EPA's Integrated Risk Information System: Updates on Process Changes and Assessments

Gina Perovich
Deputy Director, IRIS Program
U.S. EPA Office of Research and Development

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Part I

IRIS: Overview and Updates on Process Changes

- National Research Council (NRC) recommendations for IRIS (2011)
- Enhanced IRIS process (2013)
- Stakeholder engagement
- Current efforts

A More Transparent and Systematic Approach to IRIS Assessment Development

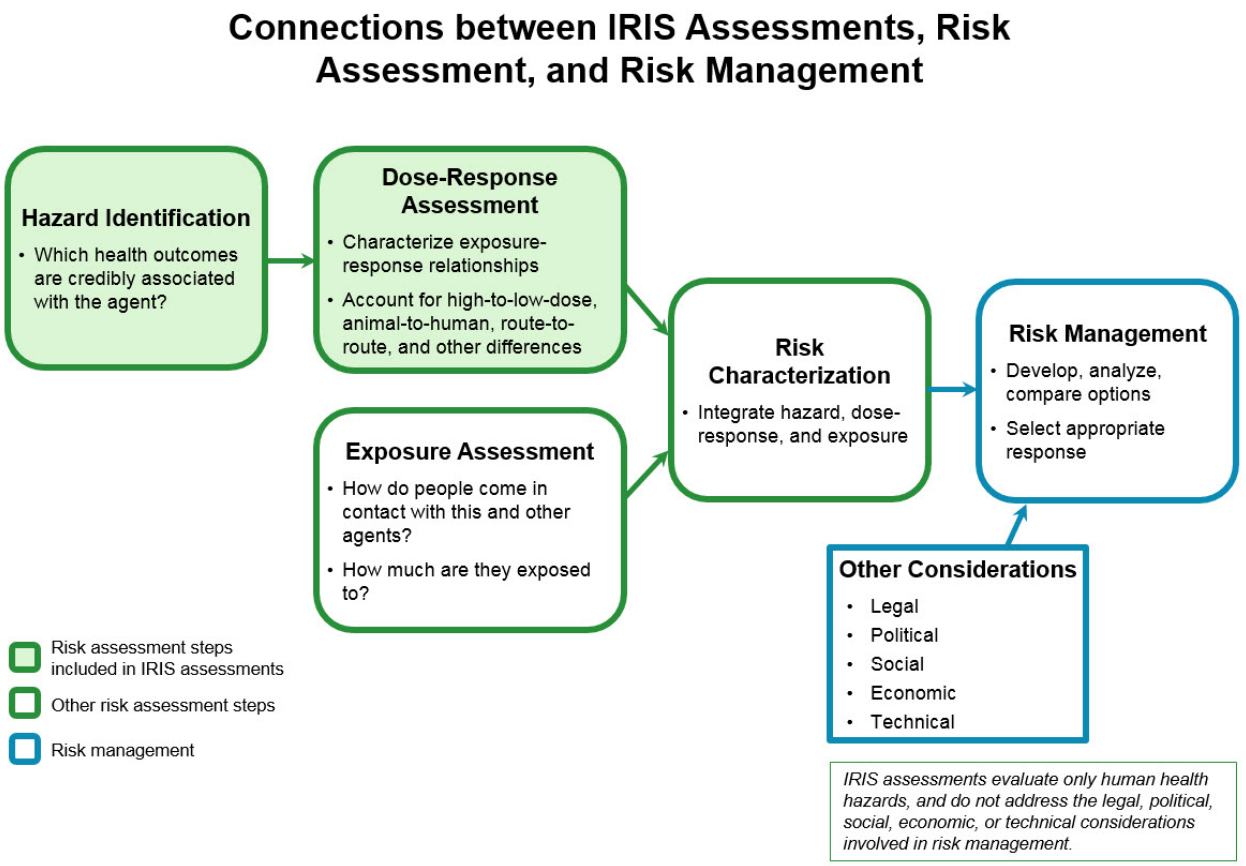
Integrated Risk Information System

- IRIS provides information on potential adverse health effects that may result from exposure to chemical substances found in the environment.
- Toxicity values for effects other than cancer: Reference Doses (RfDs) and Reference Concentrations (RfCs).
- Cancer risk: Hazard characterization, Oral Slope Factors, and Inhalation Unit Risks.

www.epa.gov/iris

- Information is posted on the IRIS database in the form of an IRIS Summary and Supporting documents (i.e., Toxicological Reviews or IRIS Chemical Assessments).
- IRIS database provides qualitative and quantitative health effects information on over 550 substances.

IRIS Assessments and Risk Assessment



2011 NRC Recommendations for Developing IRIS Assessments

- **In their review of the draft formaldehyde IRIS assessment in 2011, the NRC provided recommendations for improving the development of draft IRIS assessments, in general. For example, the NRC recommended that EPA:**
  - Provide a **fuller discussion of the methods** of the assessment; **concise statements of criteria** used to exclude, include, and advance studies for hazard evaluation and derivation of toxicity values.
  - **Clearly articulate the rationale and criteria** for screening studies and rationale for selecting studies used to calculate toxicity values.
  - Use **standardized evidence tables** to provide methods and results of studies for all health outcomes.
  - Use **uniform approaches to evaluate strengths and weaknesses** of all critical studies and **summarize findings in tables**.
  - Ensure that **weight-of-evidence descriptions** indicate the various determinants of weight to promote understanding of what elements were emphasized in synthesizing evidence.
  - **Rigorously edit documents** to reduce the volume of text substantially and address redundancies and inconsistencies.
- **The NRC did not tell EPA to stop developing IRIS assessments or to stop the IRIS Program until changes were fully implemented.**

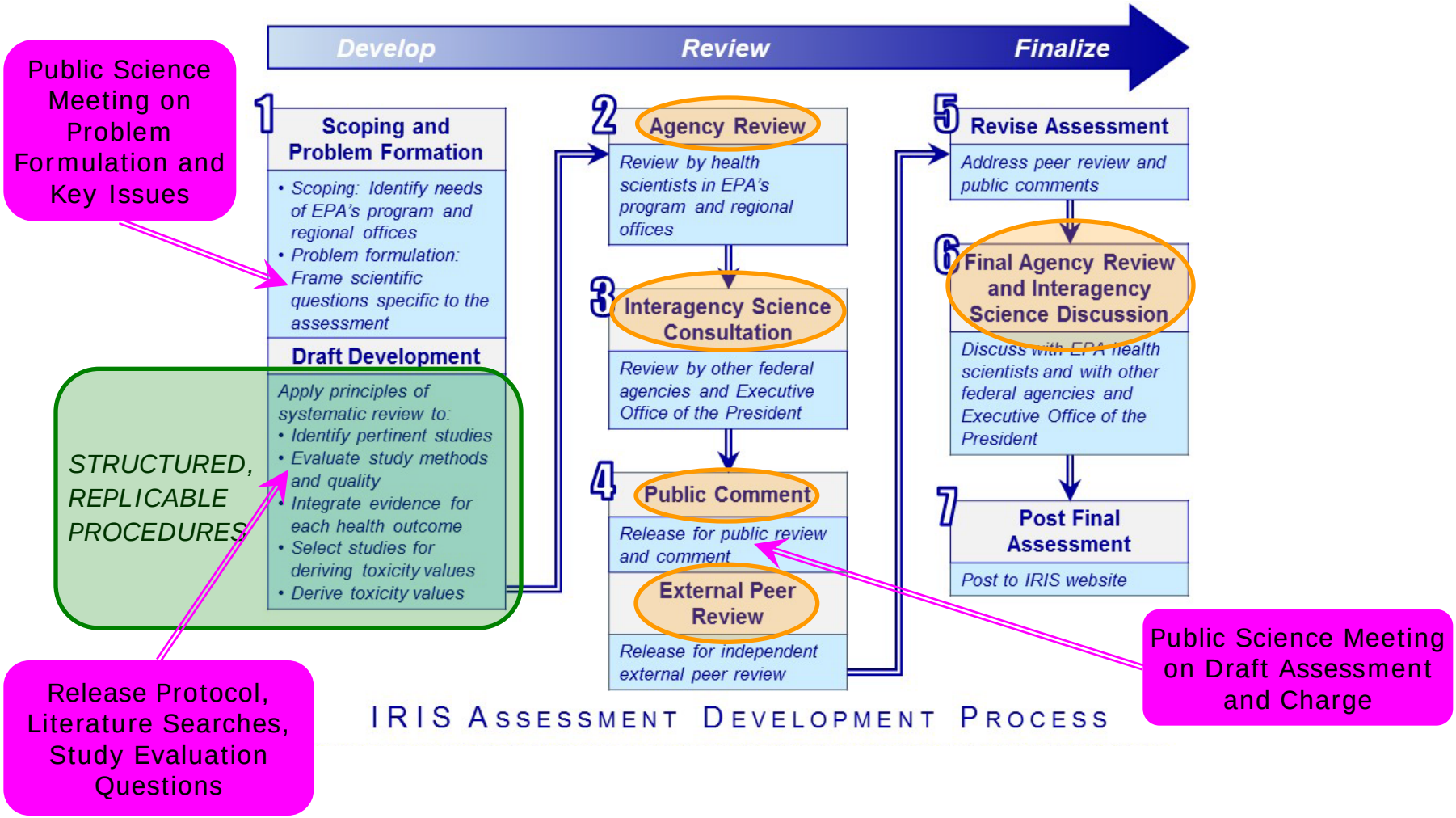
New Document Structure

- Concise, rigorously edited assessments (i.e., shorter!)
- Preamble to describe methods used
- Executive summary that presents the major conclusions and key issues in the assessment
- Detailed literature search strategy and study selection criteria
- Distinct separation of hazard identification and dose-response analysis
- Evidence tables and exposure-response arrays
- Text to focus on analysis and synthesis
- Standardized weight-of-evidence characterization for all health effects

The IRIS Process Was Enhanced in 2013

- To improve the fundamental science
  - by implementing systematic review
  - by strengthening peer review (SAB Chemical Assessment Advisory Committee)
- To increase capacity and productivity to better meet stakeholder needs
- To increase transparency so issues are identified and debated early
- To increase stakeholder engagement

The Enhanced IRIS Has Increased Opportunities for Public Engagement



Public Science Meetings

- IRIS Program encourages the scientific community and the public to participate in discussions of draft materials for IRIS assessments under development.

- The scientific information and perspectives from the meeting are then considered as the assessments progress.

<u>Public Science Meetings</u>

- Four held in 2016
- 2017 Cycle – To be determined

Stakeholder Notification and Participation

Notification

- Human Health Risk Assessment Research Program monthly bulletin which includes updates about activities in the IRIS Program
- IRIS email bulletin to regularly update stakeholders about opportunities to engage the IRIS Program; the availability of newly released draft and final assessments; and general updates about the IRIS Program
- IRIS website (www.epa.gov/iris)
- Federal Register

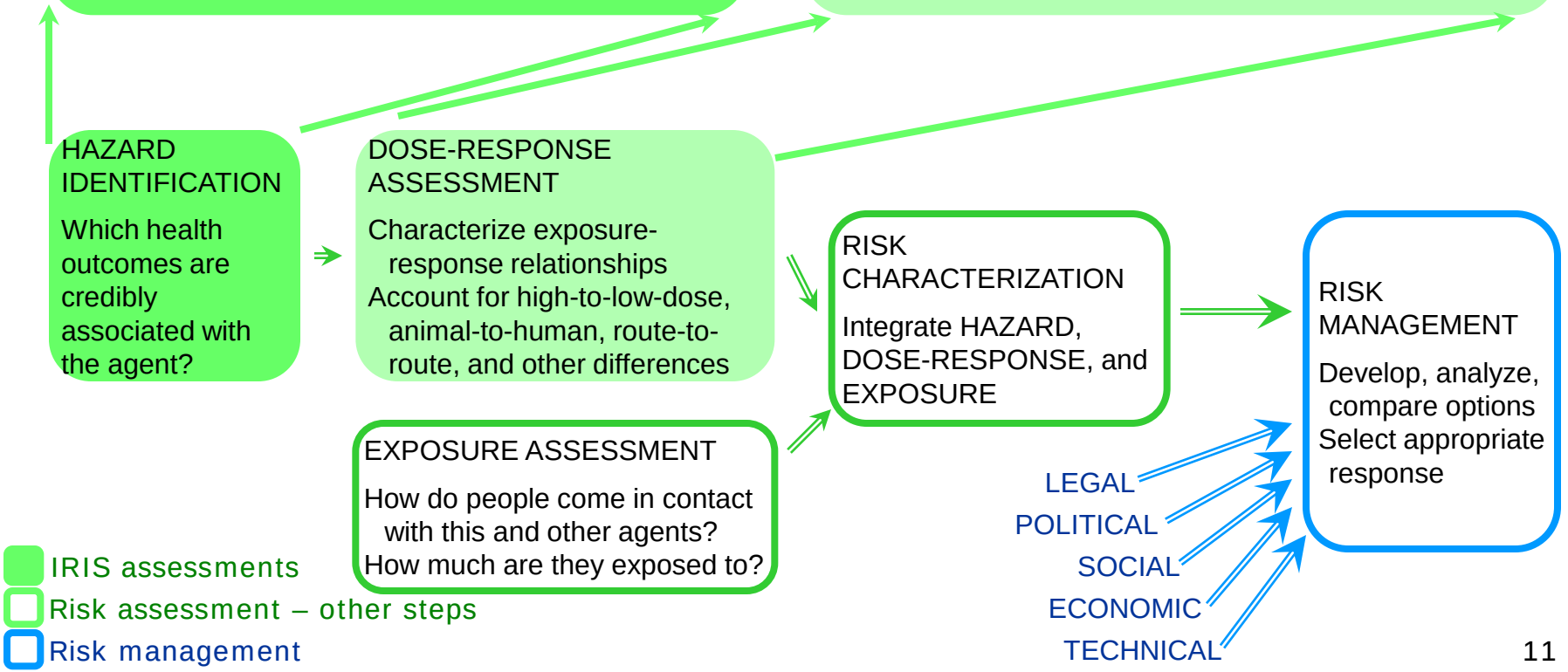
Participation Opportunities

- Submit comments and materials to the docket at http://www.regulations.gov
- Attend and participate in public meetings and scientific workshops
- Provide comments on potential topics and speakers for workshops
- Nominate peer reviewers

The Enhanced IRIS Means New Scientific Content

The HAZARD IDENTIFICATION section identifies all credible health hazards
- A workshop in Aug 2013 explored evidence-integration frameworks
- Another workshop 2014 will addressed this topic

The DOSE-RESPONSE ASSESSMENT explores toxicity values for each credible health hazard
- This will facilitate subsequent cumulative risk assessments that consider the combined effect of multiple agents acting at a common site or through common mechanisms



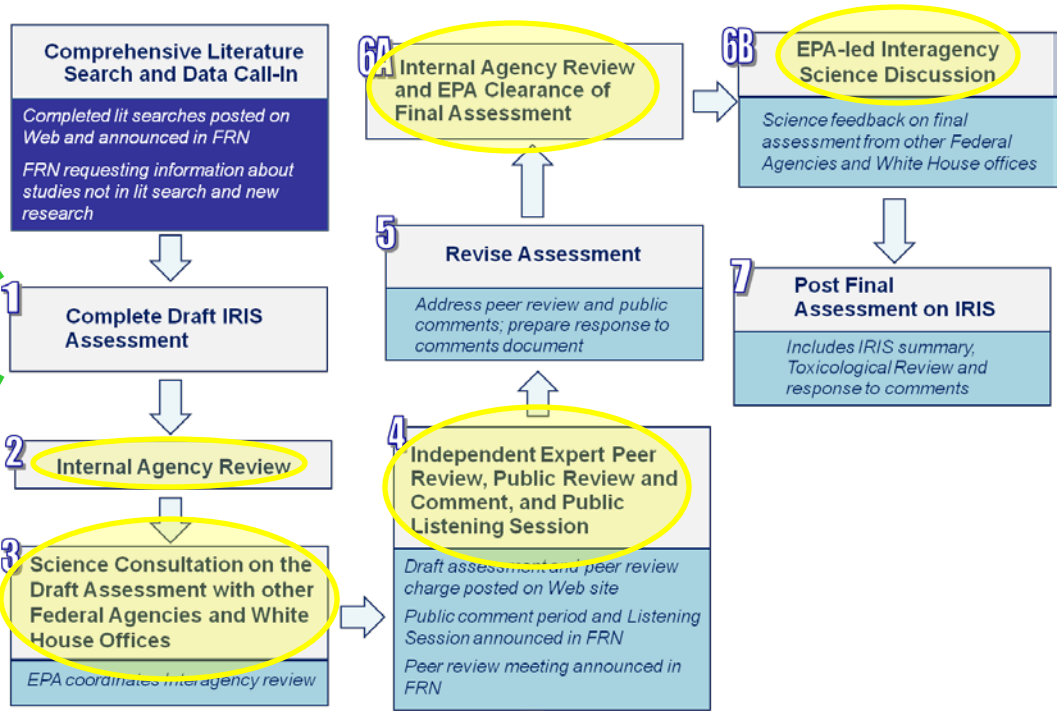
Organ/System-Specific RfDs and Proposed Overall RfD

Effect	Basis	RfD (mg/kg-d)	Confidence
Developmental	Neurodevelopmental impairments	1×10^{-4}	MEDIUM
Reproductive	Decreased ovary weight and ovarian follicles	3×10^{-4}	MEDIUM
Immunological	Decreased thymus weight and serum IgM	1×10^{-3}	LOW
Proposed Overall RfD	**Developmental toxicity**	**1×10^{-4}**	**MEDIUM**

Example. Not real data.

IRIS is Implementing Systematic Review

- Identify Pertinent Studies
- Evaluate Study Methods and Quality
- Integrate Evidence for Each Health Outcome
- Select Studies for Deriving Toxicity Values
- Derive Toxicity Values



Part II

Updates on IRIS health assessments of interest

- Trichloroethylene (TCE)
- Tetrachloroethylene (perc)
- Dioxin
- Naphthalene

Trichloroethylene (TCE)

- Stable, colorless liquid with a chloroform-like odor
- Produced since the 1920s as a dry cleaning chemical, but was largely replaced in the 1950s with tetrachloroethylene.
- Used primarily as a degreasing agent in recent decades.
- Other usages include adhesives, paint-stripping formulations, paints, lacquers and varnishes.
- Human exposure may occur due to its widespread presence in ambient air, indoor air, soil and ground water.

Trichloroethylene (TCE)

- IRIS assessment of TCE was finalized in 2011.
- Cancer and effects other than cancer were evaluated.
- TCE is characterized as “carcinogenic to humans” by all routes of exposure.

Toxicity Values	
Reference Dose (RfD):	5×10^{-4} mg/kg-day
Reference Concentration (RfC):	0.002 mg/m^3
Oral Slope Factor (OSF)	4.6×10^{-2} mg/kg-day
Inhalation Unit Risk:	4.1×10^{-6} ug/m^3

Tetrachloroethylene (PERC)

- Widely used as a solvent that is produced commercially for use in dry cleaning, textile processing and metal-cleaning operations.
- PERC has been detected in ground water, surface water, air, food and human breast milk.
- Human exposure occurs primarily via inhalation and/or ingestion of contaminated water.

Tetrachloroethylene (PERC)

- IRIS assessment of PERC was finalized in 2012.
- Cancer and effects other than cancer were evaluated.
- PERC is characterized as "Likely to be carcinogenic to humans" by all routes of exposure.

Toxicity Values	
Reference Dose (RfD):	6×10^{-3} mg/kg-day
Reference Concentration (RfC):	4×10^{-2} mg/m^3
Oral Slope Factor (OSF)	2.1×10^{-3} mg/kg-day
Inhalation Unit Risk (IUR):	2.6×10^{-7} ug/m^3

2,3,7,8-Tetrachlorodibenzo-p-dioxin (Dioxin)

- Dioxins and dioxin-like compounds are released into the environment from a number of industrial, individual, natural activities and/or events including:
  - Chemical manufacturing
  - Combustion
  - Metal processing
  - Burning of household wastes
  - Forest fires
- Human exposure occurs primarily via ingestion of contaminated foods (i.e., bioaccumulation).

2,3,7,8-Tetrachlorodibenzo-p-dioxin (Dioxin)

- IRIS assessment of dioxin was finalized in 2012.
- Only non-cancer effects were evaluated.

Toxicity Value	
Reference Dose (RfD):	7×10^{-10} mg/kg-day

As a part of the effort to develop a Multi-Year Agenda, the need for an assessment of dioxin carcinogenicity was re-evaluated by the Agency.

The IRIS Program is currently focusing other chemical assessment needs that have been identified as higher priorities to EPA program and regional offices and is deferring completion of the dioxin cancer assessment at this time.

Naphthalene

- White, crystalline solid at room temperature with an aromatic odor
- Insoluble in water, but soluble in other organic solvents
- Largest source of naphthalene is from fossil fuels (i.e., petroleum and coal).
- High levels of naphthalene can be found in coal tar, a byproduct of steel.
- Within the U.S., naphthalene is used in the production of phthalate plasticizers, resins, phthaleins, dyes, pharmaceuticals and insect repellants.
- Consumer uses include as moth repellants, toilet deodorant blocks, aerosol paints and agricultural chemicals.
- Human exposure occurs primarily via inhalation of contaminated indoor and outdoor air.

Naphthalene

- IRIS is currently reassessing the cancer and non-cancer health effects resulting from exposure to naphthalene.
- This chemical was previously assessed in 1998.
- EPA was unable to determine the carcinogenic potential of naphthalene at that time.
- Problem formulation and scoping materials were released in July 2014 for a public science meeting held on September 3-4, 2014.
- Next step will be release of protocols.

Toxicity Value	
Reference Dose (RfD):	2×10^{-2} mg/kg-day
Reference Concentration (RfC):	3×10^{-3} mg/m^3

Part III

Other Developments

Multi-Year Agenda for New Assessments

- Process – reprioritization of the 2012 IRIS Agenda
  - Surveyed EPA program and regional offices for their assessment needs
  - Evaluated the resources needed for each assessment by science discipline
  - Discussed with senior EPA officials how to meet the most high-priority needs
  - Released to the public in December 2015

https://www.epa.gov/iris/iris-agenda

Multi-Year Agenda for New Assessments

- Fifteen chemicals were identified as having the highest priority for assessment and were placed into three groups based on priority.
- Will be started over next few years as resources allow.
- With the exception of nitrate, nitrite, and perfluoroalkyl compounds, all of the high priority assessments were on the 2012 IRIS agenda.
- The dioxin cancer assessment has been deferred to focus on other, higher priority assessments.

Multi-Year Agenda for New Assessments

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

https://www.epa.gov/iris/iris-agenda

Keeping IRIS Up-To-Date

- IRIS is developing a process for updating and maintaining finalized IRIS assessments that do not warrant a full reassessment through the IRIS process.
- IRIS is developing a process for archiving pesticide assessments on IRIS that have been more recently evaluated by EPA's Pesticide Program.

The New, Enhanced IRIS

Improved science	- Systematic review - New science: hazard statement and toxicity values for each credible health outcome - Strengthened peer review
Increased transparency	- Clear, concise, systematic assessments - Opportunities for public engagement
Increased productivity	*These enhancements should enable us to complete more assessments in less time*

IRIS will continue to evolve as we receive public input and peer review advice

THANK YOU!

Gina Perovich, Deputy Director
IRIS Program
US EPA Office of Research and Development
National Center for Environmental Assessment

perovich.gina@epa.gov

Vincent Cogliano, IRIS Director	cogliano.vincent@epa.gov
Samantha Jones, IRIS Associate Director for Science	jones.samantha@epa.gov
US Environmental Protection Agency	www.epa.gov
EPA's Integrated Risk Information System	www.epa.gov/iris/