UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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DEPUTY ADMINISTRATOR

SUBJECT: Future Development and Use of Risk Assessments

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On May 23, 2025, President Donald Trump signed Executive Order 14303, "Restoring Gold Standard Science,"[1] which focuses on ensuring that science generated and used by the federal government is transparent, rigorous and impactful and that federal decisions are informed by credible, reliable and impartial scientific evidence.

EPA's mission is to protect human health and the environment, consistent with our statutory authority. The agency recognizes the critical importance of applying Gold Standard Science in all scientific activities, including research, applied science and the use of environmental information and data as part of performing EPA's statutory functions. EPA is committed to upholding the principles of Gold Standard Science.

Agency staff and external stakeholders (including states, tribes, researchers and the regulated community) have identified a need for EPA to provide more clarity as to how the agency should develop and utilize information to inform scientific risk assessments. As part of EPA's implementation of the Executive Order on Gold Standard Science, this memorandum focuses on identifying a path forward to address some of the most critical issues that have been identified related to EPA's development of risk assessments and the use of elements of risk assessments, such as hazard-based benchmarks, in regulatory and non-regulatory actions.

Additional clarity on these issues will provide the agency with the confidence to proceed to fulfill our statutory responsibilities and provide transparent and usable information to our partners and the public, ensuring we are protecting human health and the environment.

[1] https://www.federalregister.gov/documents/2025/05/29/2025-09802/restoring-gold-standard-science

Risk Assessments at EPA

EPA has utilized a structured risk assessment framework that has been foundational to agency decision-making for decades. This structure is based on four core elements:

Hazard Identification – Determination of whether a chemical can cause adverse health effects;

Dose-Response Assessment – Determination of the relations between the magnitude of exposure and the probability or severity of adverse effects;

Exposure Assessment – Estimation of the amount of exposure of a chemical, through which pathways exposure takes place, and the length of exposure; and

Risk Characterization – Estimation of risk by integrating hazard, dose-response, and exposure information to inform further decision-making.

EPA's regulatory program offices (the Office of Air and Radiation, the Office of Water, the Office of Chemical Safety and Pollution Prevention and the Office of Land and Emergency Management) typically manage various components of this process. In practice, a majority of the exposure assessment and risk characterization work is typically conducted within EPA's regulatory program offices.

EPA's IRIS Program

EPA created the Integrated Risk Information System program in 1985 to provide an internal database of human health hazard and dose-response values for chemicals found in the environment. Congress has never authorized the IRIS program in statute. The original intent of the IRIS program was to improve consistency in the evaluation of chemical toxicity across the agency. Since then, the IRIS program has attempted to serve a centralized function for the agency in developing hazard identification and dose-response assessments for environmental chemicals.

For the first decade of the IRIS program, IRIS summaries were generated from within EPA's regulatory program offices and reviewed by Agency workgroups in order to build consensus scientific positions on human health effects that may result from chronic oral or inhalation exposure to chemicals found in the environment. In 1996, EPA implemented a new process for developing Agency consensus health assessments. As part of this process, the development of IRIS summaries was consolidated and moved into EPA's Office of Research and Development. Furthermore, EPA provided for an agency-wide nomination process, independent external peer review, public comment, consensus agency review, and the posting of final assessments on the IRIS database. This new process was intended to improve efficiency in getting information onto the IRIS database, increase opportunity for public input, implement EPA's new peer review policy, and provide for external peer review.

However, criticisms of the IRIS program's human health hazard and dose-response assessments mounted, particularly from stakeholders and interagency partners. Recognizing the importance of robust hazard and dose-response values to many regulations, and to address stakeholder concerns, in 2004, the Office of Management and Budget began coordinating the review of IRIS assessments, similar to how OMB coordinates the interagency review of regulations. In 2009, EPA further revised the IRIS process, with 13 discrete steps, intended to speed the development and review of IRIS assessments and to ensure robust public and interagency engagement earlier in the IRIS assessment

development process. These changes also made EPA the coordinator of interagency review. Since 2009, EPA has continued to modify the IRIS process and the development of IRIS assessments.

Agency and Stakeholder Concerns with the IRIS Program

Changes to the IRIS process, including changes to the development of IRIS assessments, have not fully addressed many stakeholder concerns with IRIS assessments, including concerns from EPA's regulatory program offices and staff. IRIS assessments are not regulations; however, they sometimes provide a critical part of the scientific foundation for decision-making to protect public health across EPA under an array of environmental laws. And the way IRIS assessments are employed as part of regulatory decisions is often one of the areas of largest stakeholder concern and disagreement with the Agency's practices.

It is EPA's longstanding position that regulatory program offices are the best suited to integrate information to meet statutory and regulatory criteria. Likewise, program offices are in the best position to make determinations about how to conduct risk assessments and utilize risk assessment information to meet programmatic objectives. Regulatory program offices generally manage components of the risk assessment process and often conduct a majority of the exposure assessment (including exposure modeling) and risk characterization work. Historically, the IRIS program often developed hazard identification and dose-response information. However, some EPA programs routinely develop their own hazard identification and dose-response information outside of the IRIS program. For instance, EPA's pesticides program conducts full risk assessments, that include hazard identification and dose-response assessments based on the robust data sets it receives, as required by its regulations. Similarly, EPA's Toxic Substances Control Act program frequently conducts its own hazard and dose-response assessments in keeping with its rigorous statutory and regulatory requirements.

While the IRIS program was designed originally to promote consistency, the development of a risk assessment often includes science policy judgments – many of which are informed by statutory and regulatory authority and objectives. Similar to exposure assessment (which has always been conducted by EPA regulatory program offices), both hazard and dose-response assessments can often require science policy judgments. These include, for example, determining the most appropriate and fit-for-purpose uncertainty factors to apply, identifying the response level that represents adversity consistent with the statutory and regulatory framework, selecting the population of greatest concern for the decision being made, and determining what dose-response curve shape and form is appropriate. Over the years, it has become more clear that having a single program within one office at EPA make these judgments for all hazard and dose-response assessments for all of EPA is not optimal for developing fit-for-purpose risk assessments tailored to meet specific legal, statutory, and regulatory obligations.

Assumptions

Because IRIS assessments inform all populations (both domestically and internationally), under all exposure scenarios, the IRIS program has produced hazard values that have been critiqued by stakeholders, including peer reviewers, as reflecting inflated concerns for risk, identifying thresholds that are not realistic for real-world exposure scenarios, and requiring unrealistic environmental or

workplace conditions. The methodology to produce an IRIS toxicity value requires a series of science policy judgments regarding uncertainty, often including extrapolating from high-dose to low-dose or extrapolating from rodents to humans. Stakeholders have noted that IRIS has historically conservatively estimated hazard posed by many chemicals at each step, sometimes leading to counterfactual or improbable outcomes. When many conservative assumptions are stacked on top of each other, the cumulative effect can produce an estimated "safe" exposure level that is orders of magnitude below naturally occurring levels in the environment or naturally produced levels in the human body. In one example, the IRIS toxicity value for ethylene oxide (EtO), a chemical critical for medical equipment sterilization, has been criticized because it was at least 10,000 times lower than levels naturally occurring in the human body. Likewise, as explained recently in the Agency's proposal titled "National Emission Standards for Hazardous Air Pollutants: Ethylene Oxide Emissions Standards for Sterilization Facilities Residual Risk and Technology Review Reconsideration," 91 Fed. Reg. 12700 (Mar. 17, 2026), two sources of uncertainty in the IRIS value for ethylene oxide alone, dose-response model selection and the use of the statistical upper confidence limit, resulted in an EtO IRIS value that was up to five times lower (*i.e.*, EtO is five times safer than the IRIS value provided).

Modeling

Because IRIS assessments are intended to be "one size fits all" by design, stakeholders have noted that they may not adequately consider important scientific issues, such as mode of action information which describes the mechanisms by which a toxic substance causes harm. Consideration of alternative mode of action information, including mechanistic data and data from new approach methodologies (NAMs) can inform whether health protective default approaches for modeling of data are appropriate. But because IRIS assessments sought to be protective for many scenarios, some stakeholders have suggested that the IRIS program has been less inclined to consider all reasonably available information, including information which might affect the dose-response values. The Executive Order on Gold Standard Science now requires that we consider all reliable and available information and conduct a rigorous evaluation of the evidence.

EPA's regulatory program offices in the past have at times struggled with addressing the misalignment between the hazard values produced by the IRIS program and their own statutory and regulatory frameworks that direct how regulatory decisions must be made. Furthermore, EPA regulatory program office staff across the Agency have expressed concerns with the IRIS program's development process and their limited or complete lack of involvement in the development of IRIS assessments. In order to reconcile IRIS program conclusions and findings with specific regulatory or programmatic requirements, EPA program offices have required additional time for analysis and decision-making, with subsequent implications of longer timeframes for eventual EPA regulatory actions. In some instances, these longer timeframes have delayed new or revised regulatory standards from being promulgated and taking effect, postponing the resulting human health and environmental benefits of those standards.

A Path Forward for Agency Risk Assessments

The concerns and programmatic shortcomings noted above have not advanced the original goal of the IRIS program – and EPA as a federal agency – to present hazard and dose-response information in a consistent, transparent manner which represents Gold Standard Science and allows for accountability.

EPA's regulatory program offices are implementing unique regulatory programs that utilize and integrate information necessary to meet statutory or regulatory criteria, and therefore those offices are in the best position to make determinations about how best to conduct all elements of risk assessments that can be used to implement programmatic objectives and inform regulatory actions. This includes having the program offices make the science policy judgments based on their own regulatory programs that are necessary to develop fit-for-purpose hazard and dose-response assessments. EPA's regulatory program offices are best-suited to conduct these assessments with a lens toward ensuring that results accurately reflect Gold Standard Science and fit-for-purpose data and can be translated into direct action by EPA and our federal, state, tribal and local partners.

EPA's mission of protecting human health and the environment is carried out largely through rulemaking and other administrative or regulatory actions. To best support these objectives, EPA's regulatory program offices need robust science. EPA's recent reorganization brings regulatory science closer to the regulatory programs. And with the cross-agency work led by the Office of Applied Science and Environmental Solutions, EPA is taking steps to address the concerns raised about the IRIS program and to improve the quality and usefulness of scientific data developed by the Agency. Ultimately, EPA will be able to act more quickly and effectively to reduce harm to the environment and human health by ensuring that all risk assessments are fit-for-purpose.

EPA will take necessary steps to increase internal coordination and expand collaborative work at the Agency and with our partners on risk assessments. This partnership will be focused on EPA's statutory programs with support from OASES, and will enhance the agency's ability to deliver timely, credible, and Gold Standard risk assessments. This effort will ensure that EPA programs are working collaboratively with each other and other partners to accurately define their needs and focus resources to ensure they will have a direct benefit to the regulatory requirements that directly impact the everyday lives of Americans.

Addressing Previous Decisions that Utilized IRIS Values

In implementing this effort, EPA is also addressing actions conducted previously within the IRIS program. IRIS values have been developed since 1985 under different processes and procedures, using different approaches. Specific disclaimer language will be added to EPA's IRIS website to remind users that IRIS values represent only the first two steps of the four-step risk assessment process and are not necessarily intended for use as regulatory levels. Before relying on IRIS values, users should ensure that the IRIS assessments and values are fit for their intended purpose and that the values are consistent with the most current scientific literature.

Existing Final IRIS Assessments and Information

EPA Actions Informed by Existing IRIS Assessments and Information: EPA program offices that previously utilized IRIS assessments and IRIS program information as part of regulatory decision-making should review how that information was employed in their specific regulatory or programmatic actions and determine if any updates or changes are warranted. Program offices should consider whether the IRIS information is fit-for-purpose, represents best available science, was developed in a manner consistent with statutory and regulatory obligations, and meets current standards for transparency, impartiality, reliability, and credibility, in keeping with Gold Standard Science.

External Entity Actions Informed by Existing IRIS Assessments and Information: External entities that may have utilized previous assessments or information developed through the IRIS program, should consider undertaking a review similar to the reviews that will be taken by EPA program offices. Review is encouraged to ensure any decision or reliance was accurately and properly implemented.

Continued Availability of IRIS and Risk Assessment Information

Existing Final IRIS Assessments and Information: All existing final assessments and information developed through the IRIS program will continue to be available to the public.

Draft Assessments, Information, and Data: EPA will ensure that all other information developed or gathered through the IRIS program, including all information from any assessment in development, will continue to be available to the public.

Future Risk Assessments: Each program office should determine the best approach for making available hazard and dose-response information developed under each program's statutory and regulatory obligations.