IRIS Program Multi-Year Agenda

The IRIS Program multi-year agenda is providing information to the public on the following three topics:

- IRIS assessments currently underway and their status (Table 1).
- Prioritization of assessments that will be initiated over the next few years (Table 2).
- Evaluation of assessment needs and development of an update process for existing IRIS values.

IRIS assessments evaluate complex toxicity databases and integrate multiple types of evidence to provide high-quality, science-based hazard and dose-response information that is used in risk assessment. Environmental management of IRIS chemicals can have important public health and societal impacts. IRIS assessments are not regulations, but they provide a critical part of the foundation for decision-making across EPA.

Status of Current IRIS Assessments

The IRIS Program is committed to producing assessments in a timely and transparent manner to meet EPA's needs. Since the release of the IRIS enhancements in July 2013, the IRIS Program has focused on advancing a smaller number of priority assessments while simultaneously implementing recommendations from the National Research Council (NRC).[1, 2] The assessments currently under development and their status are shown in Table 1 below.

[1] http://www.nap.edu/catalog/13142/review-of-the-environmental-protection-agencys-draft-iris-assessment-of-formaldehyde

[2] http://www.epa.gov/iris/iris-and-national-research-council-nrc

Table 1. Status of chemicals currently being assessed by the IRIS Program (December 2015).

Step in IRIS Process	Assessments
6: Final Agency Review/Interagency Science Discussion	
5: Revise assessment	Ammonia (inhalation) Ethylene oxide (inhalation, cancer) Trimethylbenzenes
4: Public comment; Peer review	Benzo[a]pyrene
Pre-4: Assessments released prior to the NRC (2011). They are being revised to incorporate elements of systematic review and will be re-released to step 4.	Acrylonitrile n-Butyl alcohol Formaldehyde Polycyclic aromatic hydrocarbon (PAH) relative potency factors
3: Interagency Science Consultation	t-Butyl alcohol Ethyl t-butyl ether (ETBE) Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX)
2: Agency Review	
1: Draft development	Arsenic, inorganic Butyl benzyl phthalate Chromium VI Dibutyl phthalate Diethyl phthalate Di-isobutyl phthalate Di-isononyl phthalate Ethylbenzene Hexabromocyclododecane Naphthalene Polychlorinated biphenyls (PCBs; noncancer)
Problem formulation	

Prioritization of Assessments to be Initiated in the Next Few Years

The IRIS Program maintains an agenda of chemicals for which assessments are either underway or to be initiated. The most recent IRIS agenda, which lists over 70 chemicals, was published in May 2012. The IRIS Program has recently re-prioritized which of these chemical assessments should be initiated in the next few years. In addition, some chemicals that were not part of the 2012 agenda were identified and included in this re-prioritization. The top priority chemical assessments are those with the highest potential public health impacts and/or exposure and would be useful in anticipated EPA decision-making. A three-step process was used to determine priority: 1) collecting, analyzing, and sharing input from program and regional offices on the prioritization of chemical assessments; 2) estimating the resources and expertise needed for completing assessments; and 3) developing a cross-Agency consensus on the most important chemicals for which to begin assessment development. Each EPA program office and region prioritized chemicals based on their assessment needs. Preliminary scoping and problem formulation information was collected by the IRIS Program for the most needed assessments in order to estimate the resources required to complete the assessments. The scoping and problem formulation information included the number and types of potential adverse health endpoints that might be associated with exposure to the chemicals, the number of published epidemiologic and toxicological studies, the number of mechanistic publications and the availability of physiologically-based pharmacokinetic

(PBPK) models. This information was used to estimate the level of effort and staffing expertise needed to complete each of the assessments. The results of this effort showed that most of the Agency's highest priority needs are for major assessments, *i.e.*, the chemicals identified have many health effects studies, multiple potential health endpoints, and complex scientific issues that would likely need to be addressed.

Fifteen chemicals were identified as having the highest priority for assessment and were placed into three groups based on priority as shown in Table 2 below. The order of the chemicals within each group is alphabetical and does not reflect the priority within the group. With the exception of nitrate, nitrite, and perfluoroalkyl compounds, all of the high priority assessments are on the 2012 IRIS agenda. EPA's Office of Water is in the final stages of completing Health Advisories for two perfluoroalkyl compounds that have been found in drinking water (http://www.epa.gov/dwstandardsregulations/drinking-water-contaminant-human-health-effects-information). The IRIS Program is working with the Office of Water and other EPA programs and regions to determine the range of perfluoroalkyl compounds for which an IRIS assessment is needed.

Table 2. Groups of chemical assessments in priority order.

Group	Chemicals
1	Manganese Mercury Methylmercury Nitrate and nitrite Perfluoroalkyl compounds Vanadium and compounds
2	Acetaldehyde Ammonia (oral) Cadmium and compounds Uranium (effects not associated with radioactivity)
3	Di-(2-ethylhexyl) phthalate Dichlorobenzene isomers Methyl t-butyl ether (MTBE) Nickel and compounds Styrene

This list of chemical assessments to be initiated in the next several years is being made publicly available to inform interested parties. Offering advance notice of IRIS assessments provides the research community with an opportunity to communicate relevant ongoing research and anticipated timelines for its completion and publication.

As a part of prioritizing IRIS assessments, the need for an assessment of dioxin carcinogenicity was re-evaluated by the Agency. In 2011, EPA announced that it would conduct separate assessments for cancer and non-cancer health effects of dioxin. The non-cancer assessment was completed in 2012. The IRIS Program now intends to focus on other chemical assessment needs that have been identified as higher priorities to EPA program and regional offices and will defer completion of the dioxin cancer assessment at this time.

As a result of discussions during the development of the IRIS multi-year agenda, it was determined that an evaluation of the potential toxicity of multiple vanadium-containing compounds, including vanadium pentoxide, was a cross-Agency high priority need. For this reason, EPA has decided that the ongoing assessment of vanadium pentoxide toxicity would benefit from a concurrent, systematic evaluation of all

of the available vanadium speciation and toxicity information. Therefore, the draft vanadium pentoxide assessment will not be finalized at this time. The new assessment of vanadium-containing compounds will benefit from undergoing scoping and problem formulation steps, the application of systematic review methodology to assess human health hazards, and a peer review conducted through the standing Science Advisory Board's Chemical Assessment Advisory Committee. For more information, please see the IRIS webpage for vanadium pentoxide.

Prior to the initiation of an assessment, the IRIS Program consults with EPA program and regional offices to define the scope of the assessment, such as identifying the most important exposure pathways, and then conducts a public problem formulation step, which is intended to frame the human health endpoints and scientific issues that will likely be addressed in the assessment. EPA has begun to identify the scope of the IRIS assessments for most of the chemicals in groups 1 and 2, which will then inform the order of assessment development. The problem formulation materials for these chemicals will be released starting in 2016. The IRIS Program will provide information to the public on problem formulation meetings through the IRIS website and through email updates. In addition, as the Agency's needs and priorities evolve, changes to this list of chemical assessments will be provided on the IRIS website.

Public comments and submissions that provide information on current or planned research are encouraged to be submitted through the IRIS docket. Other comments and submissions relevant to the multi-year agenda may also be provided through the docket.

Evaluating Assessment Needs and Developing a Process for Updating IRIS Values

EPA remains committed to continue to strengthen the IRIS Program and increase transparency and productivity. The multi-year agenda, which provides information about the status of active assessments and highlights assessments scheduled to begin in the future, is a current initiative that contributes to this overarching goal. In additional efforts, the program is making further improvements that will strengthen the IRIS chemical database including:

- Beginning a project to evaluate chemical assessment needs both within and outside of EPA and the resources required to meet those needs,
- Developing a process to update and maintain finalized IRIS assessments that do not warrant a full reassessment through the IRIS process,
- Archiving pesticide assessments on IRIS that have been more recently evaluated by EPA's Pesticide Program.

All of these activities are planned or underway in concert with the implementation of enhancements to the assessment development process and improvements in response to recent NRC recommendations. Details on the above efforts and how the public can be involved will be made available on the IRIS website.