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United States
Environmental Protection
Agency

Human Health Risk Assessment

STRATEGIC RESEARCH ACTION PLAN 2012-2016

SCIENCE

Office of Research and Development
Human Health Risk Assessment

EPA 601/R-12/007

Human Health Risk Assessment

Strategic Research Action Plan 2012 - 2016

U.S. Environmental Protection Agency
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Executive Summary

This document outlines the strategic plan for EPA's Human Health Risk Assessment research efforts, and how they support and are integrated into the overall research portfolio of the Agency's Office of Research and Development.

The Human Health Risk Assessment (HHRA) research program is one of six priority National Research Program areas within the U.S. Environmental Protection Agency's (EPA) Office of Research and Development (ORD). The HHRA research program plays a unique role in serving the needs of EPA's programs and regions, as well as the broader risk assessment/management community, by identifying, evaluating, synthesizing and integrating scientific information on individual chemicals and chemical mixtures. The state-of-the-science, independently peer-reviewed human health assessments prepared under the HHRA research program serve as the foundation for EPA's regulatory and other decision-making.

Problem Statement: EPA's decisions must be based on scientifically-defensible evaluations of data that are relevant to assessing human health impacts. The current demand for human health assessments of individual chemicals and chemical mixtures is not being fully met.

Vision Statement: The HHRA research program will generate timely, credible human health assessments of individual chemicals and chemical mixtures to support priority EPA risk management decisions, thereby enabling EPA to better predict and prevent risk.

Research Themes: The HHRA research program is comprised of four complementary and integrated research themes:

1. *Integrated Risk Information System (IRIS) health hazard and dose-response assessments;*
2. *Integrated Science Assessments (ISAs) of criteria air pollutants;*
3. *Community Risk and Technical Support (CRTS) for exposure and health assessments; and*
4. *Modernizing Risk Assessment Methods (Methods).*

Theme 1 (IRIS) Outputs and Impacts: IRIS assessments are used widely by EPA's programs and regions, states, international organizations and the general public as a scientific foundation for decision-making (e.g., site-specific cleanups, rules, regulations and health policy determinations). Potential impacts that may result from these decisions include reduced environmental exposures, reduced disease burdens and improved public health. Additionally, improvements to the IRIS process and database will increase the transparency and clarity of IRIS assessments.

Examples of outputs produced under the IRIS theme include: individual IRIS assessments, scientific and technical support, and improvements to the IRIS process and database utility.

Theme 2 (ISAs) Outputs and Impacts: Under the ISA theme, HHRA scientists develop ISAs summarizing the state-of-the-science for the six criteria air pollutants—ozone, particulate matter, sulfur and nitrous oxides, carbon monoxide, and lead—and Multipollutant Science Assessments (MSAs) to support the reviews of the primary (health-based) and secondary (welfare-based) National Ambient Air Quality Standards (NAAQS), as well as to address the combined effects of nitrous and sulfur oxides. ISAs provide the scientific foundation for the EPA Administrator's decision on each of the NAAQS. Attainment of the NAAQS for these pollutants has been estimated by the Office of Management and Budget (OMB) and EPA to provide significant public health and environmental benefits to the American public that far exceed the cost of control programs. The direct benefits of EPA's air programs include the reduced incidence of a number of adverse human health impacts, including premature death and disease, improvements in visibility and avoided damage to agricultural crops and other vegetation.

Theme 3 (CRTS) Outputs and Impacts: Major outputs of the CRTS theme include quick turn-around exposure and risk assessments, crisis-level technical support, the development of Provisional Peer Reviewed Toxicity Values (PPRTVs), tools and guidance for exposure assessments and methods and tools for conducting cumulative impact assessments. The rapid response and applied technical support provided under the CRTS theme enhances the ability of EPA regional offices to quickly make sound, risk-based decisions regarding emerging issues of concern in their communities.

ORD's work in this area also ensures that EPA regional offices have the requisite tools to address community needs for screening-level decisions, records of decisions and permitting through risk-based information. EPA's ability to respond to environmental justice concerns also will be enhanced through the incorporation of nonchemical stressors into community risk assessment. The development of PPRTVs enables the Office of Solid Waste and Emergency Response (OSWER) to make informed clean-up decisions at contaminated Superfund sites, which can lead to improvements in human and ecological health in the vicinity of Superfund sites, as well as improved economic conditions and quality of life for nearby communities. Across the board, Theme 3 outputs will positively contribute to protecting the public's health, including reducing risks for sensitive populations.

Theme 4 (Methods) Outputs and Impacts: Theme 4 focuses on the translation of research, described in the Chemical Safety and Sustainability (CSS) research program and state-of-the-science methods from peer reviewed sources, into practical application in IRIS, ISA, MSA, and PPRTV assessments and in assessing special problems (e.g., hydraulic fracturing under the Safe and Sustainable Water Resources (SSWR) research program). Theme 4 products will increase the efficiency and effectiveness of EPA risk assessment programs by developing innovative approaches and applying them to mine databases and link information to users' needs in a more effective fashion. This process will enable assessments to be performed quickly and more transparently. Additionally, using quantitative estimates of incremental population

risk, along with better quantitative characterization of uncertainty and variability, will enable risk managers to more effectively use HHRA products in the context of formal decision analysis and cost-benefit analysis. This theme also includes the development of the Risk Assessment Training and Experience (RATE) Program and the application of Health and Environmental Research Online (HERO) to assessment products.

Crosscutting Issues: HHRA products rely on expertise and research conducted by the other research programs within ORD. Additionally, when developing products, HHRA scientists take into account important cross-cutting issues identified in EPA's FY 2011 – 2015 Strategic Plan: Sharing Our Vision, such as environmental justice and children's health.

Introduction

In fiscal year (FY) 2012, EPA is realigning and integrating the work of its research programs. Under the new structure, the HHRA research program will continue to provide state-of-the-science products in support of risk assessment, such as independently peer reviewed human health assessments for individual chemicals and chemical mixtures; integrated science assessments for criteria air pollutants; rapid risk assessment and technical support to meet partner and stakeholder needs; and tools to modernize human health risk assessment.

HHRA products are used extensively by EPA program and regional offices, as well as other parties, to make decisions, develop regulatory standards for environmental contaminants and manage cleanups.

The work conducted by the HHRA research program responds directly to the needs of EPA's program and regional offices, as well as to issues of shared concern among the broader risk assessment community, and falls into four complementary areas, or themes. Within each theme, HHRA scientists work with partners and stakeholders to provide science translation and technical support for HHRA's products. The HHRA research program will continue to evolve in order to meet complex environmental challenges and stakeholder needs, as demonstrated by the recent innovations in the ISAs for criteria air pollutants and through ongoing improvements to the draft development process for IRIS assessments.

Every day, the U.S. Environmental Protection Agency (EPA) must make decisions about environmental pollutants that impact human health and the environment. According to the Toxic Substances Control Act Chemical Substance Inventory, there are currently more than 80,000 chemicals in commerce, and an additional 1,000 new chemicals are introduced each year. Only a small fraction of these chemicals have been adequately assessed for potential environmental and human health risk, often because of limitations in existing data, tools and resources.

Problem Statement: EPA's decisions must be based on defensible scientific evaluations of data that are relevant to assessing human health impacts. The current demand for human health assessments of individual chemicals and chemical mixtures is not being fully met.

Vision Statement: The HHRA research program will generate timely, credible human health assessments of individual chemicals and chemical mixtures to support priority EPA risk management decisions, thereby enabling EPA to better predict and prevent risk.

Statutory Authority, Executive Orders and Policies Relevant to the Conduct of Research Under the HHRA Research Program

The HHRA research program has statutory authority to conduct its work under:

- The **Clean Air Act** (CAA) Section 103 mandates that EPA conduct a national research and development program for the prevention and control of air pollution. The 1990 CAA Amendments further require EPA to set NAAQS (40 CFR Part 50) for pollutants considered harmful to public health and the environment on a 5-year cycle and mandate the determination of risks from mobile, area and major sources of air toxics. The ISAs that are developed under the HHRA research program serve as the basis for the Administrator's decision on the individual NAAQS.

- The **Safe Drinking Water Act** (SDWA) authorizes research and assessments focusing on microbes (e.g., *Cryptosporidium*), disinfection byproducts, arsenic, sulfate and radon. The SDWA also mandates that risks are quantified for general and sensitive populations (e.g., infants, children, pregnant women) as part of cost-benefit analysis when Maximum Contaminant Levels are established. Other research provisions address risks associated with waterborne disease, complex mixtures and unregulated contaminants (e.g., development of Contaminant Candidate List).

- The **Food Quality Protection Act** (1996) requires assessment of risk from exposures to pesticides, including aggregate exposures and cumulative risk and risk to sensitive subpopulations (e.g., infants and children).

- The **Comprehensive Environmental Response, Compensation, and Liability Act** (Superfund, 1980) requires research, development and training to improve EPA's scientific capability to assess effects on and risk to human health from hazardous substances.

The HHRA research program also is responsive to Executive Orders and EPA policies, such as:

- **Executive Order 13045: Protection of Children from Environmental Health Risks and Safety Risks**, which states that each federal agency "(a) shall make it a high priority to identify and assess environmental health risks and safety risks that may disproportionately affect children; and (b) shall ensure that its policies, programs, activities, and standards address disproportionate risks to children that result from environmental health risks or safety risks."

- **EPA's 1995 Policy on Evaluating Risk to Children**, which states that "It is the policy of the U.S. Environmental Protection Agency (EPA) to consider the risks to infants and children consistently and explicitly as a part of risk assessments generated during its decision making process, including the setting of standards to protect public health and the environment."

- **Executive Order 12898: Federal Actions To Address Environmental Justice in Minority Populations and Low-Income Populations**, which states that "(a) Environmental human health research, whenever practicable and appropriate, shall include diverse segments of the population in epidemiological and clinical studies, including segments at high

risk from environmental hazards, such as minority populations, low-income populations and workers who may be exposed to, substantial environmental hazards" and "(b) Environmental human health analyses, whenever practicable and appropriate, shall identify multiple and cumulative exposures."

- **EPA's 2011 Environmental Justice Action Plan** ("Plan EJ 2014"), which established measurable commitments that address the Agency's national environmental justice priorities. These priorities created an Agency-wide focus on matters that environmental justice advocates and others have identified as critical environmental justice issues.

Addressing EPA Priorities

EPA's *FY2011–2015 Strategic Plan* (2010) identified five strategic goals to guide the Agency's work: (1) Taking Action on Climate Change and Improving Air Quality, (2) Protecting America's Waters, (3) Cleaning Up Communities and Advancing Sustainable Development, (4) Ensuring the Safety of Chemicals and Preventing Pollution, and (5) Enforcing Environmental Laws. The HHRA research program provides key contributions to Goals 1 and 4, and contributes to Goals 2 and 3.

EPA's Priorities:

Taking action on climate change

Improving air quality

Assuring the safety of chemicals

Cleaning up our communities

Protecting America's waters

Expanding the conversation on environmentalism and working for environmental justice

Building strong state and tribal partnerships

EPA's strategic plan also introduced the five cross-cutting fundamental strategies: (1) working for environmental justice and children's health; (2) advancing science, research and technological innovation; (3) strengthening state, tribal and international partnerships; (4) strengthening EPA's workforce and capabilities; and (5) expanding the conversation on environmentalism. These fundamental strategies are taken into consideration in the development of HHRA products.

Program Design

Producing an Integrated Program

HHRA is an existing multidisciplinary program that serves as a key interface between ORD and Agency decision-makers. The program's four themes and their related outputs are aligned with partner-identified needs.

The four themes are:

1. *Integrated Risk Information System (IRIS) health hazard and dose- response assessments;*
2. *Integrated Science Assessments (ISAs) of criteria air pollutants;*
3. *Community Risk and Technical Support (CRTS) for exposure and health assessments; and*
4. *Modernizing Risk Assessment Methods (Methods).*

The primary focus of the above four themes is the development of high-value health assessments. As a complement to these assessments, HHRA scientists are also contributing to the development of methods and the application of emerging science to modernize risk assessment. The HHRA research program also includes a sizable component of technical support to meet partner and stakeholder needs. The program did not require significant revisions to its major themes from the previous 2007 Multi-Year Plan. The main differences are the creation of a separate theme to address community risk and technical support and a change in emphasis in the methods development area in response to recent National Academy of Sciences (NAS) National Research Council (NRC) recommendations (NRC 2007, 2008, 2009, 2011).

Collaborating Across ORD National Research Programs

The HHRA research program occupies a critical position as the integrator of many aspects of ORD's research portfolio. While the other national programs conduct primary research and generate new data, HHRA scientists synthesize and integrate this information to develop state-of-the-science assessments and risk assessment methods. HHRA products in turn feed back into the work being done by the other national programs. For example, HHRA products help to identify research needs and data gaps, which inform the primary studies being conducted by the other national programs.

Examples of HHRA synthesis products and the ORD research programs they inform include:

- *Exposure Factors Handbook and Child-Specific Exposure Factors Handbook*—used by Sustainable and Healthy Communities (SHC) and SSWR
- IRIS health assessments—useful to SSWR; SHC; CSS; and Air, Climate and Energy (ACE)
- PPRTVs—helpful to SHC, CSS and Homeland Security
- ISAs for criteria air pollutants—inform ACE and SHC
- Cumulative risk assessments—relevant to SHC, SSWR and CSS

Developing Partnerships from the Start

Beyond EPA, HHRA products—such as IRIS assessments, ISAs, and guidance documents—are widely recognized as the principal environmental health risk assessment benchmarks in the United States and the world. Although nonregulatory and nonbinding in nature, these health risk assessment products, and the scientific analyses therein, are referenced in many federal, state, local and stakeholder environmental decisions.

The HHRA research program builds close relationships with partner federal, state and international organizations, both in accessing sources of toxicological and epidemiological data and through collaborative risk assessment development activities.

Access to data for use in risk assessments is facilitated by scientific staff networks with other federal agencies conducting primary environmental health research, particularly the National Institutes of Health-National Institute of Environmental Health Sciences National Toxicology Program and the Centers for Disease Control and Prevention's National Center for Environmental Health.

Assessment activities are coordinated through interagency working groups and collaborative relationships.

The HHRA research program has three Memoranda of Understanding (MOU); one with the California Environmental Protection Agency's Office of Environmental Health Hazard Assessment, a second with the Agency for Toxic Substances and Disease Registry and a third with the National Institute for Occupational Safety and Health. These MOUs increase communication and cooperation in the development of toxicological assessments, reduce duplication of efforts on chemical assessments, and foster harmonization and development of new risk assessment methods. In addition to these efforts, the HHRA research program is working with the Environmental Council of the State's (ECOS) Interstate Technology and Regulatory Council to develop a risk assessment training program that could be used across the 50 states.

EPA's Six Integrated Research Programs:

Human Health Risk Assessment (HHRA)

Chemical Safety for Sustainability (CSS)

Air, Climate, and Energy (ACE)

Safe and Sustainable Water Resources (SSWR)

Sustainable and Healthy Communities (SHC)

Homeland Security (HS) Research

Close relationships also are maintained with international organizations dealing with environmental health risks, including the World Health Organization through its International Programme on Chemical Safety, the International Agency for Research on Cancer and the United Nations Environment Programme through two cooperative agreements and a MOU.

EPA regularly evaluates the assessment development processes to ensure they are transparent and participatory in nature. The HHRA research program evaluates and implements recommendations made by Agency programs and regions, EPA's Board

of Scientific Counselors (BOSC), the Clean Air Scientific Advisory Committee (CASAC), the Science Advisory Board (SAB), the National Academy of Sciences (NAS), and the Government Accountability Office. The HHRA research program is committed to implementing recommendations that enhance the scientific credibility of Agency decisions, improve transparency, and increase the overall efficiency and effectiveness of the Program.

Activities conducted under the HHRA research program are responsive to the needs of EPA's program and regional offices (for a list of HHRA partners and stakeholders see Appendix A). Throughout the program development process representatives from the HHRA research program met regularly with stakeholders from across the Agency to gauge their research needs and gather feedback on HHRA products. The stated needs of Agency partners and stakeholders drove the development of the "Draft HHRA Research Framework," which is relatively broad in nature. At a more detailed level, the selection and prioritization of IRIS assessments and Provisional Peer Reviewed Toxicity Values (PPRTVs) and the timing of Integrated Science Assessments (ISAs) are also driven by stakeholder needs.

As a result, HHRA efforts are well targeted and timed to meet the needs of the Agency's programs and regions. Additionally, senior program managers were briefed on HHRA's proposed activities and outputs. The results of the planning process include alignment and prioritization of planned ORD activities during the three- to five-year cycle of the RAP, which is a living document subject to revision as programmatic needs and scientific developments alter priorities.

On a more focused scale, ongoing planning processes exist for a number of specific activities under the HHRA Strategic Research Action Plan. Regular meetings are held with representatives from the program and regional offices to determine research needs and what form HHRA outputs should take in order to most effectively respond to those needs. Formal planning of the IRIS assessment agenda occurs through a request to EPA programs and regions for nominations of priority substances for assessment. Additionally, a Federal Register Notice (FRN) is published requesting nominations for the IRIS agenda; other federal agencies, as well as any other stakeholders or members of the public, may submit nominations.

A formal planning process is used with EPA's Office of Air and Radiation (OAR) to coordinate the scope and timing of the ISAs produced by ORD with the Risk and Exposure Assessment and Policy Assessments produced by OAR. This plan and the various products from ORD and OAR are reviewed by the Clean Air Scientific Advisory Committee with opportunity for public comment. Revisions to the ISAs are planned every five years subject to the requirements of the Clean Air Act, taking into consideration resource constraints, OAR priorities and court deadlines.

PPRTVs are prepared on an ongoing basis at the request of EPA's Office of Solid Waste and Emergency Response (OSWER) for those substances found at clean-up sites and for which no IRIS value is available. An OSWER (2003) directive for site-specific assessments lists IRIS values as the first tier and PPRTVs as second tier in a hierarchy of toxicity values to be used for Superfund risk assessment. The U.S. Department of Defense and ECOS (2007) have agreed to this same hierarchy

for their health assessment programs in the context of clean-up and other health and safety decisions.

Through participation in various Agency activities, HHRA scientists gathered important input on the development of the HHRA research program. Examples of activities that yielded input include the Human Health Risk Assessment Colloquium, a symposium and workshop on the Environmental Justice Action Plan, and a workshop sponsored by ORD on children's risk issues.

In order to ensure that the RAP remains relevant and timely, stakeholder engagement will remain an integral and ongoing activity for HHRA. As we move into the implementation phase, the research coordination team (RCT) will be formalized as a means of ensuring continuous and open feedback on HHRA products. RCT members will be designated by their respective offices to represent their organizational needs and resources.

Meeting Priority Partner and Stakeholder Needs

The HHRA RAP comes from detailed information from partners and stakeholders regarding the regulatory and decision-making contexts in which they operate. Based on their feedback, it is clear that IRIS assessments are necessary for accomplishing their regulatory and decision-making needs. Additionally, the ISA program is essential to the Office of Air Quality Planning and Standards (OAQPS) and its ability to meet the 5-year deadlines for the NAAQS. OAQPS has said that ISAs have been among the best-received and most highly respected products that ORD has issued, and they are absolutely central to work on the NAAQS.

Key stakeholders also provided input regarding the importance of the work conducted under the HHRA CRTS Theme. In particular, OSWER and the regions have emphasized the importance of the development of PPRTVs, rapid risk assessment and technical support, the exposure factors program, the Superfund Technical Support Center and support for cumulative impact assessment.

Efforts taking place under HHRA's Theme 4 are particularly responsive to the priority needs stated by Agency risk managers at the Risk Assessment Forum Human Health Risk Assessment Colloquium in October 2010. Specifically, HHRA aims to address needs identified by risk managers, by incorporating recent advances in molecular biology and computational sciences into risk assessment.

For additional details see the Summary Tables below.

Research Themes and Priority Science Questions

Theme 1: Integrated Risk Information System (IRIS) Health Hazard and Dose-Response Assessments

Develop peer-reviewed, qualitative and quantitative health hazard and dose-response assessments on environmental pollutants of relevance to EPA's policies to protect human health and the environment.

Science Question

What are the important human health effects of chemicals for priority Agency decisions?

The IRIS assessments developed by HHRA scientists are peer-reviewed, qualitative and quantitative health hazard and dose-response assessments on environmental pollutants of relevance to EPA's policies to protect human health and the environment. IRIS assessments are widely used by EPA's programs and regions, as well as outside of the Agency by states, international organizations and the public, to support decision-making. EPA and the risk assessment/risk management community consider IRIS the premier source of health hazard and dose-response information for environmental pollutants. This theme also includes efforts to strengthen the IRIS process and database.

Illustrative Outputs/Products/Outcomes

Example 1: IRIS Assessments

Outcomes/Outputs: EPA's IRIS Program is a human health assessment program that evaluates quantitative and qualitative information on effects that may result from exposure to chemical substances found in the environment. IRIS health assessments meet a specific and continuing Agency need by providing a common scientific foundation for decision-making within EPA programs.

As of January 2011, the IRIS database contained information on more than 550 chemical substances that represent the first two steps (hazard identification and dose-response evaluation) of the risk assessment process. When supported by available data, IRIS provides oral reference doses (RfDs) and inhalation reference concentrations (RfCs) for chronic noncancer health effects and oral slope factors, inhalation unit risks and cancer descriptors for cancer health effects. Government and private entities combine the information on hazard and dose-response in IRIS assessments with specific exposure information to help characterize public health risks of chemical substances in site-specific or national situations.

IRIS is EPA's preferred source of health effects information. EPA's Superfund Program, for example, ranks IRIS assessments at the top of its hierarchy of sources for risk assessment toxicity values. IRIS assessments are available to EPA and the public online (http://www.epa.gov/iris). Users of IRIS include: EPA program offices and regions; other federal, state and local agencies (at national and

international levels); and the public, including academia, regulated industries, environmental organizations and individuals.

EPA decision-makers use these risk estimates when setting standards for the release of chemicals to air, water and land; determining safe clean-up levels at contaminated sites; and setting health goals and allowable levels of chemical residues in food and drinking water, consumer products, and indoor and outdoor environments. This is just one example of how IRIS assessments support risk management decisions designed to protect public health.

In May 2009, EPA released a revised IRIS process to streamline and accelerate completion of these critical science assessments (http://www.epa.gov/iris/process.htm). The IRIS process (depicted in Appendix B) includes internal EPA review, interagency review by other federal agencies and White House offices, public review and comment, and a rigorous, independent, external peer review at a face-to-face panel meeting. After each round of review, an assessment is revised to the extent necessary to address comments, and a disposition of comments is prepared. The IRIS Program is the only federal program that provides qualitative and quantitative assessments of both cancer risks and noncancer reference values. No other federal health assessment program has a similar mission and scope with a rigorous peer review process.

To ensure that the IRIS Program conducts the highest priority assessments, nominations are solicited regularly from EPA program offices and regions, other federal agencies and the public. Criteria for selection include EPA statutory, regulatory or programmatic needs; potential public health impacts; availability of science or methods to develop or update an assessment; federal, state or other user needs; availability of health assessments from other organizations to leverage resources; and availability of EPA resources to conduct the assessment.

Products: Individual IRIS assessments.

Example 2: Strengthening the IRIS process and database

Outputs/Outcomes: EPA strives to continually improve IRIS assessments. In April, 2011 the National Academy of Sciences (NAS) National Research Council (NRC), in their report reviewing EPA's draft IRIS assessment for formaldehyde, made several recommendations related to the development of IRIS assessment. EPA agrees with the NRC recommendations for the development of draft IRIS assessments and is fully implementing them consistent with the NRC's "Roadmap for Revision," which viewed the full implementation of their recommendations as a multi-year process. In July 2011, EPA announced plans to further improve the IRIS Program, both as part of an ongoing effort to strengthen the Program, but also in response to the NRC recommendations[1].

Specifically, at that time, EPA announced that:

- All new IRIS assessment documents will be shorter, clearer and more visual, concise, and transparent.

- IRIS users will see a reduced volume of text and increased clarity and transparency of data, methods, and decision criteria, as well as more graphical and tabular representations of data, in IRIS assessments.

[1] http://yosemite.epa.gov/opa/admpress.nsf/d0cf6618525a9efb85257359003fb69d/a3fcd6083819706785 2578cb00666c4d!OpenDocument

[2] www.epa.gof/hero

- Documents will be rigorously edited to eliminate inconsistencies and address redundancies, and related discussions will be consolidated into concise narrative descriptions.

In addition to changes to the draft development process, database improvements will enhance search functions within the IRIS database and modernize the computational platform. These improvements will increase database utility for both chemical managers and users of the database. Users looking for existing literature and assessments of related chemicals, adverse outcomes or modes of action will experience improved ease of access. Ongoing efforts to revise the IRIS Substance Assessment Tracking System (IRIS Track) also will increase utility and transparency. IRIS Track was created in 2005 to allow the public to monitor the status of chemical assessments that are in the development process. Additionally, literature reviews of assessments under development, which are currently made publicly available and announced in the *Federal Register,* will also be made available in the Health and Environmental Research Online (HERO) database.[2]

Products: Strengthening the IRIS process and database.

Impacts

Given the broad usage of IRIS assessments by EPA program and regional offices, as well as the general public, Theme 1 products contribute to a reduction in environmental exposures to chemicals and disease burdens and improvements in public health. Because chemicals are often considered to be safe until evaluated, the lack of hazard and dose-response assessments for many chemicals could potentially lead to a systematic bias and unintended impacts, whereby the wrong risk management options may be selected.

Research Themes and Priority Science Questions

Theme 2: Integrated Science Assessments (ISAs) of Criteria Air Pollutants

Develop ISAs summarizing the state-of-the-science for the six criteria air pollutants—ozone, particulate matter, sulfur dioxide, nitrogen oxides, carbon monoxide and lead—and Multipollutant Science Assessments (MSAs) to support the reviews of the primary (health-based) and secondary (welfare-based) NAAQS, as well as to address the combined effects of nitrogen and sulfur oxides.

Science Question

What are the human health and environmental hazards of criteria air pollutants?

Understanding the current science about the health and welfare effects of air pollutants is a critical Agency need to support decisions about the NAAQS. The ISAs and MSAs developed by the HHRA research program provide the scientific-basis for the Administrator's decisions for the NAAQS. Statutory requirements mandate the development of ISAs on a five-year cycle. Additionally, the MSAs are an important step in understanding and characterizing the health and welfare impacts of exposure to air pollutant mixtures.

Illustrative Outputs/Products/Outcomes

Example 1: Integrated Science Assessments (ISAs)

Outputs/Outcomes: The CAA provides the legislative basis for the establishment, review and revision of the NAAQS and directs the Agency to issue air quality criteria for pollutants that may be reasonably anticipated to endanger public health or welfare (i.e., environmental and other nonhuman health related effects). The HHRA research program regularly develops ISAs (formerly Air Quality Criteria Documents), which provide the scientific basis for the EPA Administrator's decisions on setting NAAQS. EPA released a revised NAAQS review process in May 2009 to accelerate the delivery of these critical science assessments and the development of the supporting documents for NAAQS. ISAs are a major component of the HHRA research program's research portfolio. They are developed on a regular 5-year cycle in response to the statutory requirements. ORD's ACE research program conducts intramural laboratory-based research and extramural research through the Science to Achieve Results grants program in support of ISA development. The ISAs incorporate and synthesize research findings from the ACE research program and others into the assessment documents.

In developing ISAs, HHRA scientists work with external scientists to evaluate, integrate and synthesize evidence from the areas of atmospheric chemistry, ecology, dosimetry, toxicology, epidemiology, exposure, sources,

ambient concentrations and measurement methods. ISAs consider life stage and other susceptibilities for exposure and/or toxicity, including identifying whether windows of susceptibility exist. In planning and developing ISAs, the HHRA research program works in very close collaboration with OAR's OAQPS, the primary client office. For example, early in the development process, HHRA will convene a workshop with the client office and the scientific community to identify the most policy-relevant science issues. A draft integrated plan for each ISA then is developed that includes the ISA (which is the responsibility of HHRA), the complementary Risk and Exposure Assessment (if warranted), and a Policy Assessment (both of which are the responsibility of OAQPS).

All external review drafts of these complementary assessment products undergo public comment and rigorous peer review by the CASAC. In addition, during the development process, draft ISAs are reviewed internally and through workshops covering specific areas of the assessment. See Appendix C for a chart of the ISA process. See Appendix D for the ISA planning chart reflecting the potential future NAAQS review timelines.

Products: Integrated Science Assessments.

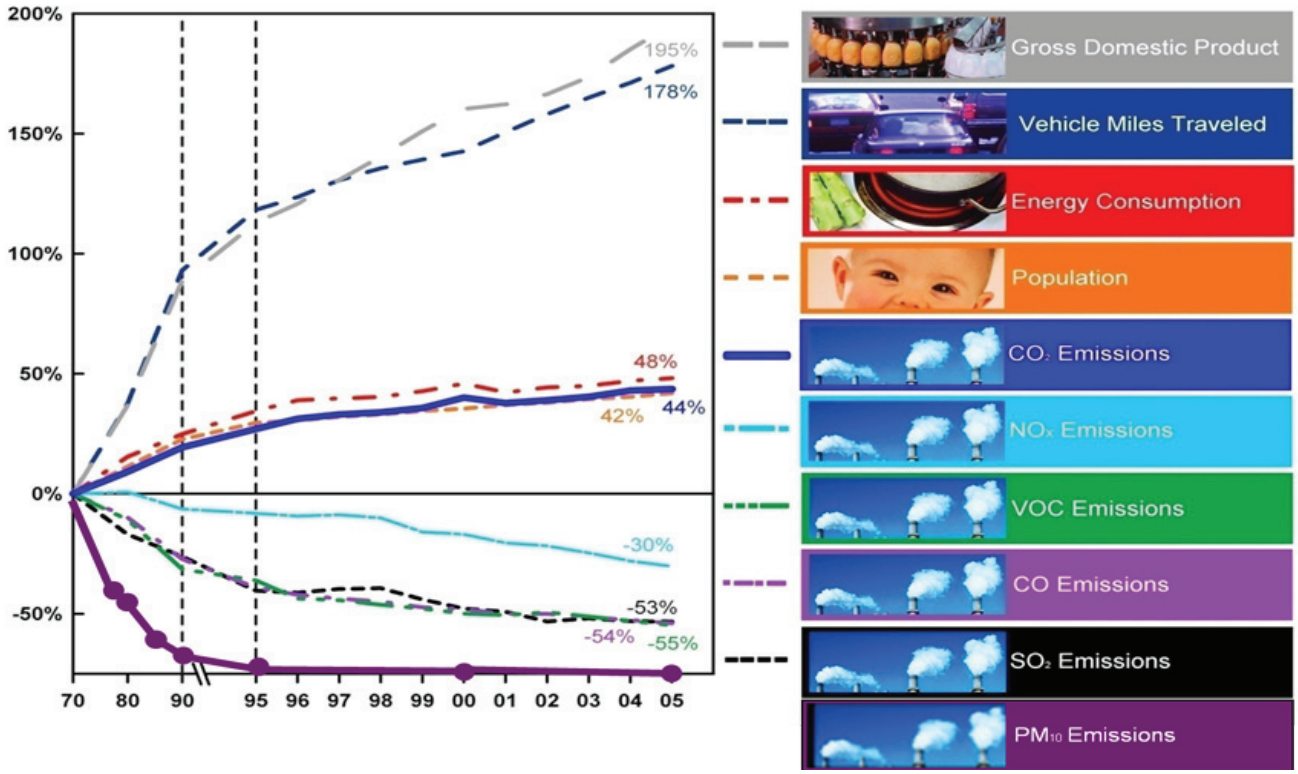
Example 2: Multipollutant Science Assessments (MSAs)

Outputs/Outcomes: The periodic review of NAAQS for the six criteria air pollutants has focused on single pollutant approaches, evaluating the independent effects of exposure to these air pollutants. It has long been recognized, however, that individuals are not exposed to a single pollutant in isolation but rather to a complex mixture of air pollution that varies in time and space. Although there has been a movement to shift from single to multipollutant approaches in evaluating air pollution-induced health effects, characterizing the health impacts of exposure to air pollutant mixtures presents a significant challenge to the scientific and regulatory communities. As an important initial step in overcoming these challenges, HHRA and ACE scientists are working in consultation with EPA offices to develop MSAs to support the reviews of the primary (health-based) and secondary (welfare-based) NAAQS. The health assessments, for example, will allow for an evaluation of the combined health effects of the exposures to mixtures of air pollutants, as well as a more effective evaluation of health effects of exposures to single pollutants in a multipollutant context than what is currently provided using single pollutant ISAs. It is anticipated that the MSAs will serve as a companion documents to the individual pollutant ISAs.

Products: Multipollutant Science Assessments (MSAs).

Impacts

Air pollution has dramatically decreased during the 40 years of the EPA's existence. The direct benefits of the CAA from 1970 to 1990 include reduced incidence of a number of adverse human health effects, improvements in visibility and avoided damage to agricultural crops and other vegetation. These results have been accomplished in the face of a growing population, number of vehicles and economy (See Figure 1).



According to OMB, EPA's Clean Air Program is the largest nonmilitary federal program in terms of economic benefits to society. ISAs contribute directly and significantly to this national effort to reduce the adverse health and ecological effects caused by air pollution, directly resulting in healthy communities that have clean air and sustainable ecosystems. In spite of these successes, public health and the environment continue to be negatively impacted by air pollution. More than 100 million people live in areas that exceed current air pollution standards, and many ecosystems are imperiled by atmospheric pollutants. Children, people with preexisting diseases and high-exposure groups are particularly at risk. Economically disadvantaged populations can experience higher exposures and be at increased risk because they often reside in less desirable, polluted areas (e.g., near freeways). Additionally, as science progresses more sensitive methods and a more robust understanding of human and ecologic health continue to reveal previously unknown impacts even while pollution levels are decreasing.

Research Themes and Priority Science Questions

Theme 3: Community Risk and Technical Support (CRTS) for Exposure and Health Assessments

Develop tools and analyses to help EPA programs and communities assess exposure and rapidly scope the risks of emerging issues, as well as directly support the regions by improving their ability to quickly find technical assistance on human health risk issues within ORD.

Science Question

What tools and analyses can ORD provide to help EPA programs and communities assess exposure and rapidly scope the risks of emerging issues?

Communities are often faced with an urgent need for coordinated assistance to assess and address issues of chemical and other environmental contamination. EPA's HHRA research program is often called upon to assist in these situations to provide the science to support decision-making at cleanup sites, develop tools to help understand community risk, or provide rapid responses to ensure that decision-makers have the tools they need to address emerging community concerns about environmental chemicals.

Work under this theme includes quick turn-around exposure and risk assessments, crisis-level technical support, the development of Provisional Peer Reviewed Toxicity Values (PPRTVs), tools and guidance for exposure assessments, and methods and tools for conducting cumulative impact and risk assessments. Taken together, this work helps ensure that EPA's regions have the tools and information they need to make decisions and address community concerns.

Illustrative Outputs/Products/Outcomes

Example 1: Quick turn-around exposure and risk assessments

Outputs/Outcomes: Environmental contamination issues impact real people with legitimate concerns about potential health risks in their community. Contamination situations can potentially result in very high exposures to significant segments of the population by chemicals or other substances known to be hazardous or suspected of being hazardous. EPA is asked to respond quickly, often in the face of large scientific uncertainties. Formalizing and more clearly articulating HHRA's ability to provide rapid risk assessment and technical support will improve the regions' and program offices' ability to access critical applied expertise when dealing with environmental health problems.

In many cases, there is a concerned public demanding answers about exposure, hazard and risk mitigation. These situations may

include risks to sensitive populations—like children—and to communities with underlying environmental justice issues. EPA must find ways to respond to these emerging, crisis-level, chemical/substance issues with sound science that allow for quick action and, ultimately, quick decisions and effective solutions. Responding to these types of real-world issues is a key part of EPA's mission to protect human health and the environment and represents the heart of what EPA does.

In order to respond to these urgent needs, HHRA scientists:

- Perform rapid risk assessments of contaminated sites, for instance following the Gulf Oil Spill;
- Provide guidance to EPA regions, states and localities on how to assess contamination risks, such as by developing a PCB exposure estimation tool for school building contamination; and
- Advise on field studies to gather data for risk assessment.

Scientists in the HHRA research program are also working to better understand how nonchemical stressors – such as socioeconomic status – may impact the health effects that may result from exposure to environmental chemicals. An important component of work under this theme includes developing methods to incorporate the impacts of nonchemical stressors into community risk assessments, better positioning the Agency to respond to community environmental justice concerns as called for in EPA's Plan EJ 2014.

Products: Quick turn-around exposure and risk assessments.

Example 2: Exposures Factors Handbook
Outputs/Outcomes: An important component of the exposure assessment process is the selection of appropriate exposure factors for use in an exposure assessment. Exposure factors are related to human behavior and characteristics that help determine an individual's exposure to an agent. The *Exposure Factors Handbook (2011)* is a key source of exposure factor information and has served to promote consistency among risk assessments conducted by the Agency and others. It provides a unique synthesis of exposure factor data for the U.S. population that is unavailable in any other single source.

Efforts related to the handbook have traditionally focused on two main endeavors: (1) development of the *Exposure Factors Handbook* and related products, and (2) directed research and assessment activities supporting the development of new and improved exposure factors, the use of which will decrease exposure assessment uncertainties. Products developed by HHRA (e.g., *Exposure Factors Handbook* (U.S. EPA 1989, 1997, 2011), *Child-Specific Exposure Factors Handbook* (U.S. EPA 2008)) are used in nearly every exposure assessment developed by the Agency.

Products: Exposures Factors Handbook.

Example 3: Provisional Peer Reviewed Toxicity Values (PPRTVs)
Outputs/Outcomes: PPRTVs are toxicity values derived for use in EPA's Superfund program when a value is not available in the IRIS database. PPRTVs are used by the Superfund program and regional decision-makers when making site-specific clean-up decisions. This well-established part of the HHRA research program will be highlighted as a feature of the CRTS theme.

PPRTVs are derived following a review of the

relevant scientific literature using the same methods, sources of data and guidance used by the IRIS program to derive values. All PPRTVs receive internal review by a panel of EPA scientists and external peer review by independent scientific experts and are publicly available (http://hhpprtv.ornl.gov).

The purpose of PPRTV documents is to provide hazard and dose-response assessments pertaining to chronic and subchronic exposures to substances of concern, present the major conclusions reached in the hazard identification and derivation of the PPRTVs and characterize the overall confidence in these conclusions and toxicity values. The use of the HERO database, developed under Theme 4, in the development of PPRTVs provides transparency to that program by allowing users of those assessments to access the literature on which the PPRTVs are based. PPRTV assessments are updated approximately on a 5-year cycle for new data or methodologies that might impact the toxicity values or characterization of potential for adverse human health effects and are revised as appropriate.

Products: PPRTVs.

Impacts

The rapid risk assessments and technical support provided under the CRTS theme will ultimately contribute to protecting the public's health and cleaning up contaminated communities, key to EPA's mission and one of its strategic goals. Additionally, the development of tools and guidance for exposure assessment will provide HHRA's customers with critical information to help understand the extent and route of exposure. PPRTVs enable OSWER to make clean-up decisions at contaminated Superfund sites. The implications of these decisions include improvements in human health in the vicinity of Superfund sites, reduction or reversal of damages to natural resources, reduction of harm in emergency situations, improved economic conditions and quality of life in communities affected by hazardous waste sites, improved environmental practices by industry and advances in science and technology. Theme 3 activities also support EPA's ability to positively respond to environmental justice concerns through the incorporation of nonchemical stressors into community risk assessment, contributing to reduced risks for sensitive populations.

Research Themes and Priority Science Questions

Theme 4: Modernizing Risk Assessment Methods

Address high-priority Agency needs identified by risk managers, incorporate recent advances in molecular biology and computational sciences into risk assessment, and tackle specific scientific issues using approaches informed by recommendations from a number of expert advisory bodies.

Science Question

> *How can EPA's Office of Research and Development better meet the needs of decision-makers by modernizing risk assessment to incorporate recent scientific innovations, including molecular biology and computational sciences?*

Theme 4 focuses on the translation of research, described in the CSS research program and elsewhere, into practical application in HHRA assessments (IRIS, ISA, MSA, and PPRTV assessments) and in assessing special problems (e.g., hydrofracturing under the Safe and Sustainable Water Resources research program). Recently completed research is now being utilized to develop prototype assessments that will allow Agency risk managers to become more familiar with the use of molecular biology and the use of powerful, new computational methods, thus facilitating cheaper, faster and more robust risk assessments.

Recent recommendations from the National Research Council (NRC), the Science Advisory Board (SAB) and the Board of Scientific Counselors (BOSC) have highlighted unmet needs and discussed use of these new data and approaches to advance risk assessment. For instance, *Toxicity Testing in the 21st Century* (NRC 2007) lays out a vision and strategy for using recent scientific advances to more efficiently prioritize and assess a large number of chemicals. The need for advancements in risk assessment was reiterated in *Science and Decisions: Advancing Risk Assessment* (NRC 2009), which also recognized the need for improved approaches to dose-response quantification across both cancer and noncancer effects to better support Agency decisions. In addition, *Phthalates and Cumulative Risk Assessment: The Task Ahead* (NRC 2010) advocated expansion of the scope of cumulative risk assessments. Recognizing the complexity of the Agency and assessment decisions, NRC (2009) along with the SAB (2010) and the BOSC (2009) recommended expanding the use of decision-support sciences to determine the risk assessment approach best suited to inform each risk management situation.

In October 2010, Agency risk managers were asked to identify key unmet risk assessment needs in their decision-making at the Risk Assessment Forum Human Health Risk Assessment Colloquium. Three priority needs were consistently identified by the diverse

group of risk managers:

- Making informed decisions about the large number of compounds lacking health assessments;
- Considering cost-benefit and risk-risk tradeoff for chemicals and effects lacking quantitative estimates of the incremental risk/benefit with changing exposure; and
- Considering the combined effects of multiple chemical and nonchemical stressors without cumulative assessments of sufficiently wide scope.

Illustrative Outputs/Products/Outcomes

Example 1: Tools to advance hazard identification and efficiency of assessment development

Outputs/Outcomes: To create more comprehensive and transparent assessments within a shorter timeframe, the Agency must utilize informatics technologies to extract, summarize and evaluate information from the literature; store and manage data and knowledge; and leverage existing databases and data sources. This research project will create tools to automate these activities. In particular, this project will capture and apply what is known about various disease processes and chemical influences on disease processes to inform hazard identification and dose-response for specific chemical assessments. These efforts will rely on CSS and other research efforts to develop chemically induced disease signatures or fingerprints. HHRA will apply this information on a case-by-case basis.

By providing risk assessors and decision-makers with access to summarized, policy-relevant scientific information that includes data grading schemes and visualization tools (e.g., data arrays), the time to review the literature, integrate the evidence and incorporate new knowledge into hazard and risk assessments will decrease. Thus, this project will streamline and facilitate basic functions of risk assessment and management in addition to moving HHRA toward the goal of effective capturing, sharing, discussing and debating of knowledge across the program.

Products: Tools to advance hazard identification and efficiency of assessment development.

Example 2: Dose-response characterization

Outputs/Outcomes: Although dose-response analysis is an integral part of human health risk assessment, it has been decades since there have been any major fundamental changes in how dose-response is characterized. The combination of increased demands on risk assessment and the recent explosion of scientific knowledge presents unique opportunities to modernize the practice of dose-response analysis. This has been echoed in several NRC recommendations to advance dose-response analyses, particularly in the areas of increasing the throughput of chemical assessments, characterizing uncertainty and variability, quantifying incremental risk and addressing susceptibility. During the October 2010 Human Health Risk Assessment Colloquium, risk managers indicated that advancing dose-response analysis would be useful for their decision-making needs.

HHRA is taking a systematic, step-wise approach to addressing several decision-maker needs for quantitative dose-response characterization, including maximizing the use of available data and methods, better characterizing uncertainty and variability, and developing a better understanding of how to quantitatively address susceptibility. Thus, the

focus of this effort is on products that facilitate the translation of scientific concepts and data specifically for use in dose-response analysis while simultaneously utilizing and providing feedback to the generation of scientific concepts and data occurring in the other parts of ORD and the greater scientific community.

Products: Dose-response characterization.

Example 3: Risk Assessment Training and Experience (RATE) Program and the application of Health and Environmental Research Online (HERO)

Outputs/Outcomes: To support the development of the IRIS assessments, ISAs, MSAs, and PPRTVs, EPA also develops capabilities within and external to EPA to ensure full understanding and utilization of science. These capabilities are developed by advancing the methods used in assessment development and through targeted risk assessment training activities. Two examples of HHRA products that contribute to these capabilities are the development of the RATE program and the application of HERO to assessment products.

A critical need and problem that faces risk assessment professionals throughout the United States is having sufficient, up-to-date information and training on state-of-the-art principles and practices focusing on human health and exposure. Additionally, during times of scarce resources and the continuously evolving knowledge in risk assessment, HHRA and state environmental agency staff members need comprehensive guidance on how to understand and conduct risk assessments, which, in turn, enables effective and efficient implementation of their duties to safeguard environmental and public health. In response to these needs, EPA is developing the RATE program. RATE is a comprehensive risk assessment guidance and training course that includes modules in the following areas: fundamentals of risk assessment, hazard identification, dose-response assessment, exposure assessment, risk characterization, communication and management.

HERO represents a transformational approach in using the world's scientific literature in the risk assessment process. HERO is a comprehensive system to identify, compile, characterize, analyze, synthesize and prioritize scientific studies used in IRIS health hazard and dose-response assessments. The HERO database is a repository of the scientific studies considered and used in assessments. This evergreen database provides a system for searching and importing new literature as new studies are added continuously. HERO facilitates complete and effective assessment development by: employing advanced searching, screening and classification techniques using natural language processing and innovative, efficient technologies for intelligent information extraction and synthesis; meeting the evolving needs of scientists, collaborators and stakeholders with agile development practices; involving public participation in the assessment development process by soliciting input; and providing transparency and accessibility to the stakeholders and public.

Products: HERO and RATE.

Impacts

Theme 4 products will increase the efficiency and effectiveness of EPA risk assessment programs by developing innovative approaches and applying them to mine databases and link information to users' needs in a more effective manner. These products also will contribute to the quality, timeliness

and transparency of IRIS assessments, ISAs and PPRTVs. Theme 4 products also will provide additional and needed information to risk managers and decision-makers, leading to more informed decisions. For example, presenting additional dose-response approaches, particularly for noncancer endpoints, will allow more comparisons of risk relationships between and among chemical-induced adverse health outcomes. Additionally, using quantitative estimates of incremental population risk, along with better quantitative characterization analysis of uncertainty and variability, will enable risk managers to more effectively use HHRA products in the context of formal decision analysis and in cost-benefit analysis.

Conclusion

As a result of extensive input from stakeholders during the planning phase, the outputs of the HHRA research program are very closely linked to their programmatic use in hazardous site assessments and regulatory considerations. For example, IRIS quantitative cancer risk and noncancer reference values are accorded priority consideration in OSWER and regional site clean-up evaluations and are a critical consideration in many regulatory determinations by EPA's other programs. ISAs constitute the scientific basis for review of the NAAQS for criteria air pollutants. Rapid risk assessments enable regional decision-makers to respond quickly to emerging and crisis-level issues. The HHRA research program's models, methods and guidance outputs generally serve as the standard for Agency health hazard assessment practice and are influential on national and international scales.

Summary Tables of Outputs and Outcomes

The following tables list the expected outputs from the HHRA research program along with the associated partner outcomes. Although each output is listed under a single theme and science question, many of them serve to answer multiple questions. The third column lists other science questions that an output addresses. It also lists other ORD research programs that the output addresses and external organizations with which the HHRA research program will collaborate.

Theme 1 – Integrated Risk Information Systems (IRIS) Health Hazard and Dose-response Assessments

Science Question 1: What are the important human health effects of chemicals for priority Agency decisions?

Outcomes: IRIS assessments are used widely by EPA's programs and regions, states, international organizations and the general public as a scientific foundation for decision-making (e.g., site-specific cleanups, rules, regulations and health policy determinations). They also directly support decisions by the EPA Administrator under CERCLA, RCRA, TSCA, the Clean Air Act, the Clean Water Act, the Safe Drinking Water Act, and other environmental statutes.

Outputs	Output Year	Relevance to other HHRA Themes
Dichloromethane IRIS Assessment	FY12	Information from IRIS feeds into Theme 3 CRTS outputs in quick turn-around exposure and risk assessments, which result in the development of unique products and advances in science, such as reports, memos, fact sheets, briefing, and presentations
Tetrahydrofuran IRIS Assessment	FY12	
Halogenated platinum salts IRIS Assessment	FY12	
Tetrachloroethylene IRIS Assessment	FY12	
Ethylene oxide IRIS Assessment	FY12	
Dioxin (non-cancer) IRIS Assessment	FY12	
Methanol (non-cancer) IRIS Assessment	FY12	
n-butanol IRIS Assessment	FY12	
1,4-dioxane IRIS Assessment	FY12	
Trimethylbenzene, 1,2,4- IRIS Assessment	FY13	
Trimethylbenzene, 1,3,5- IRIS Assessment	FY13	
Ammonia IRIS Assessment	FY13	
Vanadium pentoxide IRIS Assessment	FY13	
Biphenyl IRIS Assessment	FY13	
PAH mixtures IRIS Assessment	FY13	
Benzo(a)pyrene IRIS Assessment	FY13	
Uranium IRIS Assessment	FY13	
Acrylonitrile IRIS Assessment	FY13	
t-Butanol IRIS Assessment	FY13	
PCBs IRIS Assessment	FY13	

Outputs	Output Year	Relevance to other HHRA Themes
RDX IRIS Assessment	FY13	Information from IRIS feeds into Theme 3 outputs in quick turn-around exposure and risk assessments, which result in the development of unique products and advances in science, such as reports, memos, fact sheets, briefing, and presentations
Libby asbestos IRIS Assessment	FY13	
Acetaldehyde IRIS Assessment	FY13	
Diethylphthalate IRIS Assessment	FY13	
1, 2-Dichlorobenzenes IRIS Assessment	FY14	
1, 3-Dichlorobenzene IRIS Assessment	FY14	
1, 4-dichlorobenzene IRIS Assessment	FY14	
Statistical and dose-response technical support for IRIS Chemical Managers	TBD	Feeds into IRIS Assessments
Updated Benchmark dose Modeling Software (BMDS)	TBD	
Standalone Software (e.g. CatReg)	TBD	
Communicate with stakeholders on approaches to recurring statistical and dose-response issues in IRIS Assessments	TBD	
Pharmacokinetic technical support for IRIS Chemical Managers	TBD	Feeds into IRIS Assessments
PBPK model evaluation	TBD	
Model scoping reports for new assessments	TBD	
MOA scientific support for IRIS Chemical Managers	TBD	
Communicate with stakeholders on approaches to recurring MOA issues in IRIS Assessments (e.g. memorandum and white papers)	TBD	
Streamlined and more transparent IRIS assessment documents	TBD	
Enhanced search functions for IRIS database	TBD	
Modernize computational platform for IRIS database	TBD	

Theme 2 – Integrated Science Assessments (ISAs) of Criteria Air Pollutants

Science Question 2: What are the human health and environmental hazards of criteria air pollutants?		
Outcomes: ISAs provide the scientific foundation for the EPA Administrator's decision on each of the primary and secondary NAAQS. Attainment of the NAAQS for these pollutants has been estimated by the Office of Management and Budget and EPA to provide significant public health and environmental benefits to the American public that far exceed the cost of control programs. The direct benefits of EPA's NAAQS include the reduced incidence of a number of adverse human health impacts, including premature death and disease, improvements in visibility and avoided damage to agricultural crops and other vegetation.		
Outputs	**Output Year**	**Relevance to other HHRA Themes**
Workshop on PM	FY14	Feeds into Multipollutant Science Assessment (MSA)
Final PM ISA	FY16	
Scientific support related to PM NAAQS decision-making	FY18	
Workshop on CO	FY13	Feeds into MSA
Final CO ISA	FY15	
Scientific support related to CO NAAQS decision-making	FY17	
Final Ozone ISA	FY12	Feeds into MSA
Scientific support related to Ozone NAAQS decision-making	FY14	
Workshop on Nox	FY12	Feeds into MSA
Final NOx ISA (Health Criteria)	FY14	
Scientific support related to NOx NAAQS decision-making	FY16	
Workshop on SOx	FY12	Feeds into MSA
Final SOx ISA (Health Criteria)	FY15	
Scientific support related to SOx NAAQS decision-making	FY17	
Workshop on Lead	FY11	Feeds into Theme 3 outputs
Final Lead ISA	FY12	
Scientific support related to Lead NAAQS decision-making	FY14	
Outcomes: MSAs inform the EPA Administrator's decisions on the primary and secondary NAAQS, as well as considerations for potential future multipollutant standards.		
Workshop on NOx/SOx Eco ISA	FY13	
Final NOx/SOx Eco ISA	FY16	
MSA Workshop	FY11	
Final Health MSA	FY16	
MSA Workshop	FY13	
Final Welfare MSA	FY15	

Theme 3 – Community Risk and Technical Support for Exposure and Health Assessments

Science Question 3: What tools and analyses can ORD provide to help EPA programs and communities assess exposure and rapidly scope the risks of emerging issues?		
Outcomes: Feeds into regional or site specific decisions and into Programs exposure assessments; Rapid assessment of potential exposures and risks allow program offices, regions, or EPA senior management to make informed decisions in addressing emerging or unanticipated environmental contaminants.		
Outputs	**Output Year**	**Relevance to other HHRA Themes**
Quick turn-around exposure and risk assessments, which result in the development of unique products and advances in science, such as reports, memos, fact sheets, briefing, and presentations	TBD	Information from these Theme 3 CRTS outputs are also used to inform quick turn-around exposure and risk assessments, which result in the development of unique products and advances in science, such as reports, memos, fact sheets, briefing, and presentations.
Crisis-level technical support (conveyed in the form of memorandum offering technical advise, formal response letters, fact sheets, briefings, and technical reports)	TBD	
Applied technical support to inform risk-based decision-making	TBD	
Exposure Factors Handbook	TBD	
Supporting documents and analyses	TBD	
Outcomes: RAF will provide a conduit for guidance to EPA's regions and programs; The toolbox will allow scientists to more easily identify and access available exposure and risk characterization resources necessary to perform assessments; Tools and Guidance developed under Project 3 are used in exposure assessments and guidance developed by the Agency; Expo-Box will provide Agency exposure assessors with a web-based compendium of exposure assessment and risk characterization tools. Comprehensive exposure assessment documents feed into exposure assessments conducted by programs and regions; Development of chemical-specific, or chemical class-specific exposure summaries may be used by Agency program and regional offices, environmental decision makers, industry, and the public interested in support of human health risk assessments.		
Expo-Box will synthesize and integrate exposure assessment tools developed within HHRA (as well as those developed in other parts of the Agency)	TBD	
Comprehensive exposure assessment documents, such as reports, memos, fact sheets, briefing, and presentations	TBD	Feeds into work being conducted by the Exposure Factors Program, which is also under HHRA Theme 3.

Outputs	Output Year	Relevance to other HHRA Themes
Outcomes: Feed into Exposure assessments conducted by programs and regions		
Chemical exposure sections in IRIS toxicological reviews	TBD	Feeds into Theme 1 IRIS assessments
Communicating advances in chemical exposure science to stakeholders	TBD	
Report on dioxin-like compounds and releases	FY15	
Outcomes: The development of PPRTVs enables the Office of Solid Waste and Emergency Response (OSWER) to make informed clean-up decisions regarding the screening of chemicals of concern, conducting human health risk assessments, and evaluating alternative clean-up actions at federal and state Superfund sites, which can lead to improvements in human and ecological health in the vicinity of Superfund sites, as well as improved economic conditions and quality of life for nearby communities; PPRTVs are also used by EPAs regions when making site specific clean-up decisions.		
Final individual PPRTVs (50 per year)	Per annum	
Peer-reviewed ecology "white-papers" posted at www.epa.gov/erasc, technical assistance responses (TARs) for human health issues including: documented telephone "hotline" advice, email responses, formal written responses, distribution of existing NCEA publications, technical and peer reviews of non-EPA toxicity values.	FY15	
Technical support on community-based cumulative risk assessments		
Chemical specific risk estimates (conveyed in the form of memoranda offering technical advice, formal response letters, fact sheets, briefings, and technical reports)	FY15	
Outcomes: The qualitative and quantitative approaches to grouping and analyzing risks from chemical and non-chemical stressors that are developed under this theme inform regional and local decision makers. Developing methods teaching workshops will aid EPA programs and regional offices in conducting and in evaluating opportunities to conduct cumulative risk assessments (CRAs). The publication of case studies provides strategies and tools to address grouping and risk analytic strategies for use by program offices in regulatory efforts (e.g. OW). The publication of the methods and models developed will aid regulators in the integration of health effects data into risk assessment activities; focus on vulnerability factors will allow for better characterization of variability and uncertainty in risk assessments.		
Methods and tools to improve regional and programmatic cumulative risk assessments, including a peer-reviewed publication in the scientific literature on methods in FY15	FY15	
Case studies published in the peer-review scientific literature that characterize exposures to (or outcomes related to) combined chemical and non-chemical stressors	FY15	

Outputs	Output Year	Relevance to other HHRA Themes
A publication in the peer-reviewed scientific literature that describes methods and models for evaluating associations between health outcomes and chemical and non-chemical stressors (and assessing interactions between stressors): analyses of socio-economic status and other vulnerability factors	FY15	
Outcomes: Development of guidelines will provide defensible approaches for EPA program and regional offices to conduct cumulative risk assessments. Publications will improve and disseminate Cumulative Risk Assessment practice information needed for EPA programs and regional offices to conduct cumulative risk assessments. Tools and guidance for cumulative risk assessment data analysis will allow EPA programs and regions to organize information and estimate human health and ecological risks. In concert with CSS, predictive/ computational models and toolboxes will provide data that can be used to facilitate hazard identification and inform quantitative dose-response assessment and associated uncertainties.		
Internal Technical Report to support the Risk Assessment Forum's Cumulative Risk Assessment guidelines development	FY14	
A peer-reviewed publication to improve cumulative risk assessment practices	FY14	
A web-based tool describing methods and resources that support data analyses for program office and regional cumulative risk assessments	FY14	
Methods to Integrate CSS-based biomarker and Cumulative Risk Outcomes	FY14	

Theme 4 – Modernizing Risk Assessment Methods

Science Question 4: How can ORD better meet the needs of decision makers by modernizing risk assessment to incorporate recent scientific innovations, including molecular biology and computational sciences?

Outcomes: Theme 4 outputs will increase the efficiency and effectiveness of EPA risk assessment programs by developing innovative approaches and applying them to mine databases and link information to users' needs in a more effective fashion. Using quantitative estimates of incremental population risk, along with better quantitative characterization of uncertainty and variability, will enable risk managers to more effectively use HHRA products in the context of formal decision analysis and cost-benefit analysis.

Outputs	Output Year	Relevance to other HHRA Themes
Natural language processing method to mine chemical mode of action data from existing IRIS assessments and the toxicology literature	FY14	Contributes to developing PPRTVs, IRIS, and ISAs in a more transparent manner based upon the state-of–the-science approaches and methods to meet programmatic needs.
Health hazard ontology and MOA knowledgebase (part of the HERO System) of common chemical modes of action to generate mode of action pathway maps (knowledge maps) and to capture the literature associated with modes of action	FY14	
HERO NLP - used to develop automated exposure response arrays from graphical and tabular data sources in peer reviewed literature	FY14	
Enroll HERO Systems into the ORD Federated Data System (FROST)	FY16	
Toolbox for health assessors to generate mode of action pathway maps that demonstrate the size and strength of associations graphically using the MOA knowledgebase to graphically display what is known about toxicity/disease pathways and modes of action to inform weight of evidence analysis for hazard characterization of assessments	FY13	Contributes to developing PPRTVs, IRIS, and ISAs in a more transparent manner based upon the state-of–the-science approaches and methods to meet programmatic needs.
Bioinformatics Toolbox that includes semi-automated workflows for standardized bioinformatics analyses using NIH, European Bioinformatics Institute (EBI) and other external tools	FY13	
Utilize HERO Systems to build chemical specific exposure response arrays for adverse outcomes to inform dose response analysis	FY13	
Integration of CSS Dashboards, CSS and HHRA Toolboxes, and HERO Systems into a standard HHRA Risk Informatics Platform	FY13	

Outputs	Output Year	Relevance to other HHRA Themes
Inventory of existing needs, data, and methods for dose-response used in NCEA	FY14	Contributes to developing PPRTVs, IRIS, and ISAs based on appropriate scientific data and methods to meet programmatic needs
Gaps analysis of unmet dose-response needs and methods development for NCEA	FY14	Contributes to developing PPRTVs, IRIS, and ISAs based on appropriate scientific data and methods to meet programmatic needs
Based on inventory and gaps analysis, provide technical support of application of existing data and methods in PPRTVs, IRIS, and ISAs	FY14	Contributes to developing PPRTVs, IRIS, and ISAs based on appropriate scientific data and methods to meet programmatic needs
Framework and case studies for characterizing uncertainty and variability in dose-response analysis for cancer and non-cancer effects	FY15	Contributes to developing PPRTVs, IRIS, and ISAs based on appropriate scientific data and methods to meet programmatic needs; Contributes to developing more comprehensive cost-benefit analyses that address uncertainty and variability, and benefits from reducing non-cancer effects.
Expert workshop coordinated by WHO seeking external input on draft framework and case studies	FY14	Contributes to developing PPRTVs, IRIS, and ISAs based on appropriate scientific data and methods to meet programmatic needs; Contributes to developing more comprehensive cost-benefit analyses that address uncertainty and variability, and benefits from reducing non-cancer effects.
Provide technical support for incorporating approaches to characterizing uncertainty and variability in PPRTVs, IRIS, and ISAs	FY15	Contributes to developing PPRTVs, IRIS, and ISAs based on appropriate scientific data and methods to meet programmatic needs
Provide technical support for incorporating approaches to characterizing uncertainty and variability in cost-benefit analyses in various programs	FY15	Contributes to developing more comprehensive cost-benefit analyses that address uncertainty and variability, and benefits from reducing non-cancer effects.

Scoping key science areas where susceptibility issues impact dose-response	FY13	Contributes to developing PPRTVs, IRIS, and ISAs based on appropriate scientific data and methods to meet programmatic needs.
Conducting state-of-the-science reviews on key areas where susceptibility issues impact dose-response	FY15	Contributes to developing PPRTVs, IRIS, and ISAs based on appropriate scientific data and methods to meet programmatic needs.
Provide technical support for incorporating approaches to better incorporate susceptibility issues in dose-response in PPRTVs, IRIS, and ISAs	FY15	Contributes to developing PPRTVs, IRIS, and ISAs based on appropriate scientific data and methods to meet programmatic needs.
Materials and documentation associated with the training modules (e.g., instructor notes, reading packets, PowerPoint presentations) for classroom and internet-based applications	FY15	Contributes to training of staff that are developing PPRTVs, IRIS, and ISAs based on state of the science approaches and methods to meet programmatic needs.
Training on the fundamentals of scientific disciplines that are relied upon for risk assessment	FY15	
Application of HERO to HHRA assessments	FY15	Feeds into Theme 1 assessments; Theme 2 ISAs and MSAs, and Theme 3 PPRTVs.

Appendix A – Research Program Partners and Stakeholders

EPA Research Program Partners

Regions 1-10

Office of Solid Waste and Emergency Response (OSWER)
- Office of Emergency Management (OEM)
- Office of Underground Storage Tanks (OUST)
- Office of Superfund Remediation and Technology Innovation (OSRTI)
- Office of Resource Conservation and Recovery (ORCR)
- Office of Program Management (OPM)

Office of Air and Radiation (OAR)
- Office of Air Quality Planning and Standards (OAQPS)
- Office of Transportation and Air Quality (OTAQ)

Office of Water (OW)
- Office of Ground Water and Drinking Water (OGWDW)
- Office of Science and Technology (OST)

Office of Chemical Safety and Pollution Prevention (OCSPP)
- Office of Pesticide Programs (OPP)
- Office Pollution Prevention and Toxics (OPPT)
- Office of Science Coordination and Policy (OSCP)

Office of Children's Health Protection (OCHP)

Office of the Science Advisor (OSA)

Office of Policy (OP)
- National Center for Environmental Economics (NCEE)

Office of Environmental Justice (OEJ)

Office of Chief Financial Officer (OCFO)

Other Governmental Stakeholders

EPA's Board of Scientific Counselors (BOSC)
Clean Air Science Advisory Committee (CASAC)
Science Advisory Board (SAB)
National Academy of Sciences (NAS)
Government Accountability Office (GAO)
National Institutes of Environmental Health Sciences & National Toxicology Program (NIEHS & NTP)

Centers for Disease Control and Prevention (CDCP)
Agency for Toxic Substances and Disease Registry (ATSDR)
National Institutes of Health (NIH) Chemical Genomics Center
California's Environmental Protection Agency (Cal/EPA), Office of Environmental Health Hazard Assessment
FDA National Center for Toxicological Research
Department of Defense
National Institute of Occupational Health and Safety (NIOSH)

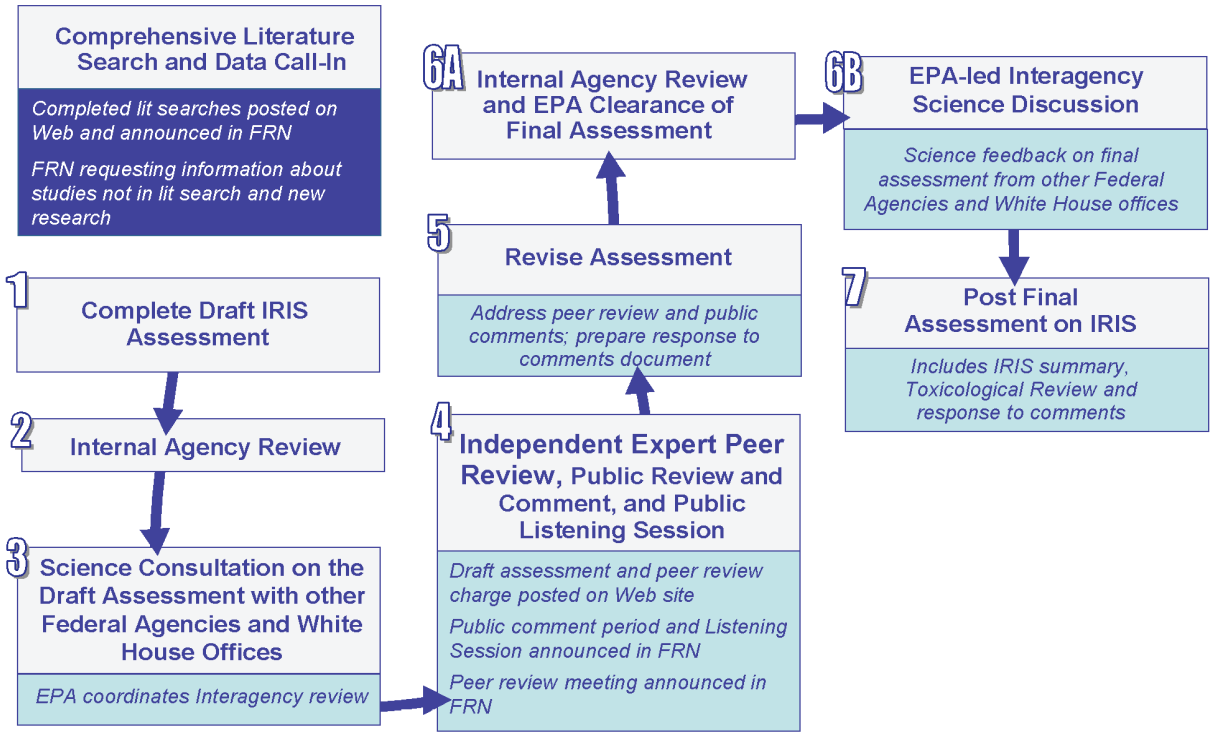
Nongovernmental Organizations

Environmental Working Group (EWG)
National Resource Defense Council (NRDC)
Environmental Defense Fund (EDF)
Environmental Council of the States (ECOS)
Interstate Technology and Regulatory Council (ITRC)
American Public Health Association (APHA)
American Chemistry Council (ACC)
Integrated Life Sciences Institute (ILSI) – Risk 21

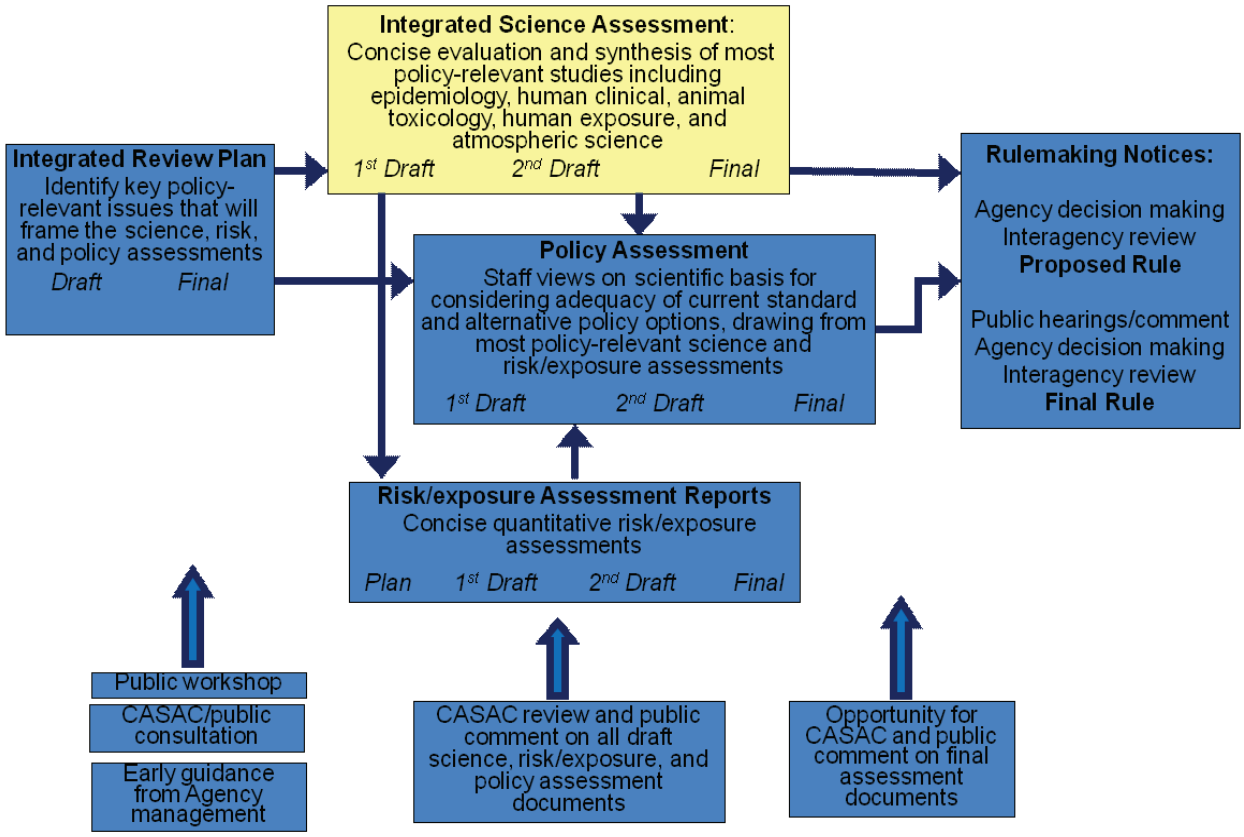
This is a preliminary list, which will be updated regularly.

Appendix B – IRIS Process

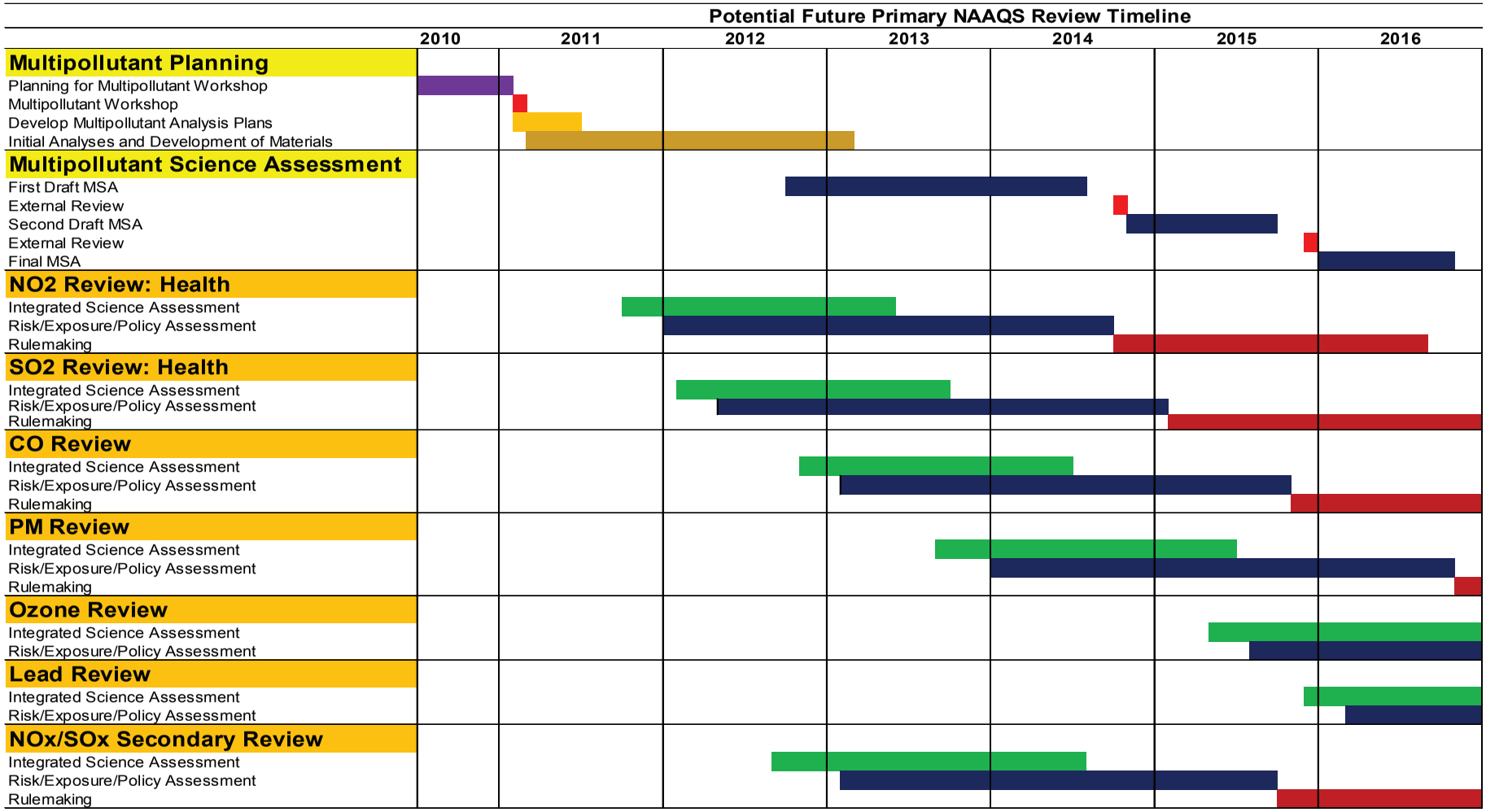
Assessment Development Process for New IRIS



Appendix C – ISA Process



Appendix D – ISA Planning Chart



FINAL DRAFT

Appendix E – List of Definitions

Outputs are synthesized and/or translated from Products into the format needed by the End User. Outputs should be defined, to the extent possible, by Partners/Stakeholders during Problem Formulation.

Product - A deliverable that results from a specific Research Project or Research Task. This may include (not an exhaustive list) journal articles, reports, databases, test results, methods, models, publications, technical support, workshops, best practices, patents, etc. These may require translation or synthesis for inclusion as an Output.

Partner/Stakeholder Outcome - The expected results, impacts, or consequence that a Partner or Stakeholder will be able to accomplish due to ORD research.

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