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EPA's Flawed IRIS Program Is Far from Gold Standard

EPA's Integrated Risk Information System Produces Counterproductive Results

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Environmental activists claim that the U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) represents the gold standard for risk assessment.[1] In reality, IRIS has a long history of sloppy research and lack of transparency that has advanced faulty and often counterproductive regulations that impose needless burdens on the public.[2] In addition, poorly conducted IRIS assessments have sounded false alarms about risk and produced unwarranted health scares.

IRIS is a research program that assesses chemical toxicity that EPA program offices use to develop regulations under federal laws such as the Safe Drinking Water Act, the Clean Air Act, Superfund, and other laws. It operates outside the regulatory framework; therefore systems to ensure the scientific integrity of IRIS assessments are limited. Many of its findings have tended to be excessively cautious based on questionable and incomplete science.

Efforts to reform IRIS have been ongoing and debated for several decades, but only recently have serious reform efforts gained traction. In particular, the Improving Science in Chemical Assessments Act (H.R. 6468), sponsored by Rep. Andy Biggs (R–Ariz.) in the 115th Congress, would move most IRIS functions to program offices. It passed the House Science, Space, and Technology Committee in August 2018, but did not reach the floor. Under this legislation, the EPA's Office of Research and Development, which houses IRIS, would continue to maintain a database using the assessments from the program offices. The bill would require EPA offices to operate under the scientific standards set within the laws they implement. It would also require that risk assessments rely on the best available science and deploy practices to improve the quality of the science via policies that promote transparency, reproducibility, and weighing of the evidence.

This paper offers an overview of the IRIS program and makes the case for how reforms like the Improving Science in Chemical Assessments Act offer the opportunity for significant improvement of the EPA's approach to chemical risk assessment.

Background on IRIS. EPA officials created IRIS administratively in 1986 as an agency-wide program run by two inter-office scientific work groups to provide unanimous consensus information on chemical risks that all of EPA could use for regulatory purposes. Accordingly, IRIS assessments had tremendous influence on myriad EPA policy decisions related to such things as cleanup of hazardous waste sites, drinking water standards, clean

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air rules, regulatory and market impacts around the world, and many other issues. Initially, IRIS represented an agency-wide database of chemicals and relevant data, but in 1995 the inter-office workgroups were disbanded and this agency-wide focus was lost. The EPA's research office continued to conduct its own chemical risk assessments, but without the agency-wide focus, these assessments were not uniformly used by the EPA. In addition, this research office had no legal guidelines based on legislation to follow.
IRIS information does not represent a full risk assessment, which usually involves several steps. The EPA identifies four:[3]

1. **Hazard Identification**. Researchers consider whether a chemical has the *potential* to cause harm at some exposure level.
2. **Dose-Response Assessment**. To determine if there is any relationship between exposure to the chemical and health conditions.
3. **Exposure Assessment**. If the dose-response assessment finds a relationship, researchers assess at what exposure levels it occurs, considering such factors as a chemical's potency, estimated public exposure levels, and frequency or duration of exposures.
4. **Risk Characterization**. Using information collected in the prior three steps, researchers assess actual risk levels based on estimated public exposure.

IRIS assessments perform the first two steps. For each chemical it sets a "reference concentration (RfC) "of a continuous inhalation exposure" and a reference dose (RfD) "of a daily oral exposure" at which the chemical is expected to pose no risk of non-cancer-related health risks.[45] Risk-specific doses (RSDs) are also established for cancer toxicity. Other EPA offices are supposed to conduct the last two steps when applying the reference concentration or dose for regulatory and other purposes.

In addition to setting reference doses and concentrations, IRIS classifies chemicals within one of the following categories based on EPA (2005) guidelines:[6]

- Carcinogenic to humans
- Likely to be carcinogenic to humans
- Suggestive evidence of carcinogenic potential
- Inadequate information to assess carcinogenic potential
- Not likely to be carcinogenic to humans[7]

IRIS Controversies. IRIS and its assessments have proven controversial, and concerns about the program have only grown over the past decade. The Government Accountability Office (GAO) raised concerns about IRIS' productivity and procedures more than a decade ago.[8] Since then, IRIS reform has continued to be the subject of GAO reports, an Inspector General Report, and congressional hearings.[9]

In 2011, a National Academies of Sciences (NAS) panel report on IRIS' formaldehyde risk assessment criticized the program for "recurring methodologic problems," including repeated failures to provide "clarity and transparency of the methods," along with inconsistencies, poor research documentation, failure to follow EPA research guidelines,

and other issues.[10] At the end of its report, the NAS panel included a special section to provide suggestions for IRIS to improve its science.

IRIS staff have been working to implement the NAS recommendations since 2011, but progress has been sluggish at best. In particular, the NAS urged IRIS staff to implement "systematic review" of the scientific literature and to operate in a more transparent way. Originally designed for review of medical research, systematic reviews go beyond simple narrative literature reviews, employing procedures to ensure a more comprehensive review of the literature in an attempt to reduce researcher bias involved with selecting studies.[11]

Operating in a systematic and transparent way should be a given, yet three years after the first NAS review, the EPA was still trying to make its research systematic when the NAS conducted yet another review, indicating that the agency made improvements but still had work to do.[12]

Reform efforts supposedly have picked up pace since President Obama selected Kristina Thayer—a former contractor/employee of the left-of center Environmental Working Group, which has a long history of exaggerating risks and supporting regulations that raise prices and limit consumer choice—to take over the office in January 2017.[13] Shortly before leaving office, Obama also selected Tina Bahadori to head the National Center for Environmental Assessment (NCEA), which houses IRIS within EPA's Office of Research and Development.

In early 2018, President Trump's budget proposed significant cuts and the Senate Omnibus reconciliation bill proposed IRIS elimination. Working to save the program, Thayer and Bahadori called for a NAS workshop and review.[14] For a day and a half in February 2018, Thayer and Bahadori briefed the NAS panel on the procedural reforms and activities they were implementing.[15] NAS released this review in April 2018. This time the EPA managed to get some modest praise for its reforms. EPA staff apparently wanted to use the NAS review to demonstrate that the IRIS has finally made some real progress, but a closer look suggests otherwise.

IRIS staff garnered some praise and avoided a critical review by keeping the scope of the NAS review extremely narrow. They asked the committee to assess only whether the "current trajectory of the program agrees with past recommendations of the National Academies" in 2011 and 2014. The NAS report explains further that the committee "was not asked to evaluate the overall value of the IRIS program," and it "was not tasked with conducting a comprehensive review of the IRIS program."[16] In other words, all the NAS was asked to do was validate the efforts the EPA has undertaken to improve the process, not whether it finally achieved its goals or whether it had substantially improved its assessments.

The EPA got what it requested, as the 2018 NAS report appears very positive but actually says little. Of the 130 pages, about 90 simply republish EPA presentations and posters, and much of the rest includes background information, title pages, and appendices. Twelve pages provide a history of the issue. The report offers a few sentences of praise for some

procedural reforms, but also points out that IRIS has still not achieved some basic goals. For example, IRIS has not even finalized a handbook outlining its process, which NAS asked for in 2014.[17]

The 2018 NAS report may have helped IRIS program staff generate good press, but it raises the question of whether their limited process reforms have translated into sound assessments or improved productivity. That information is not part of the NAS report.

IRIS' Excessive Caution. Even if IRIS were able to improve its procedures, the program suffers from a fundamental, agency-wide flaw. EPA risk assessments, by and large, focus on preventing worst-case scenarios—even absurd ones—and ignore more plausible scenarios, while ignoring more serious risks created by the EPA's own regulations.

A short but helpful paper by scientists at the American Chemistry Council (ACC) details some examples of excessively cautious IRIS reference doses. For example, the IRIS reference dose for the chemical acetone is below the level that is naturally found in breast milk. ACC notes, "The human body normally produces 2,000 to 3,000 mg of acetone each day, which is more than 40 times the IRIS-estimated levels." The IRIS assessment of methanol also sets the reference dose lower than the amounts that naturally occur in healthy foods like orange juice. This assessment implies that Americans are already at risk of methanol-induced developmental effects from such things as drinking seven ounces of orange juice.[18]

The key point is that the dose makes the poison. Some things that can be dangerous at relatively high exposures, particularly over many years or a lifetime, pose little danger at intermittent and lower exposures. We should be able to use these products if they provide benefits at these lower levels. Accordingly, we should apply the best science to determine safe exposure levels so that we can both ensure public safety and benefit from the use of these chemicals.

Some may argue that it is sensible to be overly precautionary, but excessive caution can lead to regulations and market changes that can undermine safety and quality of life,[19] ultimately doing more harm than good.[20] For example, excessively precautionary policies can contribute to malnutrition and hunger around the world by undermining agricultural innovations necessary to produce enough food for growing populations.[21] That was the case in 2002 when the government of Zambia deprived food aid to its starving populations during a famine because they feared some of the food might have contained genetically modified corn.[22] Such anti-GMO policies are precautionary rather than science-based; there's no evidence that these foods are any less safe than food from conventionally grown crops.[23] In addition, overly cautious health assessments can lead to unwarranted public health scares that have adverse impacts, as the examples below demonstrate.

Formaldehyde. The debate about IRIS' formaldehyde assessment has never simply been about its procedural failings. Rather, it strikes at the heart of IRIS' unhelpful bias toward excessive caution. The Trump administration has yet to release the final IRIS formaldehyde assessment, which appears to be highly flawed, warranting revisions that delay its release.

To start with, formaldehyde is created by all living organisms, from plants to animals to the human body, so exposure is unavoidable. Rather, the key is finding at what it level is poses a risk. It is reasonable to assume that dangerous levels would greatly exceed that which occurs in naturally in the human body and in healthy foods we consume. Yet, the draft formaldehyde assessment proposed a reference concentration that is multitudes lower than the amount that humans naturally exhale with each breath. The World Health Organization estimates that humans exhale 8.0 parts per billion (ppb) per breath while IRIS proposed setting a standard below 0.008 ppb. So if you want to avoid allegedly "dangerous" levels of this chemical, stop breathing. And forget about cooking or eating Brussels sprouts, cabbage, or shiitake mushrooms. The mushrooms alone can contain more than 300 parts per million (ppm) of formaldehyde.[24] Note that is parts per *million*, much higher than the parts per *billion* noted in the IRIS standard. But even then, these exposures pose no significant health concerns.[25]

As a result, the EPA's suggested reference dose is likely to be too low, as it was in the draft risk assessment. Critics maintain that delays indicate that the Trump administration is engaging in a cover-up about formaldehyde risks.[26] But political hype aside, IRIS should only release reports that are in line with the best science.

An assessment that overstates formaldehyde risks may lead to bans and regulations that would do more harm than good. Formaldehyde is used for medical purposes, such as in the manufacture of vaccines. In some cases, it is used to inactivate viruses that cause the flu and to detoxify bacterial toxins necessary to produce safe vaccines for diphtheria and other diseases. The levels of formaldehyde left in these vaccines are low and not dangerous. The FDA explains:

> The body continuously processes formaldehyde, both from what it makes on its own and from what it has been exposed to in the environment. When the body breaks down formaldehyde, it does not distinguish between formaldehyde from vaccines and that which is naturally produced or environmental. The amount of formaldehyde in a person's body depends on their weight; babies have lower amounts than adults. Studies have shown that for a newborn of average weight of 6 - 8 pounds, the amount of formaldehyde in their body is 50-70 times higher than the upper amount that they could receive from a single dose of a vaccine or from vaccines administered over time.[27]

Formaldehyde is also used as a preservative in personal care products to prevent the development of bacteria, mold, and other dangerous pathogens. It provides these benefits, but exposure remains very low. For example, the tiny trace of formaldehyde released when shampooing your hair is about the same amount as that contained in one medium-sized apple or pear.[28]

Ethylene Oxide. IRIS issued a new reference dose and reference concentration for ethylene oxide (EtO) in 2016, which has put some key uses of this product at risk. EtO is used to make a variety of personal care products, plastics, and household cleaners. It is also used in

the sterilization of more than 20 billion medical products, which is more than half of all medical products in use in the United States today.[29] Ethylene oxide is ubiquitous and can be found even where industrial activity is absent. In addition to small releases from medical equipment facilities sterilization and consumer products, it is produced by the human body and is released into the air from combustion and other natural sources such as vegetation.

The EPA's National Air Toxics Assessment (NATA) office uses IRIS assessments to compile its periodic report on air toxics. NATA reports estimated levels of so-called "toxics" found in outdoor air across the United States, broken down by community and zip code. These reports are supposed to help state and local officials focus on potential problem areas.

In August 2018, NATA released its sixth report for using emission data collected and estimated for 2014. In a fact sheet about the report, the EPA noted: "The 2014 NATA shows that several areas could have elevated cancer risks from long-term exposure to the chemical ethylene oxide. These elevated risks are largely driven by an EPA risk value that was updated in late 2016."[30] In other words, IRIS released such a low and excessively cautious reference concentration for EtO that this chemical was highlighted in the NATA report as a possible problem. In a petition to the EPA to correct the science underlying the NATA report, the American Chemistry Council explains:

> A simple comparison of the results of the EtO IRIS Assessment to the "real world," however, demonstrates its lack of credibility. Specifically, the RSC [relative source contributions] is 19,000 times *lower* than the normal, endogenous levels of EtO in the human body. Likewise, the RSC is orders of magnitude *lower* than ambient levels of EO. Thus, if the EtO IRIS Assessment is to be believed, normal human metabolism and/or breathing ambient air, without more, is sufficient to cause cancer. It strains scientific credibility to conclude that the EtO IRIS Assessment presents a legitimate basis for determining risk for EO.[31]

Nonetheless, after the release of the NATA report, panic has ensued in communities located near medical equipment sterilization plants that use EtO. *The Chicago Tribune* has fueled the flames of hysteria within the Illinois communities of Willowbrook, where the Sterigenics plant uses EtO to clean medical equipment, and Lake County, home to Vantage and Medline medical sterilization plants. In a series of articles, the *Tribune* developed a narrative that the Trump administration is working to allow emissions and relax regulations from medical sterilization plants that poison communities and cause cancer.[32] Such hype has promoted some local activists to call for shutting down the Willowbrook plant completely rather than assessing the real world risks.[33] In addition, personal injury lawyers are stirring the pot with frightening commentary on the topic, perhaps hoping they can cash in by bringing lawsuits.[34]

Some Democratic lawmakers have jumped on the alarmist bandwagon. Illinois Sens. Dick Durbin and Tammy Duckworth and Rep. Bill Foster have called on the EPA inspector general to conduct an independent investigation of the Trump EPA's handling of the issue.[35] Former Illinois Attorney General Lisa Madigan also sought to politicize the issue by

bringing lawsuits against the Sterigenics plant.[36] Rather than grandstanding, lawmakers should focus on advancing policies that help determine actual exposures and risks.

"The driving message of why we are fighting is no level of ethylene oxide emissions is safe," one activist told the *Chicago Tribune*.[37] Again, such fearmongering ignores the fact that *the dose makes the poison*. The question is not whether there are any emissions. The question is whether the level of human exposure is high enough to pose significant risks. The IRIS assessment has fueled the alarmism by setting absurdly low reference doses and concentrations. Combined with alarmist hype, it has done a disservice to individuals living in these communities, many of whom now live in fear.

The EPA has been testing the EtO levels within the Willowbroook community since May 2018. It recently announced that tests conducted before October 2018 may have overestimated the levels because of EtO's similarity to another chemical (trans-2-butene). Tests conducted in November 2018 found no detectible levels of EtO in residential areas and parks. At a few places near the facility, the agency found six cases where EtO was detected ranging from 0.284 to 6.62 parts per billion.[38] The EPA continues to monitor the issue and will eventually use the data to develop a risk assessment, which it says will be available in the spring of 2019.

The EPA explains on its website it does not yet have enough data to draw any conclusions. However, initial results from November are anything but alarming. The fact that no detectible levels have been measured near human populations alone should be reassuring. But if the EPA is going to produce a truly accurate final report about the risk levels, it also needs to reassess the original IRIS assessment, which was excessively cautious. As noted, EtO is produced by both manmade and natural sources, so traces are bound to be found in the environment. While such trace levels may pose little or no risk, they may continue to generate fear because of the faulty IRIS assessment.

Unfortunately, EtO uses for sterilization around the nation are now at risk because of the IRIS assessment and surrounding hype. Without EtO, many medical products would have to be destroyed rather than reused because there are no good sterilization alternatives for many types of medical equipment. As the Ethylene Oxide Sterilization Association explains, EtO sterilization is the "most effective and efficient, and often the only viable, sterilization technology," available for most of its applications. The elimination of EtO for medical product sterilization would be "significant, and likely disastrous" for public health and "would introduce the real risks of increased morbidity and mortality."[39] Similarly, in a November 2018 public statement, the medical supply company Medline explained the significant risks associated with potential shutdowns of medical sterilization facilities:

> Any disruption of EtO sterilization facilities would cause a near-immediate public health crisis. Illinois hospitals would lose access to sterilized medical packs needed for life-saving surgeries. The enormous disruption in the supply chain would put catastrophic impact on Illinois' hospital system. Hospitals would be forced to cancel surgical procedures and even shut down operating rooms. Critical care facilities with

> high volumes of emergent surgeries would be impacted immediately. Conducting non-sterile surgeries is not an option for obvious patient risk and hospital liability.[40]

Regulations or fearmongering alone that eliminates EtO sterilization could even hurt our pets. In public comments submitted to the EPA on the draft assessment, Albert E. May, CEO of the sterilization equipment manufacturer Anderson Products, explained that EtO is essential to controlling disease transmission inside veterinary practices. He noted:

> Animal health care practices are struggling with the growing problems of antibiotic resistance, MRSA prevalence and the increase in nosocomial and zoonotic infections (infections which can be transmitted from animals to humans). EtO has a long history in veterinary medicine, and there is no economically viable substitute for the wide range of instruments and materials that may be sterilized with this method.[41]

The importance of EtO to medicine should be weighed against any possible emission-related risks. A reasonable approach would seek to ensure emissions are low enough to protect public health, while benefiting from EtO uses, particularly for important medical applications. Yet the excessive caution in IRIS assessments has basically thrown such rational approaches out the window.

Conclusion. Clearly, IRIS is *not the gold standard* that many of its supporters claim. Rather, it has long produced assessments that have little basis in reality. Procedural reforms are unlikely to address the program's overly cautious culture. Rather, it is time to shut down IRIS, or at the very least give it a massive overhaul.[42] The Improving Science in Chemical Assessments Act offers one opportunity to reform the program. The EPA can also reform IRIS from within, since it was created administratively.

In July 2018, acting EPA Administrator Andrew Wheeler said that he has called for a program review to better define IRIS' mission and who its "customers" are—referring to which EPA offices its assessments are supposed to serve. "I have asked them to come back to me with some information about how we are going to use the assessments for the regulatory program," he said. He also noted that he needs to understand how IRIS fits in with the newly reformed Toxic Substances Control Act (TSCA), which he said represented the "state of the art on risk assessments."[43]

Wheeler would be wise to roll IRIS functions into the TSCA program, a possibility he seems to be considering. Recently reformed by Congress in 2016 with broad bipartisan support, TSCA has stronger language directing the agency to use the "best available science," rather than rely on outdated approaches that misrepresent actual risks. Accordingly, there are good reasons to believe that TSCA's approach would be superior to that of IRIS. Meanwhile, IRIS program functions could easily be transferred to the TSCA program.

Notes

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