EPA'S IRIS PROGRAM REQUIRES MAJOR OVERHAUL.

American® Chemistry Council

In the mid-1980s, the U.S. Environmental Protection Agency (EPA) created the Integrated Risk Information System (IRIS) to facilitate the development and dissemination of risk assessments for chemicals. This platform was intended as a tool to support and guide scientifically sound and consistent risk management decisions.

Since its inception, IRIS has become a point of contention, rather than an asset, for EPA, due to conclusions on risk that are not supported by science in all cases. The IRIS program must be overhauled to improve its scientific rigor if it wants to be credible and an asset to risk managers. In fact, many IRIS risk assessments have been referred to the National Academy of Sciences (NAS), which recently concluded that systemic flaws in IRIS methodology lead to poor quality assessments. The NAS and other expert panels frequently criticize the IRIS assessments for their poor scientific quality – a result of the IRIS's unnecessary reliance on overly conservative and default assumptions and outdated scientific information. These weaknesses are most clearly seen when IRIS-recommended "safe" levels for chemical exposures are below the levels formed every day in our bodies or are below environmental background levels.

Below are just a few of the examples that illustrate the illogical challenges the IRIS risk assessments create for risk assessors, and how these inconsistencies further undermine the credibility of the IRIS program.

ACETONE
IRIS Risk Assessment Level: 0.9 mg/kg/day
Naturally Occurring Level in Humans: 1.5 mg/kg/day

The estimated daily dose to infants from the acetone normally present in mother's milk (1.5 mg/kg/day) exceeds the IRIS-estimated safe level of 0.9 mg/kg/day by nearly two-fold. Thus, the IRIS analysis suggests that the daily doses of acetone in mother's milk are unsafe to the nursing child. This analysis also does not account for the fact that 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 – information that was available to IRIS in 2003,[1] but was not used in their revised risk values.

FORMALDEHYDE
IRIS Risk Assessment Level: 0.008 parts per billion (ppb)
Naturally Occurring Level in Humans: Up to 8.0 ppb

The World Health Organization reports that humans form formaldehyde in their bodies and exhale it at concentrations up to 8.0 ppb. The IRIS-proposed cancer risk value of 0.008 ppb would set a cancer risk value that is significantly below the levels that naturally occur in the environment. The EPA's proposed cancer risk value would suggest that human breath poses an unacceptable risk of cancer, yet experience, common sense and science tell us that this couldn't possibly be the case. In fact, a comprehensive National Academy of Sciences report recommends that the IRIS risk assessment be consistent with the World Health Organization's guidelines.

ACRYLAMIDE
IRIS Risk Assessment Level: RfD of 2 µg/kg/day
Naturally Occurring Level: 0.3 to 1 µg/kg/day

This chemical is created from the cooking process of bread and cereals. IRIS established a Reference Dose (RfD) for acrylamide at 2 µg/kg/day based on findings from a study reporting degenerative nerve changes in rats.[2] Yet acrylamide exposure estimates for a USDA-recommended diet range are up to 1 µg/kg/day. These estimates indicate a very small margin of exposure, meaning that there is very little difference between recommended dietary intake of acrylamide and the dose at which we'd expect to see toxic effects.

There has not been a sudden increase of degenerative nerve changes occurring in any population associated with the introduction of manmade acrylamide over the last few decades, calling into question the validity of IRIS results. In fact, this IRIS guideline level would suggest the USDA advocates dietary consumption of unacceptable levels of acrylamide.

ARSENIC
The inorganic arsenic IRIS review inappropriately uses a linear, no threshold approach based on a single epidemiology data set, although all available evidence on carcinogenic mode of action points to non-linear mechanisms. The arsenic IRIS document does not consider any literature after 2007, excluding over 300 articles, including detailed mechanistic data and epidemiology studies of U.S. populations. In this IRIS assessment, EPA failed to conduct an "integrative analysis" of newer epidemiology studies of U.S. and other western populations as had been requested by an independent peer review panel. Instead, the IRIS program ignored this peer review finding and chose to rely only on very dated (1968 and 1977), high exposure data from Taiwan. The "acceptable exposure levels" derived from the proposed new IRIS cancer risk evaluation would be below background levels in many soils and water supplies. Food grown and produced in the U.S. contains inorganic arsenic from natural sources, and the cancer slope factor currently being proposed by IRIS would indicate background levels of arsenic in soil and food would pose more than a minimal cancer risk and this could create unnecessary and unreasonable concerns about the safety and wholesomeness of the U.S. food supply.

METHANOL
IRIS Risk Assessment Level: RfD of 0.4 mg/kg/day
(producing an estimated blood level of 0.08 mg/L)
Levels in the Blood Stream[3]: 0.25 to 4.7 mg/L

Methanol is ubiquitous in the environment and in many foods that make up a healthy diet. It is also metabolized differently by different species. EPA has acknowledged these facts, yet recently re-released a draft assessment on methanol that does not consider the range of background/endogenous levels or currently accepted data on comparative pharmokinetics.

Studies have shown that even people on diets restricting methanol-producing foods have background blood levels ranging from 0.25 to 4.7 mg/L. Higher levels would most certainly be expected in the general population. Yet IRIS has proposed an RfD of 0.4 mg/kg/day, which clearly falls within the range of background/endogenous levels.

The IRIS assessment thus implies that Americans are already at risk of methanol-induced developmental effects – without being exposed to external methanol – and that consuming certain foods and beverages, such as orange juice, may put them at even greater risk. For example, a single 6.6 oz serving of orange juice would exceed the RfD of methanol for an adult; in children, a single 1.9 oz serving would exceed it.[4]

Risk Values Should Be Based on Best-Available Science, Not Simple Assumptions: Revise the IRIS Process

The IRIS process must be revised to follow appropriate and transparent guidelines and incorporate best-available science rather than convenient assumptions. When appropriate data are available, they should be used, not ignored, to drive realistic risk evaluation. The EPA should also offer meaningful opportunities for diverse stakeholders to contribute, including EPA managers, government and non-government agencies, industry and others so the IRIS program can be a credible and comprehensive tool for risk managers.

For information regarding the government agencies supporting these policies, go to:
The U.S. Environmental Protection Agency (www.epa.gov)
The Integrated Risk Information System (www.epa.gov/IRIS/)

[1]American Chemistry Council Acetone Panel – Submission to EPA's Voluntary Children's Chemical Evaluation Program (VCCEP): Acetone (CASRN 67-64-1), September 10, 2003.

[2]Based on degenerative nerve changes in a chronic rat study with a point of departure dose of 0.053 mg/kg/day, which was calculated as the Benchmark Dose Lower-Confidence Limit (BMDL), and applying a total uncertainty factor of 30 (3 for uncertainty in toxicokinetic differences, 10 for interindividual differences).

[3]Background/endogenous levels in people on diets that restricted methanol-producing foods.

[4]Methanol Institute – Comments on the U.S. EPA Draft Toxicological Review of Noncancer Effects of Methanol (IRIS), June 17, 2011, p. 23