of Agrochemicals," *Pest Management Science* 78, no. 12 (December 2022): 5049-5056, https://doi.org/10.1002/ps.7148; Amy J. Clippinger et al., "Pathway-Based Predictive Approaches for Non-animal Assessment of Acute Inhalation Toxicity," *Toxicology in Vitro* 52 (October 2018): 131-145, https://doi.org/10.1016/j.tiv.2018.06.009; Amy J. Clippinger et al., "Alternative Approaches for Acute Inhalation Toxicity Testing to Address Global Regulatory and Non-regulatory Data Requirements: An International Workshop Report," *Toxicology in Vitro* 48 (April 2018): 53-70, https://doi.org/10.1016/j.tiv.2017.12.011.

9 Nicholas Chartres et al., "Conducting Evaluations of Evidence That Are Transparent, Timely and Can Lead to Health-Protective Actions," *Environmental Health* 21, no. 123 (2022), https://doi.org/10.1186/s12940-022-00926-z; Alliance of Nurses for Healthy Environments et al., "The Role of NAMs and Rodent Studies"; National Academies of Sciences, Engineering, and Medicine, *Building Confidence in New Evidence Streams for Human Health Risk Assessment: Lessons Learned from Laboratory Mammalian Toxicity Tests* (Washington, DC: National Academies Press, 2023), https://doi.org/10.17226/26906; OECD, *Initial Recommendations*; Children's Health Protection Advisory Committee, "Protecting Children's Health."

10 Coming Clean, Inc. "The Louisville Charter for Safer Chemicals," accessed July 2024, https://comingcleaninc.org/louisville-charter/endorse#:~:text=The%20Louisville%20Charter%20consists%20of,the%20environment%2C%20or%20the%20climate.

11 Alliance of Nurses for Healthy Environments et al., "The Role of NAMs and Rodent Studies." https://www.nrdc.org/sites/default/files/2023-03/epa-letter-tsca-nams-20230315.pdf