Overview

- Human Health Risk Assessment (HHRA) Role in ORD research portfolio
- Vision and Link to EPA Priorities and mandates
- Program design
- Community and Site-specific Risk
- Research to Advance Analyses and Applications
- Supplementary Materials (IRIS, ISAs)
ORD Research Programs

Air, Climate & Energy

Sustainable & Healthy Communities

Homeland Security

Chemical Safety for Sustainability

Human Health Risk Assessment

Safe & Sustainable Water Resources
## Aligning Research with EPA Strategic Goals

### Cross-Agency Strategies
- Sustainable Future
- Visible Difference in Communities
- New Era of Partnerships
- High-Performing Organization

### EPA Goals 2014-2018
- Addressing Climate Change and Improving Air Quality
- Protecting America’s Waters
- Cleaning Up Communities and Advancing Sustainable Development
- Ensuring the Safety of Chemicals and Preventing Pollution
- Enforcing Laws, Ensuring Compliance

### Research Programs
- Air, Climate & Energy
- Safe and Sustainable Water Resources
- Sustainable and Healthy Communities
- Chemical Safety for Sustainability
- Human Health Risk Assessment
- Homeland Security
**Problem Statement:** Predicting impacts and protecting human health and the environment depend on bringing the best available science to describe potential hazards and to characterize risks for a variety of exposure scenarios. The wide range of decisions made daily by EPA and other stakeholders requires a comprehensive suite of application products and analytical approaches that tailor assessments to fit the purpose of these various management decisions.
Risk-based decisions by the EPA, State/local/tribal agencies and the public to protect public health and the environment are based on reliable, transparent and high-quality risk assessment methods, models, and data.

- HHRA research program supports this vision by identifying, evaluating, integrating, and applying relevant data from a variety of scientific disciplines to characterize the risk from exposures of individual chemicals, mixtures and non-chemical stressors.

- Assessments generated by the HHRA research program inform a variety of risk management decisions, and serve to identify critical scientific issues and advance analytical approaches for their resolution.
HHRA Addresses all of EPA’s Priorities and Mandates

- Clean Air Act (CAA)
- Safe Drinking Water Act (SDWA)
- Food Quality Protection Act (FQPA)
- Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA)
- Resource Conservation and Recovery Act (RCRA)
- Toxic Substances Control Act (TSCA)

Broad Input to Support
- Agency Strategic Goals
- Children’s Health, Environmental Justice, Climate and Nitrogen Roadmaps
- Sustainability
HHRA Program Design

ISA = Integrated Science Assessment
MSD = Multipollutant Science Document
IRIS = Integrated Risk Information System

SCIENCE AND DECISIONS
Advancing Risk Assessment

Stakeholder Engagement & Cross-Program Integration Planning / Problem Formulation and Scoping

Research to Advance Analyses and Applications

IRIS
ISA MSD
Community and Site-Specific Risk

Stakeholder Engagement & Cross-Program Integration Evaluation / Outreach and Training

Look Inside
ORD – Human Health Risk Assessment Research Program

Resources

FY12 – FY15 Dollars and FTE

DOLLARS (K)

2012 ENA  $42,647
2013 ENA  $40,051
2014 ENA  $43,050
2015 PB   $40,713

FISCAL YEAR

HHRA Research Program Dollars

HHRA Research Program FTE

FTE

ORD – Human Health Risk Assessment Research Program

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FTE
Risk Assessor’s Toolbox
Assessment context and data availability linkage

- Human studies
- Chronic animal studies
- Adverse outcome pathways, biomarkers, knowledge mining
- QSAR, in vitro HT/HC assays
- Short duration in vivo studies

Integrated Science Assessments
Integrated Risk Information System
Provisional Peer-Reviewed Toxicity Value
Rapid Tox Assessments
Screening and Ranking

Number of chemicals

Adapted from Ivan Rusyn
Community and Site-specific Risk

• Provisional Peer-reviewed Toxicity Values (PPRTV)
  – Coordination with OSWER
  – ≥ 12 annually
• Superfund Technical Support Center
  – Human health
  – Ecological
• Rapid risk assessment
• Cumulative risk assessment (CRA) methods
Community and Site-specific Risk:
Cumulative Risk Assessment (CRA)

- Cumulative risk assessment (CRA) methods
  - Considerable Agency experience
  - Guidance for mixtures
  - Case studies and publications
  - Training

- Well-vetted platform to
  - Advance place-based community assessment
  - Address environmental justice issues
Community and Site-specific Risk: Advancing CRA

• Extend with ecological assessment
  – General ecological assessment endpoints (GEAE)
  – Ecosystem services
  – Adverse outcome pathways (AOP)
• Collaboration with other programs to incorporate
  – Resiliency
    • (Homeland Security)
  – Well-being
    • (Sustainable and Healthy Communities)
Research to Advance Analyses and Applications: Updating Exposure and Dosimetry

  - Web-based tool box
  - Annotated links to Over 800 Resources
    - Data
    - Models
    - Guidance
    - References
    - Organized by Topic Area
    - Related Website Links
- Update approaches to translate doses of different study types (epidemiological, *in vitro*, laboratory animal) to various human exposure scenarios
- Dosimetry
  - Update with mature models to support description of key events at different levels of biological organization
  - Facilitate interpretation of biomonitoring and reverse dosimetry
Research to Advance Analyses and Applications: Dose/Duration/Response Complexity

- Flexibility required to
  - Characterize different exposure scenarios
    - Acute
    - Episodic
    - Chronic
  - Address different scales
    - Geographical
    - Temporal
    - Biological
  - Describe disease dimensions (e.g., early or late event)
  - Develop prognostic significance for key events and probabilistic approaches
- Provides support to benefits analysis for all effects
Research to Advance Analyses and Applications: Applying New Data

- Integration area with CSS
- Rapid tox approaches
  - Prioritization
  - Hazard ID
- Applications for other chemical domains and additional endpoints
  - Air, water, land
  - Respiratory, liver, cardiovascular, ...
- Decision criteria for utility across applications
New Data: New Challenges
New Data: New Opportunities

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- **10s-100s/yr**
- **10s-100s/day**
- **1000s/day**
- **10,000s-100,000s/day**

**Human Relevance/Cost/Complexity**

**Throughput/Simplicity**
Chemical Safety for Sustainability (CSS)

QSAR/Read-Across/ToxCast/RTK/IVIVE

High Throughput POD → Screening Reference Values → PPRTV Appendix

PPRTVs/IRIS/ISAs

RapidTox Assessment
Disease-Chemical Data Integration

Human Health Risk Assessment (HHRA)

External diverse data sources (e.g., Tox21, ‘omics data)
RapidTox Assessment

- Semi-automated data mining and data integration outputs
- Expert judgment integrates data and applies causal framework
- Data sources are existing electronic databases, CSS output, and models
  - HTS/HC/QSAR
  - HT-PODs
  - Cellular signaling/metabolism pathways, AOPs, MOAs
  - Human clinical and epidemiology data (rare)
  - REACH
Disease-based Data Integration

- Disease-based context for other critical endpoints of interest
  - Respiratory, liver, cardiovascular, …
- Data from diverse sources and approaches
  - High Throughput/Content Screening
  - Adverse outcome Pathway/Mode of Action
  - Biomonitoring
  - Laboratory animal (ex vivo, in vivo)
  - Human (clinical, epidemiological)
  - Clinical chemistry
  - Virtual tissues

AOP and biomarkers serve to link elements and describe disease pathogenesis
Assessment Development Methods

- Continue to improve technologies to enhance data access and management systems to support transparency and efficiency of assessment document development
  - Improve understanding of risk assessment basis, issues and methods
  - Health and Environmental Research Online (HERO) system (www.epa.gov/HERO)

[Modified from 2014 NRC Report (Figure S-1)]
Stakeholder Engagement: Outreach

- Develop and apply methods for stakeholder engagement and risk assessment training to varied audiences via the Risk Assessment Training and Experience (RATE) program
  - Outreach efforts as public workshops, seminars and training sessions and varied communication approaches (e.g., web posting, emails, blogs)

- Recent workshops/seminars
  - Benefits assessment workshop for non-cancer endpoints
  - Mouse lung tumor workshop
  - Hexavalent Chromium workshop
  - IRIS Bimonthly meetings
  - Upcoming: workshop on 2014 NAS IRIS Program Report
Human Health Risk Assessment Research

Supporting communities with environmental and health risk assessments

Developing assessments for improved public health

Providing the science to support the air quality standards

Modernizing risk assessment
Supplemental Materials

- Integrated Risk Information System
- Integrated Science Assessments
Provide a concise review, synthesis, and evaluation of the most policy-relevant science to serve as the scientific foundation for review of the National Ambient Air Quality Standards (NAAQS) for criteria pollutants

Prepared in close coordination with EPA air office
“All NAAQS All the Time”

• Complete current ISAs:
  – Oxides of Nitrogen – Health Criteria
    • Second draft release (October 2014)
    • Final FY 2015
  – Oxides of Sulfur – Health Criteria
    • First draft due to be released December 2014
    • Final FY 2016
  – Oxides of Nitrogen and Sulfur – Ecological Criteria
    • Final FY 2016

• Initiate upcoming reviews:
  – Particulate Matter – Workshop on Science Policy Issues (early 2015)

• Advance multipollutant science (Multipollutant Science Documents):
  – MSD for the Effects of the Criteria Air Pollutants on Climate Forcing
    • First Draft FY 2015
    • Final FY 2016
  – MSD on Human Health
    • Exploratory literature search activities, multipollutant analyses, and preliminary publications underway
ISA for Ozone

- Final released February 2013
  - 4,000+ studies considered; 2,270 studies cited
  - 1,038 new since 2006 Ozone Air Quality Criteria Document (AQCD)

- Multiple peer-reviewed journals spawned from this review

- Implemented new weight of evidence framework for at-risk factors
  - Which individual- and pollutant-level factors result in increased (decreased) risk of an air pollutant induced health effect?
  - Four level classification of evidence for potential at-risk factors
• Final released June 2013
  – 7,400+ studies considered; 3,188 studies cited
  – 1,714 new since 2006 Pb AQCD (745 health, 543 eco, 426 other)

• Multiple peer-reviewed journals spawned from this review
  – Lassiter et al. (Submitted). Cross-Species Coherence in Effects and Modes of Action in Support of Causality Determinations in the U.S. Environmental Protection Agency’s Integrated Science Assessment for Lead. Toxicol.

• Integrated health and ecological effects based on mode of action
• Characterized blood-lead/air-lead relationships to inform policy assessment
• Identify and summarize the state-of-the-science for the criteria air pollutants, focusing on effects in the context of air pollutant mixtures

• Primary purpose of the MSD is to inform future ISAs on the individual pollutants
  – Example: Oxides of nitrogen and sulfur, PM, CO, O₃ → Climate forcing
  – The ISA for Oxides of Nitrogen and Sulfur - Ecological Criteria provides the scientific basis for the EPA Administrator’s decisions on the secondary (welfare-based) NAAQS for oxides of nitrogen and sulfur
  – Workshop on Science Policy Issues – March 4-6, 2014
  – Peer-input Workshop – January 2015 (tentative)
  – First Draft ISA due to be released – May 2015 (tentative)

• MSD for the Effects of the Criteria Air Pollutants on Climate Forcing
  – Workshop on Science Policy Issues – May 1, 2012
  – Peer-input Workshop – late 2014 (tentative)
Review of the Integrated Risk Information System (IRIS) Process (NRC, May 2014): “EPA has made substantial improvements to the IRIS Program in a short amount of time”
IRIS Enhancements

- **Development process** [http://epa.gov/iris/](http://epa.gov/iris/)
  - Planning and scoping
  - Public meetings on released literature search and strategy, evidence tables, and exposure-response figures

- **Improving the science**
  - Systematic review
  - Concise, compact and clear document structure
  - SAB Chemical Assessment Advisory Committee (CAAC) [http://yosemite.epa.gov/sab/sabpeople.nsf/WebCommitteesSubcommittees/Chemical%20Assessment%20Advisory%20Committee](http://yosemite.epa.gov/sab/sabpeople.nsf/WebCommitteesSubcommittees/Chemical%20Assessment%20Advisory%20Committee)

- **Improving productivity and transparency**
  - Workforce planning
  - Agency needs assessment
New Disciplinary Workgroups and Workflow
Cross-cutting Issues and Scientific Workshops

• Challenges arise in specific assessments
  – Factors influencing the uptake and carcinogenicity of ingested hexavalent chromium (2013)
  – Approaches to meta analysis for inorganic arsenic (on-going)
• Issues also identified by disciplinary groups
  – Mode of action for development of mouse lung tumors by selected solvents (2014)
• Evidence integration and risk of bias
• Extending cumulative risk assessment (CRA) methods to address community concerns and support “place-based” assessments and sustainability
• Advancing approaches for benefits analysis of noncancer endpoints
• Incorporating new data and emerging advances in biotechnology and computational toxicology