

Office of Research and Development

Human Health Risk Assessment Research Program

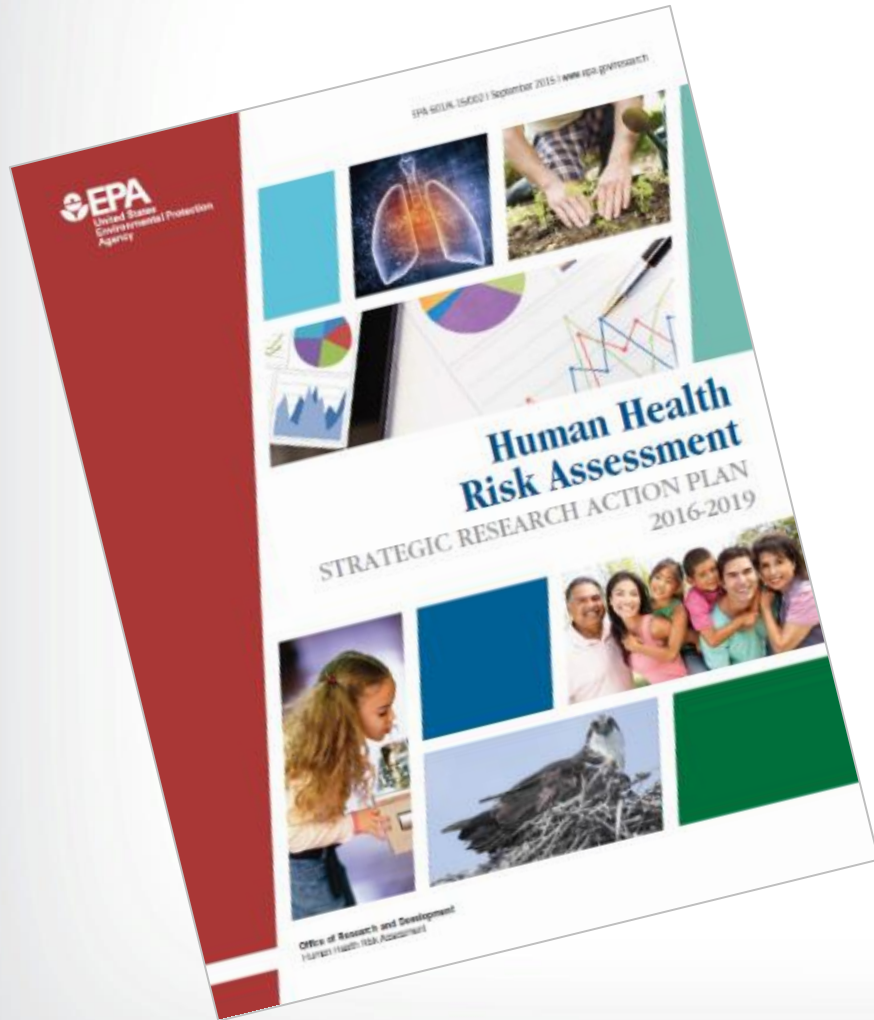


**HHRA Charge Questions 2, 3 and 6
EPA Board of Scientific Counselors (BOSC)
September 1, 2015**

John J. Vandenberg, National Program Director (NPD)
Annie M. Jarabek, Deputy NPD



Charge Questions #2, 3 and 6



- **How effective are the approaches for involving the EPA partners in the problem formulation stage of research planning?**
- **How well does the program respond to the needs of EPA partners (program office and regional)?**

HHRA Addresses all Agency Priorities and Mandates

HHRA

- **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)**

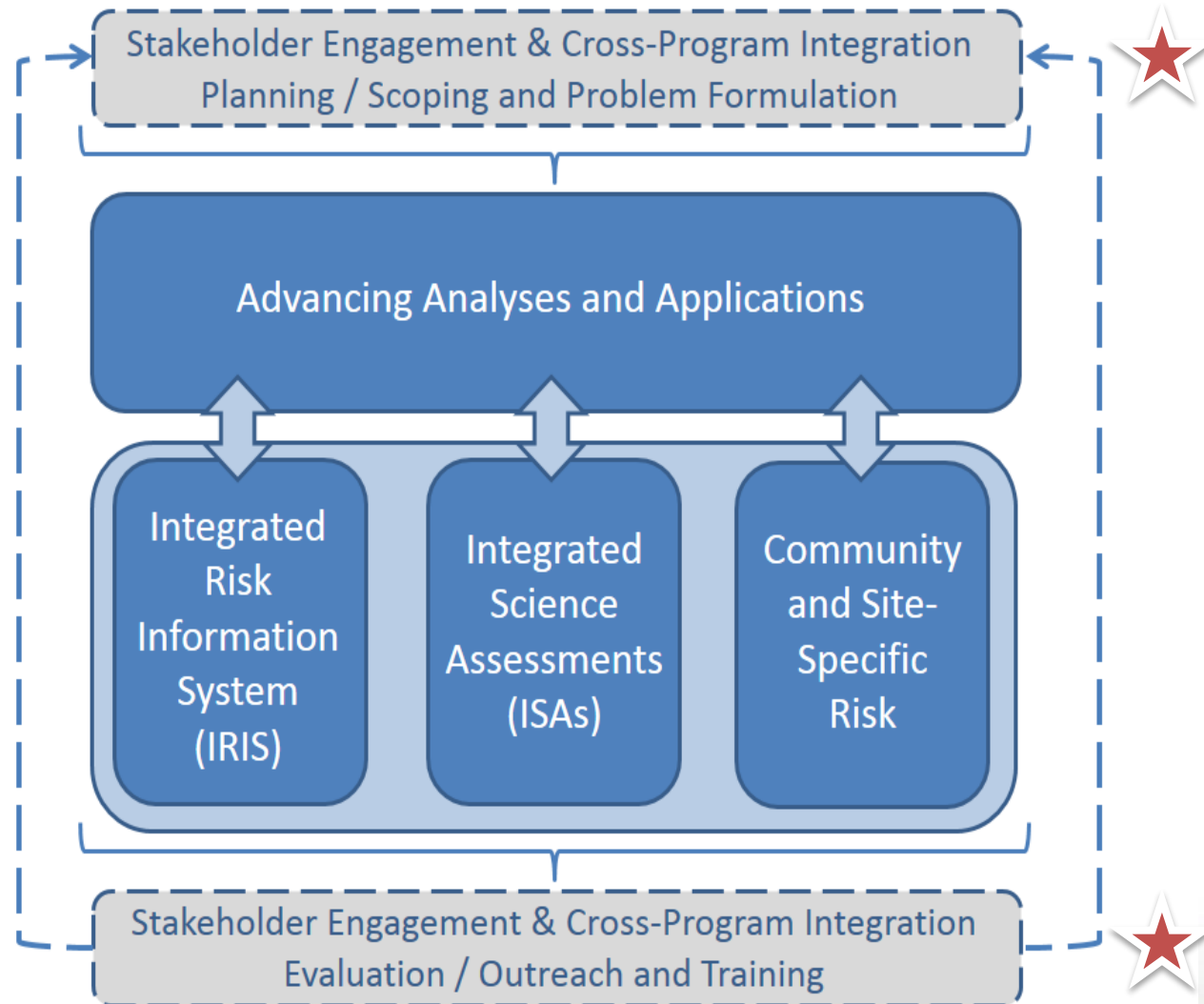
**Broad
Input to
Support**

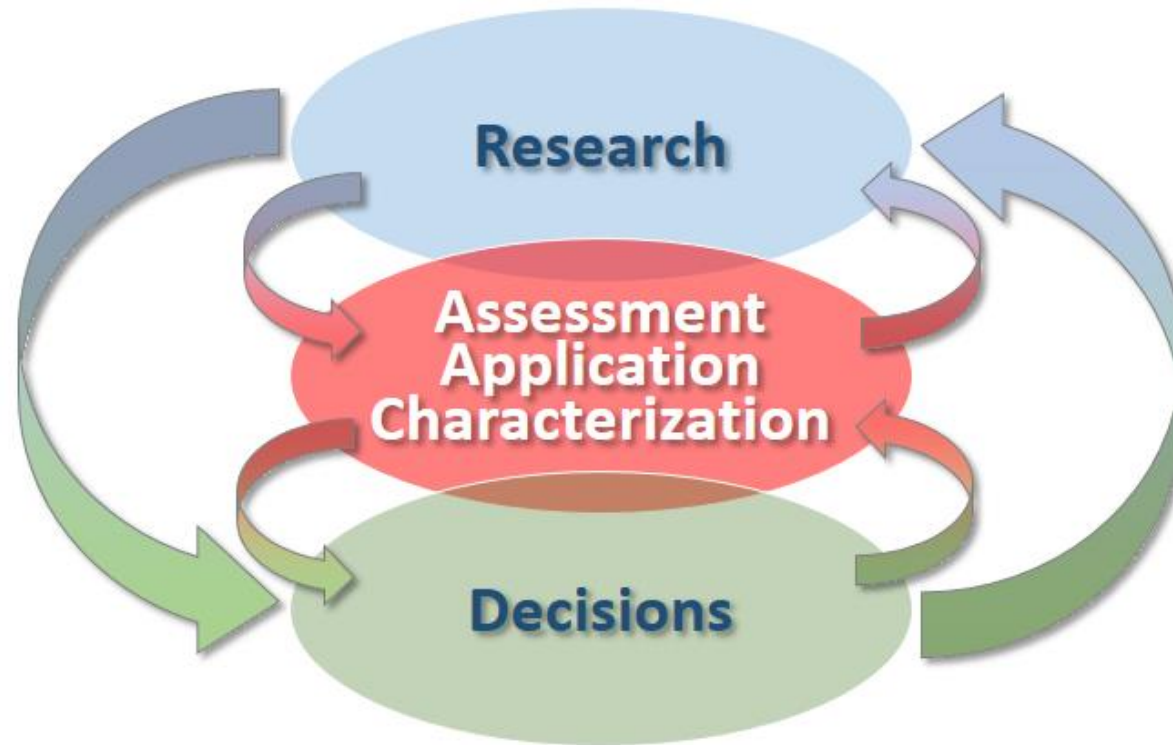


- **Agency Strategic Goals**
- **Children's Health, Environmental Justice, Climate and Nitrogen Roadmaps**
- **Sustainability**



HHRA Program Design





HHRA Vision: 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.

Research Planning Partner Meetings

- “*Risky Business*” face-to-face cross-program planning meetings
 - StRAP Project proposal presentations and feedback from OAR, OSWER, OW, OCSP, OA, and the regional offices
- Programmatic updates quarterly (most programs); 2-3 per month (OAR)
- Annual Senior-level meeting of Assistant Administrators
- On-going meetings to review revisions and to target and communicate products

Monthly HHRA Highlight and Support Bulletins (Sept 2015)

- HHRA Bulletin (7,211 recipients)
- BMDS – News (5,087 recipients)
- IRIS Updates (2,008 recipients)
- ExpoBox Bulletin (806 recipients)



Public Meetings and Workshops (examples):

- Science Advisory Board (SAB) Chemical Assessment Advisory Committee (CAAC) public peer review meetings
- IRIS public science meetings
- Clean Air Scientific Advisory Committee (CASAC) public peer review meetings
- Integrated Science Assessment (ISA) kickoff workshops
- Scientific workshops to address challenges and emerging issues (Task 7.5)
 - Epigenetics (2015)
 - Advancing systematic review (2015)
 - Temporal exposure issues (2016)

Risk Assessment Support to Programs, Regions and NCEA (Task 9.1)

- Integrated Risk Information System (IRIS) Website and database
- Integrated Science Assessments (ISA) Websites and database
- Peer-reviewed Toxicity Value (PPRTV) Website and database
- Health and Environmental Research Online (HERO) database (> 3 million references)
- Benchmark Dose Software (BMDS) Modeling website and training system
- EPA's-Expo-Box Website (EXPO-Box) and database
- Ecological Risk Assessment Support Center (ERASC) website
- Risk Assessment (Risk) Web Portal collection of human health risk assessments website and databases, including:
 - All-Ages Lead Model (AALM) Website
 - BioMarkers database
 - Database of Sources of Dioxin-like Compounds in the US
 - Dioxin Website and database
 - Epigenetics reference compilation
 - Next Generation of Risk Assessment (NexGen) website
 - Physiologically Based Pharmacokinetic (PBPK) modeling Website
 - Physiological Information (PID) database.



<http://www2.epa.gov/risk>

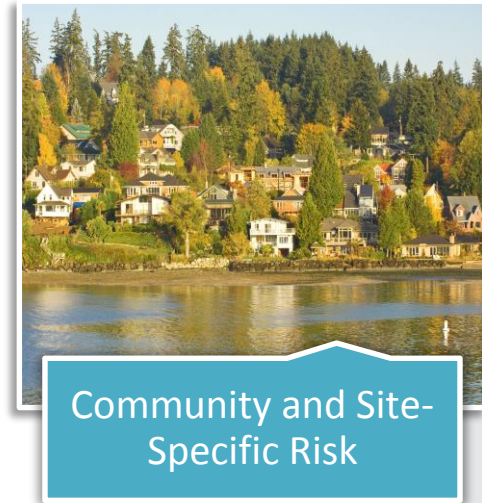


Outreach and Communication

Training (Task 9.2): Risk Assessment Training and Experience (RATE) program for internal partners and external stakeholders

- Updating the current risk assessment training and experience (RATE) training database based on the new developments in risk assessment science
- Developing new training modules such as application of risk assessment in food matrices, microbial risk assessment, implementation and use of computational toxicology methods in risk assessment, cumulative risk assessment to support sustainability and environmental justice, and risk communication
- Providing risk assessment to interested divisions in various USEPA's program offices and regions
- Providing risk assessment training to state, tribal, national and international audiences as resources permit
- Project via the Interstate Technology and Regulatory Council (ITRC) of the Environmental Council of States (ECOS) to develop specialized training for state risk assessors.
 - The ITRC risk assessment training team completed the technical document entitled *Decision Making at Contaminated Sites: Issues and Options in Human Health Risk Assessment* (<http://www.itrcweb.org/risk-3/>)
 - Training course development was solely led by state risk assessors with EPA input on products
 - First live training for the new document was held on March 10th, 2015. Schedule is at this URL: http://www.itrcweb.org/Documents/TeamResources_OutreachMaterials/ITRC-2015-Classes-010615.pdf

- **Rapid response assessments and cumulative risk methods to address emergency response, Superfund site assessment, sustainability characterization, and community concerns**
- **Project 5 - Site-specific and Superfund Regulatory Support**
 - Quarterly reports to Superfund Technical Support Center (STSC) and Ecological Risk Assessment Support Center (ERASC)
 - Technical support, consultation and review for Superfund and other Agency priorities
- **Project 6 - Cumulative Risk Assessment (CRA) Methods and Applications**
 - Approaches to cross-species data integration to support CRA
 - Incorporating multiple stressors
 - Applying genetic and epigenetic data to inform susceptibility
 - Apportioning multimedia exposure and risk across human and ecological receptors





Rapid Response to Support Communities Freedom Industries (Charleston, WV)

- **Crude 4-methylcyclohexanemethanol (MCHM) was spilled from a corroded storage tank into the Elk River on January 9th, 2014.**
- **HHRA in collaboration with HS provided support to WV Dept. of Environmental Protection**
 - **Contributed to drinking water health advisory by CDC/ATSDR**
 - **Developed recommended inhalation screening level**
- **Approach to derive short-term inhalation level involved a route-to-route extrapolation of CDC/ATSDR's drinking water advisory**
- **These efforts informed emergency response actions and remediation work at the Freedom Industries site and provided the capability to interpret air emissions for elevated MCHM levels.**
- **Assessment work was recognized with the Philadelphia Federal Executive Board's Excellence in Government Gold Medal Award for Outstanding Technical Support Accomplishment.**



Kenny Kemp | Charleston Gazette

- **Cumulative risk assessment (CRA) methods**

http://www.epa.gov/raf/publications/pdfs/frmwrk_cum_risk_assmnt.pdf

- **Considerable Agency experience**

- **Guidance for mixtures**
- **Case studies and publications**

- Evans et al. (2014). Joint Exposure to Chemical and Nonchemical Neurodevelopmental Stressors in U.S. Women of Reproductive Age in NHANES. *Int. J. Environ. Res. Public Health* 11(4), 4384-4401; doi:[10.3390/ijerph110404384](https://doi.org/10.3390/ijerph110404384)<http://www.mdpi.com/1660-4601/11/4/4384>

- **Training**

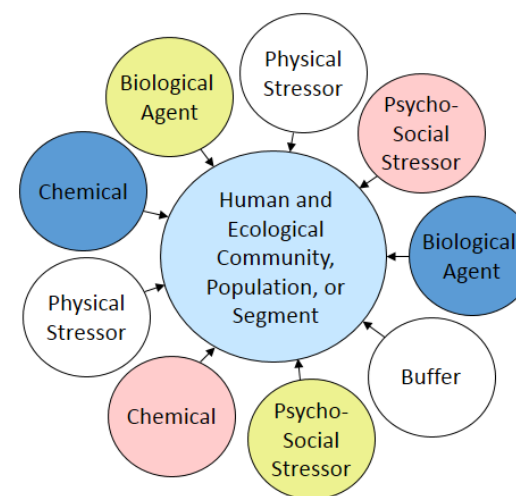
- **Well-vetted platform to**

- **Evolve place-based community assessment**

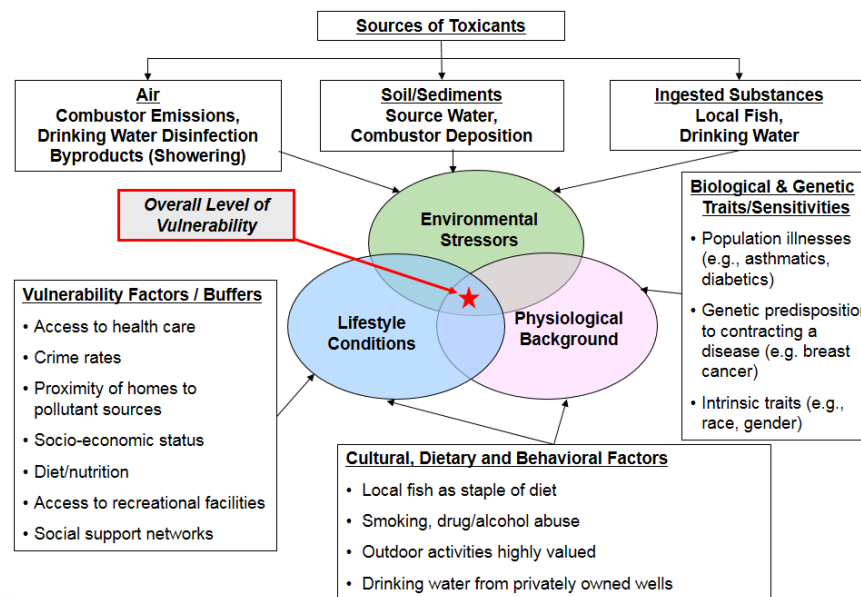
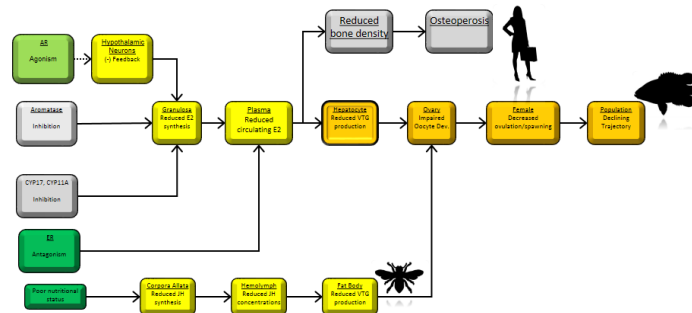
- **Address environmental justice issues**

- Olden et al. (2014). *Epigenome: Biosensor of Cumulative Exposure to Chemical and Non-Chemical Stressors Related to Environmental Justice*. *J Am Public Health Assoc* Oct;104(10):1816-21.

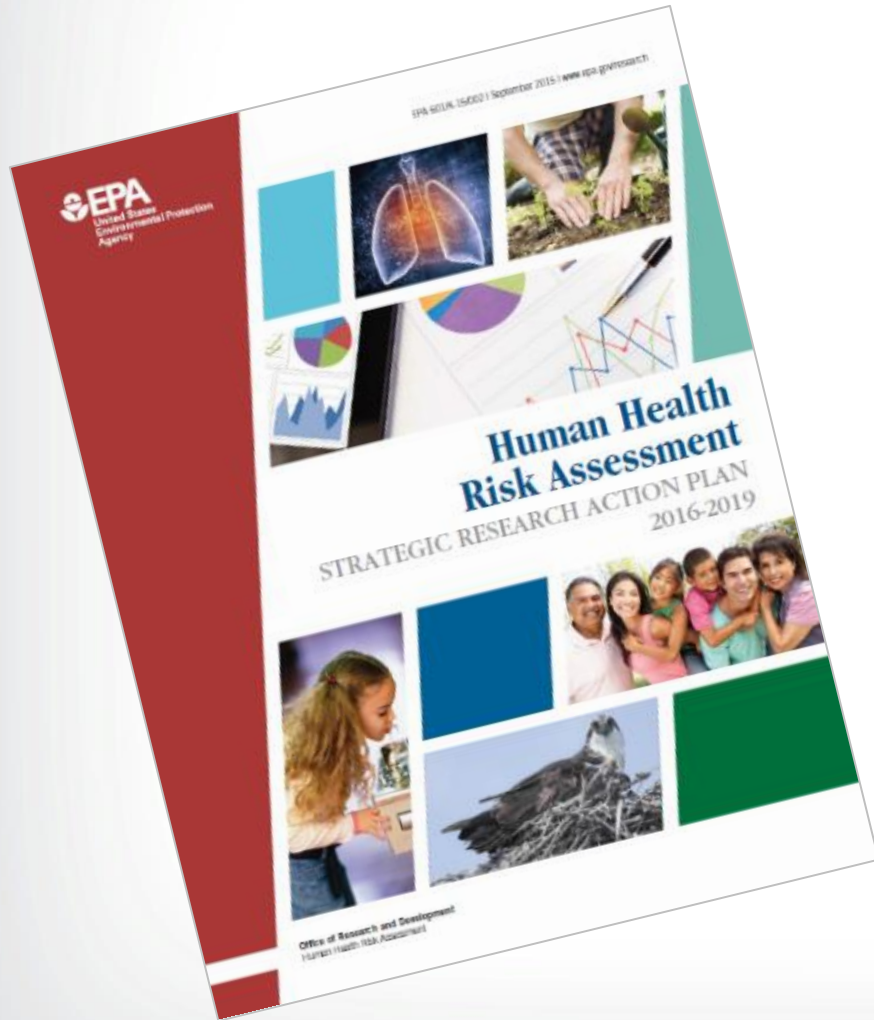
<http://www.ncbi.nlm.nih.gov/pubmed/25122010>



- Expand understanding of stressor interactions
- Integrate ecological assessment
 - General ecological assessment endpoints (GEAE)
 - Adverse outcome pathways (AOP)
 - Ecosystem services
- Apportion multimedia exposure and risk to receptors
- Collaboration with other programs to incorporate
 - Resiliency (HS)
 - Well-being (SHC)



Charge Question #6



- **Please comment on the research dimensions of the HHRA program and, in particular, the proposed approaches for characterization of new data and computational methods to improve confidence and build capacity for their application in the context of risk assessment.**

➤ **Address science challenges affecting hazard, exposure or dose-response analyses and application of scientific, technical and communication innovations to improve characterization of human and environmental impacts**

- **Project 7 – Advancing Hazard Characterization and Dose-Response Methods**

- Advancing Methods
 - Systematic review and evidence integration
 - Quantitative methods
 - Methods for benefits and uncertainty analyses
 - Characterizing determinants of risk: response surface and probabilistic approaches
- Science workshops on major risk assessment methodology issues

- **Project 8 – Applying Emerging Science to Inform Risk Screening and Assessment**

- Disease-based integration of new data types
- Application characterization of high-throughput platforms
 - CSS and HHRA scientists won best 2015 manuscript from the Society of Toxicology
- Dosimetry21: Advancing multi-scale dosimetry models to incorporate AOP/MOA and biomarker data
- Evaluation and application of new exposure data and methods
 - Sensor data: Analytical considerations and interpretation strategies: Collaboration with NIOSH and ACE

- **Project 9 – Risk Assessment Support and Training**

- Development and maintenance of essential software and support tools (e.g, HERO, BMDS, ExpoBox, IRIS website)



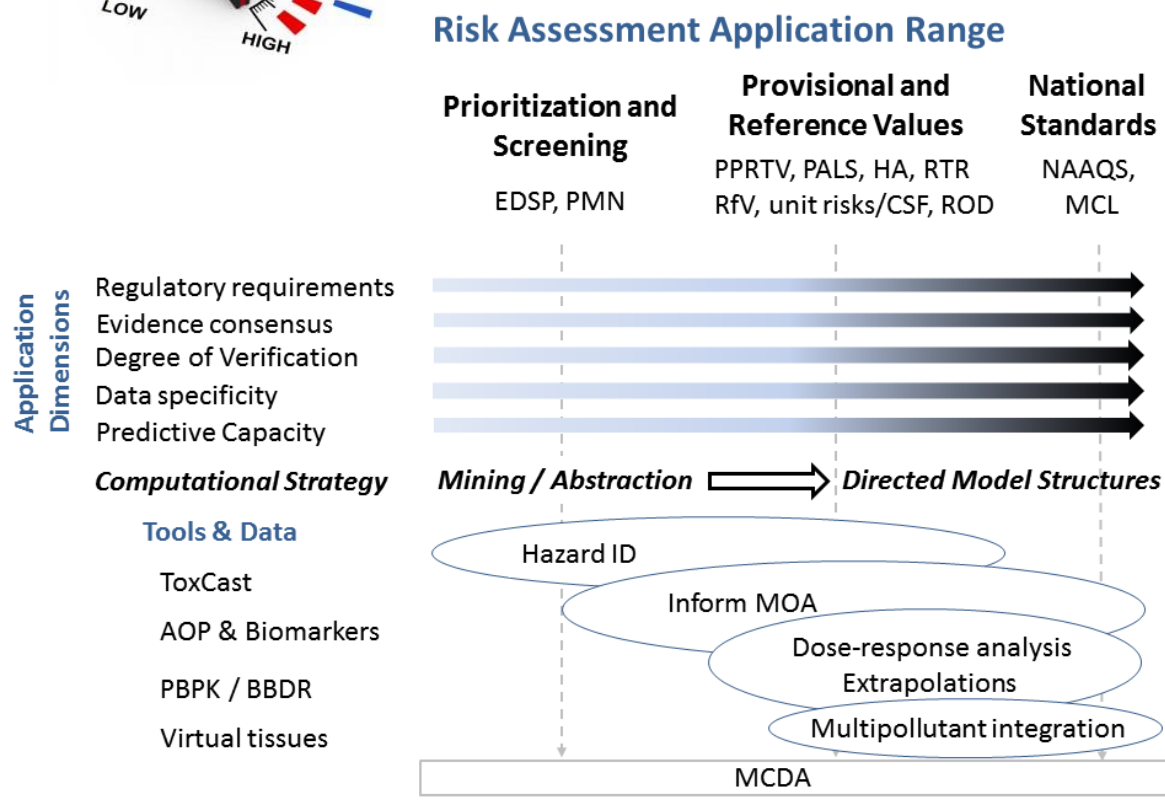
Advancing Analyses
and Applications



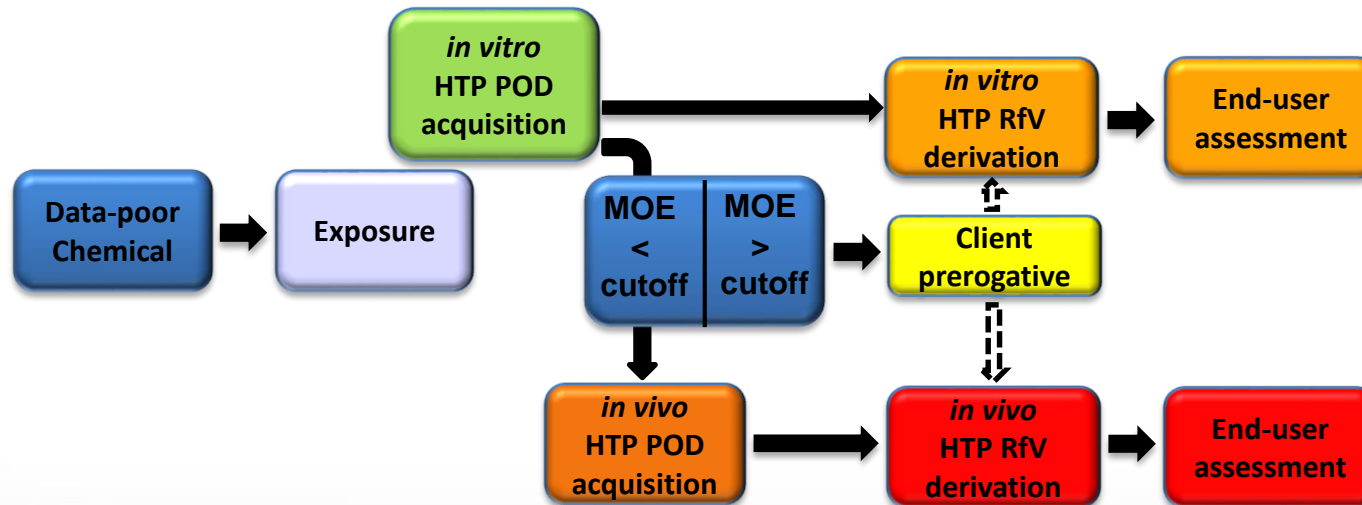
- **Scope of review was limited to application characterization of CSS-type tools to modernize assessments**
 - **SAB/BOSC review found the CSS and HHRA research programs to be scientifically robust and well-aligned to the overarching EPA Strategic Plan...***“considered to be on a path to revolutionize chemical safety assessment and viewed as leading the field”*
 - *“...an iterative approach to tool creation, evaluation, and application is strongly recommended in order to maintain confidence during this period of transition”*
- **Building confidence will require an iterative and integrated approach to foster understanding and trust of new techniques**
- **HHRA characterizations will provide a flexible portfolio and address fit-for-purpose applications:**
 - **High-throughput platforms to aid prioritization**
 - **Multiple platforms to enhance evidence integration and disease-based evaluations**
 - **Updated dosimetry models to quantify AOP / MOA key events and biomarkers**
 - **Response surface analyses to address acute and episodic exposures**
- **HHRA also anticipates advancing cumulative risk methods**
 - **Pivot assessment approaches to “place-based” on community scale**



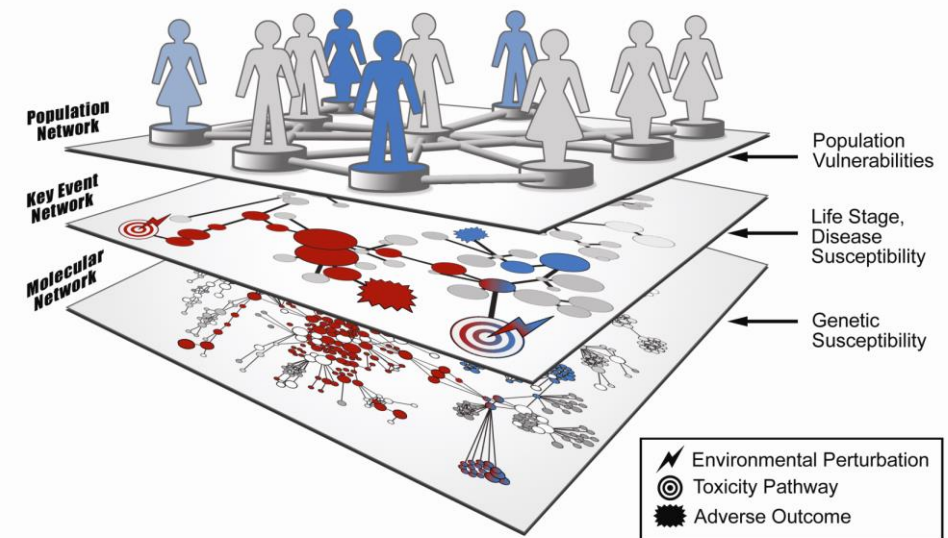
- Characterize application of emerging data and computational approaches across the risk assessment landscape
 - NAAQS > IRIS > PPRTV > screening/prioritization
 - Gain understanding and build capacity
- Integrate mechanistic knowledge into assessment products
 - High Throughput Screening (HTS) to aid hazard identification and provide points of departure for PPRTV assessments
 - Adverse outcome pathways (AOP) to inform evidence integration
- *Decision context for assessment product defines “fit for purpose” need and drives application of data or approaches*



- **CSS data/outputs from read-across/SAR, QSAR, ToxCast, and IVIVE rTK will feed collectively into the development of high-throughput points-of-departure (PODs)**
- **High-throughput PODs (HTP) incorporated into chemical dossiers in the HHRA program and evaluated for use in margin-of-exposure (MOE) and/or screening reference value (sRfV) derivations**



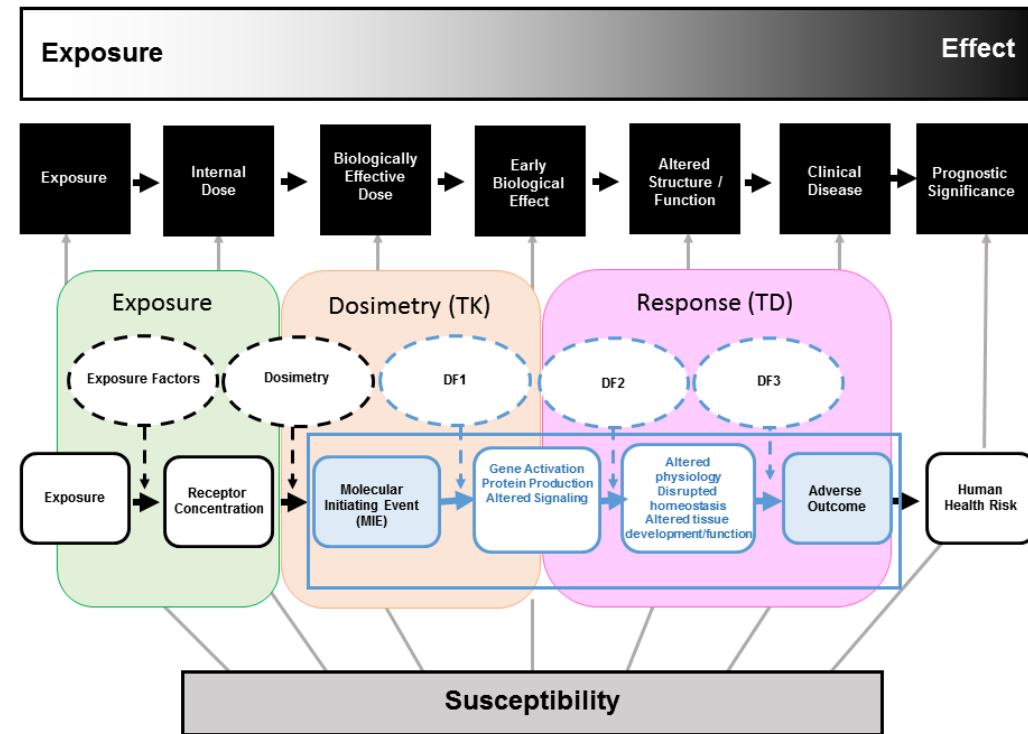
- **Disease-based context for other critical endpoints of interest**
 - Respiratory, liver, cardiovascular, ...
- **Data from diverse sources and approaches**
 - High Throughput Screening / High Content
 - Adverse Outcome Pathways / Mode of Action
 - Biomonitoring
 - Clinical chemistry
 - Laboratory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



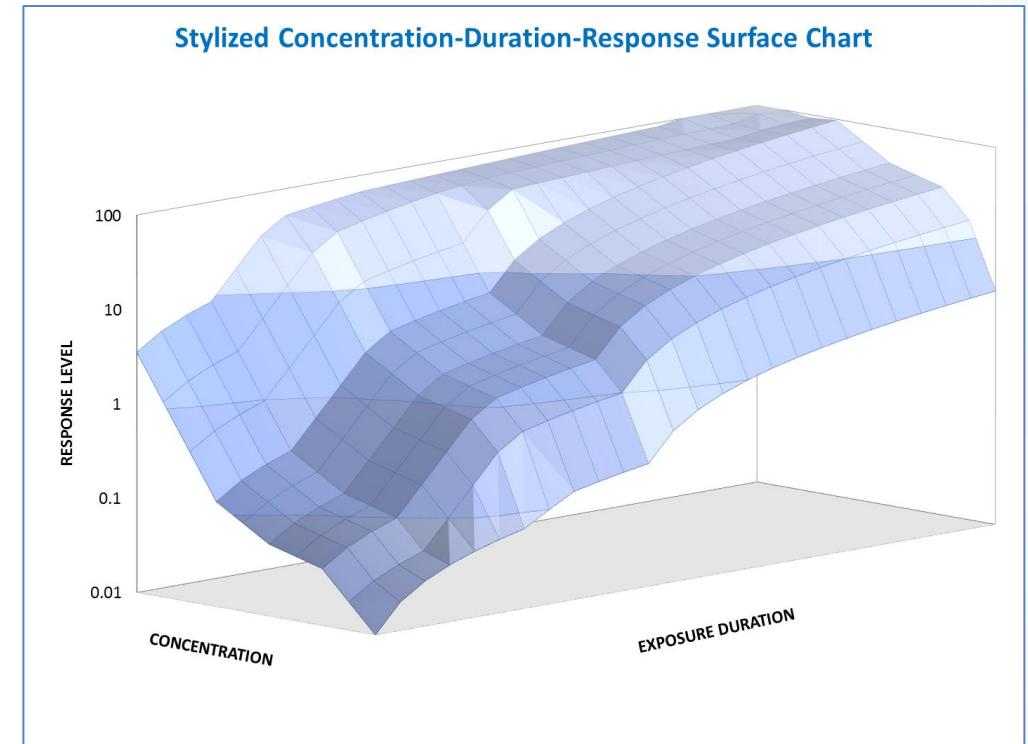
Adapted from Edwards & Preston (2008), *Tox Sci*, 106(2):312-318

Project 8: Multi-scale Dosimetry to Advance Application of AOP and MOA

- We anticipate the need to define different dose metrics in order to apply key events of adverse outcome pathways (AOP) and mode of action (MOA) in risk assessment
 - Screening dosimetry insufficient for quantitative response analysis
 - Portal-of-entry descriptions across routes required
 - Broad context re: both endpoints and chemical classes
- Supports transparency, evidence integration, causal linkage and interoperability of computational models along exposure to dose-response continuum



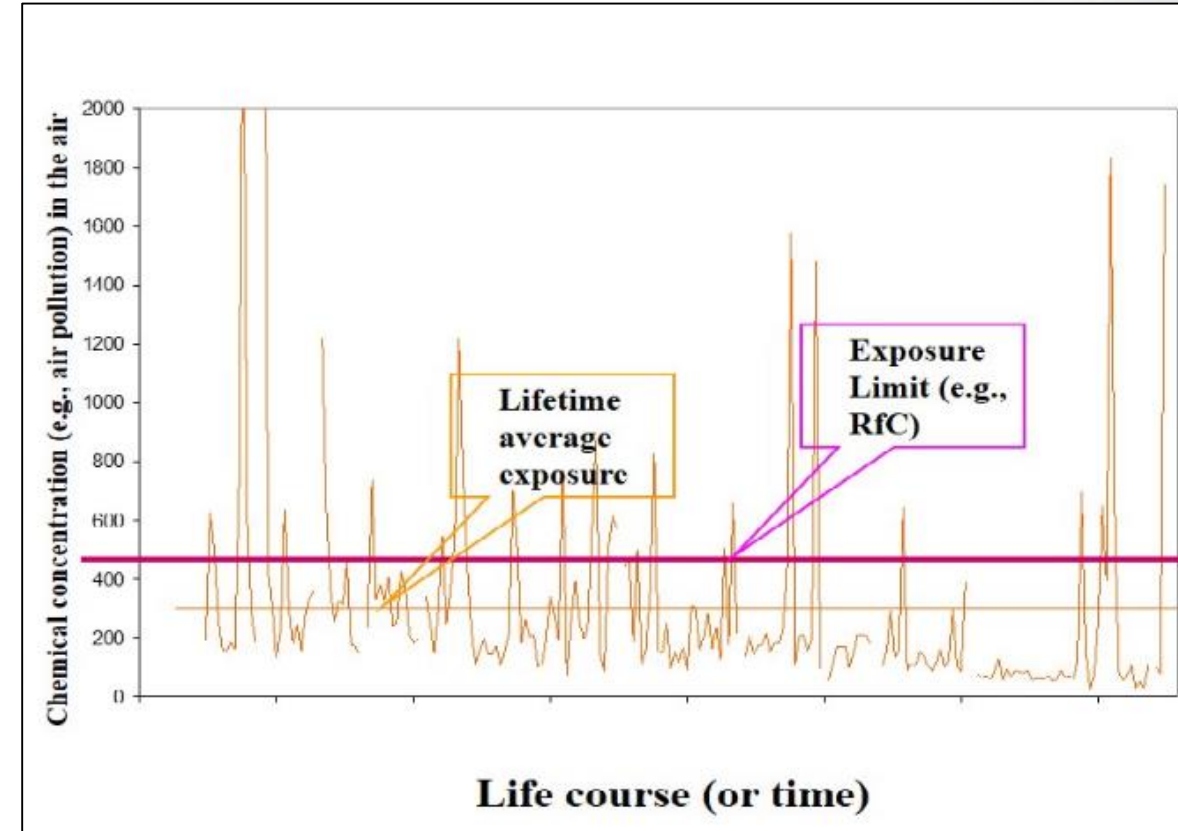
- **Characterization of responses across duration and concentration**
 - Address trajectory of different lesions
 - Create context for evaluating assessment approaches to acute and episodic exposures
- **Best bridge to systems biology and computational models**
 - Key events understood as part of pathogenesis
 - Aids application of **MOA** and **AOP**
 - Informs case studies on benefits-cost assessment





Task 7.4. Characterizing Determinants of Risk: Concentration, Duration and Timing of Exposure

- **Support to develop acute risk estimates**
- **Address different exposure scenarios**
 - **Characterize damage accumulation and/or irreversible effects**
 - **Define dose metrics**
- **Case study approach across chemical categories / endpoints of concern**
 - **Reactive gases / solvents / metals**
 - **Developmental / neurological**

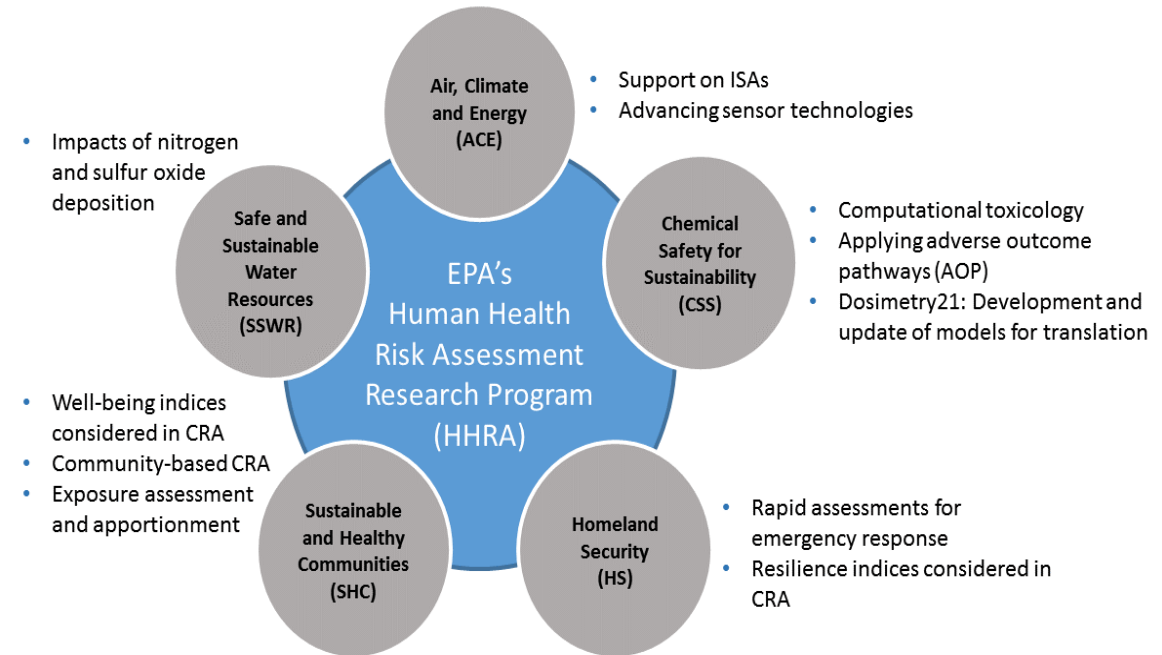




Cross-Cutting Collaborations

HHRA Cross-Cutting National Program Work:

- **Chemical Safety for Sustainability (CSS)** – Application and characterization of new data, tools and concepts in risk screening and assessments; update of dosimetry modeling
- **Air, Climate and Energy (ACE)** – Incorporation of NAAQS research (including climate as a welfare effect) into Integrated Science Assessment; IRIS assessments of air toxics; interpretation of sensor data
- **Safe and Sustainable Water Resources (SSWR)** – Assessment of deposited oxides of nitrogen and sulfur on surface water quality
- **Sustainable and Healthy Communities (SHC)** – Development of Cumulative Risk Assessment (CRA) methods and decision analytic software to support “place-based” community assessment and to link health and ecology to wellbeing
- **Homeland Security Research Program (HSRP)** – Rapid response assessment and incorporation of resiliency into cumulative risk assessment methods





Cross-Cutting Collaborations

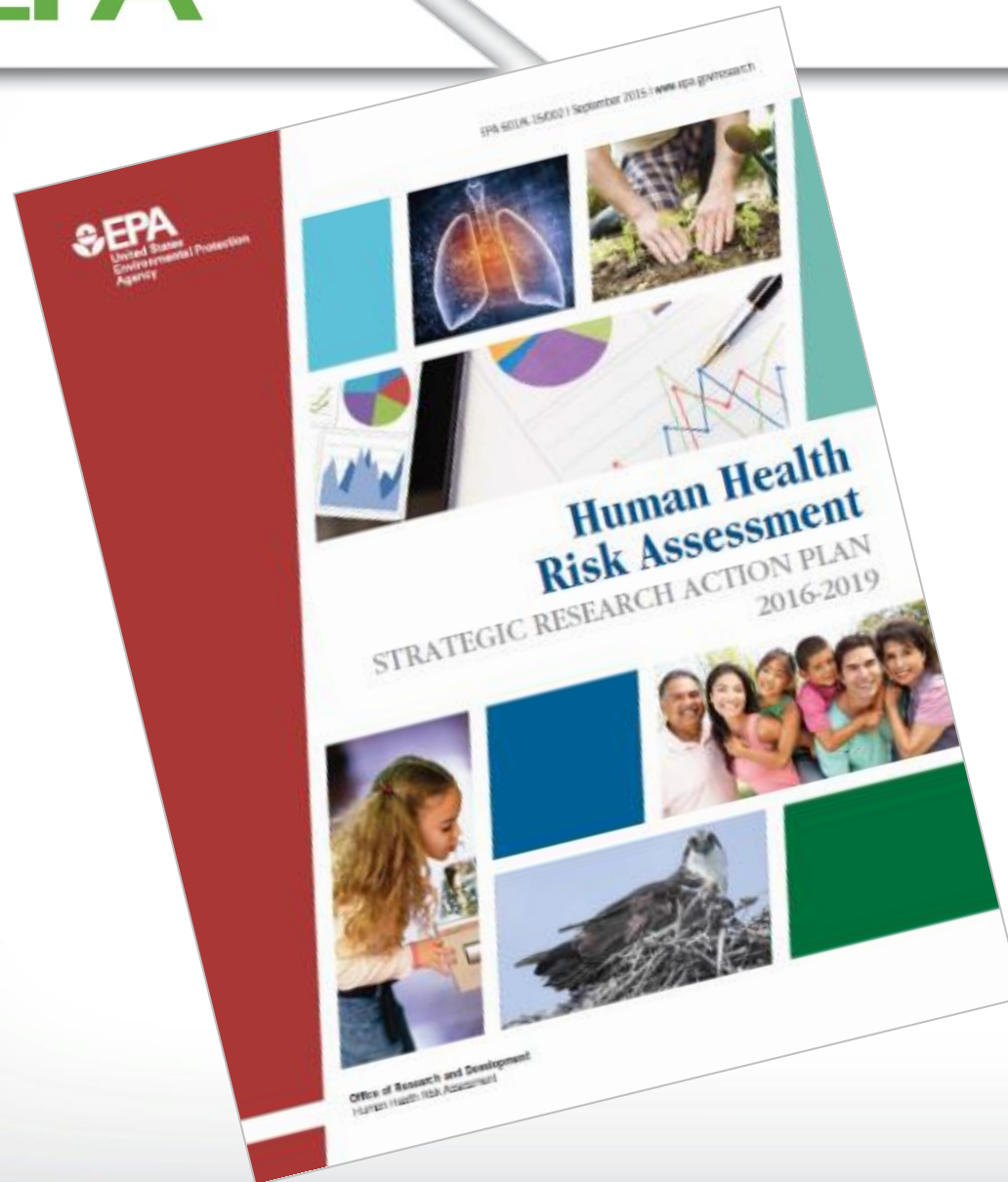
ORD Roadmap	HHRA Topic Area			
	IRIS Assessments	ISA Assessments	Community and Site-specific Risk	Advancing Analyses and Applications
Climate Change		✓ ✓	✓	
Environmental Justice	✓	✓	✓	✓
Children's Health	✓	✓ ✓	✓	✓
Nitrogen & Co-Pollutants	✓	✓ ✓		

HHRA Cross-Cutting Roadmap Work:

The HHRA research program is a full partner with collaborations with all of ORD's cross-cutting research roadmaps:

- Children's Environmental Health;
- Nitrogen and Co-Pollutants;
- Climate Change; and
- Environmental Justice (EJ).

Summary



- **Developing a portfolio of assessment products for improved public health**
- **Identifying issues and advancing approaches to arrive at solutions**
- **Applying new technologies and data to refine analyses**
- **Supporting communities with cumulative risk characterization of multiple stressors on human and ecological health**
- **Educating and engaging stakeholders to build capacity**

Extra Slides

- **Project Charters** – A short description of the project (project formulation, EPA context, focus areas)
- **Project Plans** – Detailed implementation plan prepared by labs/centers (incl. QA/QC, resource allocation)
- **PLs – Project Leads** – Key leadership positions in the labs & centers; they prepare project plans
- **Tasks** – A unit of research within a project; SHC averages 5 tasks per project
- **TLs** – Task Leads – key position in the labs/centers under direction of PL
- **Product** – A tangible item from research (report, model, tool, database, website, journal article)
- **Output** – A synthesis of a body of work representing multiple products
- **Outcome** – The good that comes from the research



Matrix Nomenclature

- **Strategic Research Action Plans (StRAP)** – 4 years of planned research for 6 national research programs
- **NPD** – National Program Director (6), plans the “what” as described in the StRAP (planning)
- **Labs and Centers** – determine the “how” (implementation); conduct the research
- **MI** – Matrix Interface, a scientist serving as the pivot point in the matrix (planning & implementation) reporting to a Lab/Center and the NPD
- **Topics** – Broad areas of research within a national program; 4 in SHC
- **Projects** – Key operational unit in a national program; 11 in SHC
- **Focus Areas** – Subordinate unit within a project

- TASK
- PRODUCT
- OUTPUT
- OUTCOME



Labs/Centers develop the tasks & products

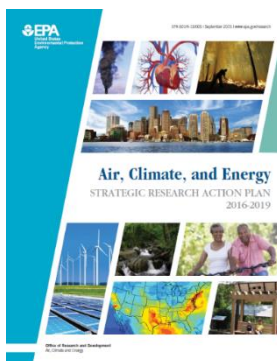


NPD Designs the Output

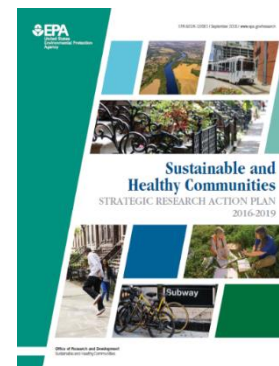


- **What is a Strategic Research Action Plan (StRAP)?**
 - Describes our research program for internal and external audiences
 - Serves as our guide for resource planning activities
 - First generation covered 2012-2016
 - Currently completing 2nd generation to over FY16-19 (final release October 1, 2015)
 - Developed in consultation with advisors (Science Advisory Board and Board of Scientific Counselors), EPA partner offices, other stakeholders

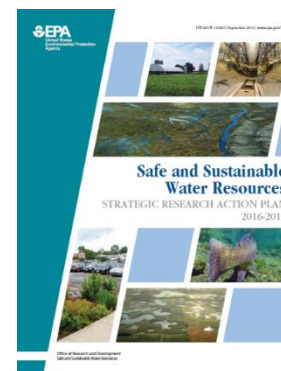
Air, Climate & Energy



Sustainable & Healthy Communities



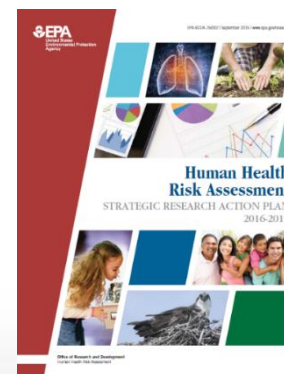
Safe & Sustainable Water Resources



Chemical Safety for Sustainability



Human Health Risk Assessment

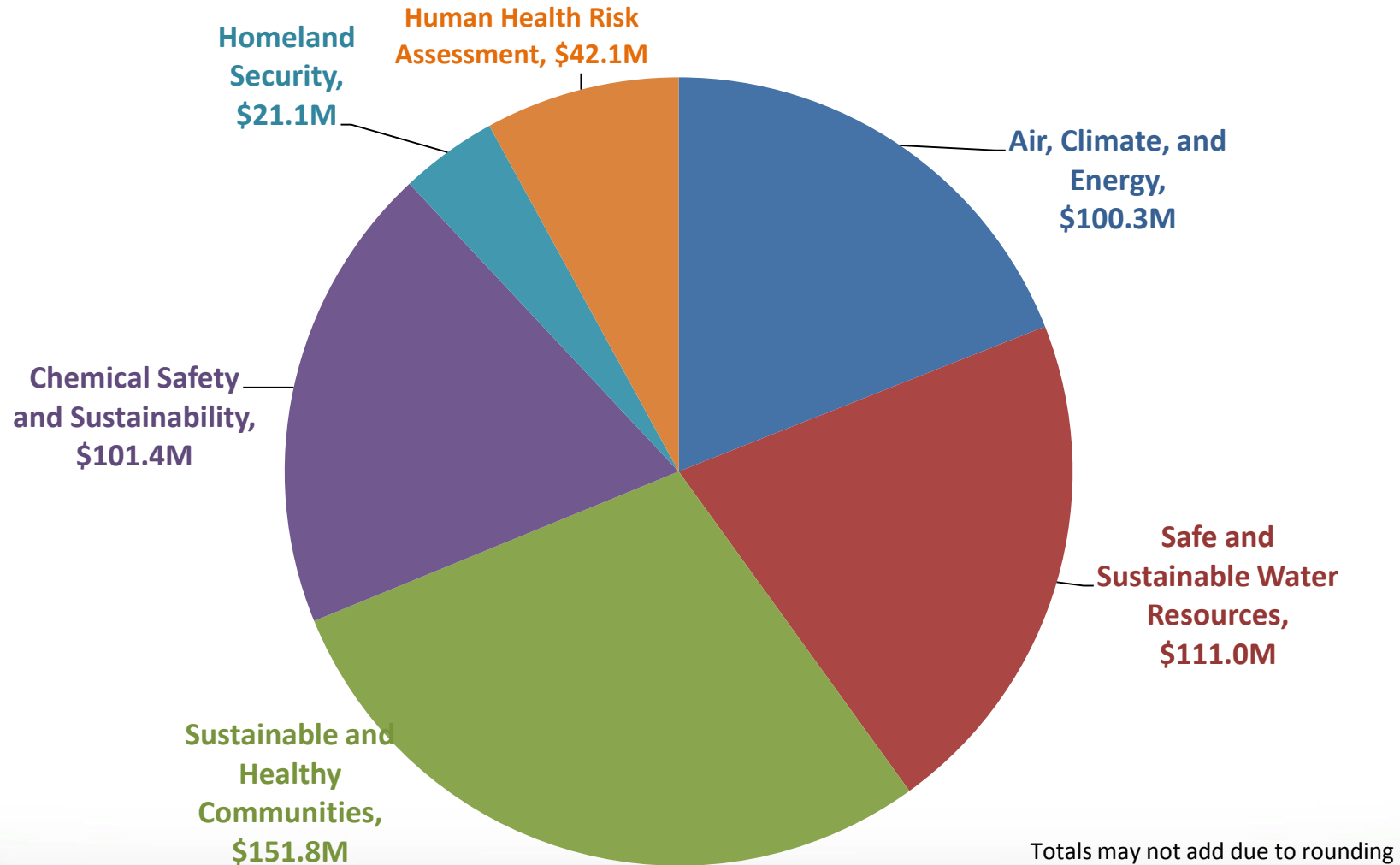


Homeland Security



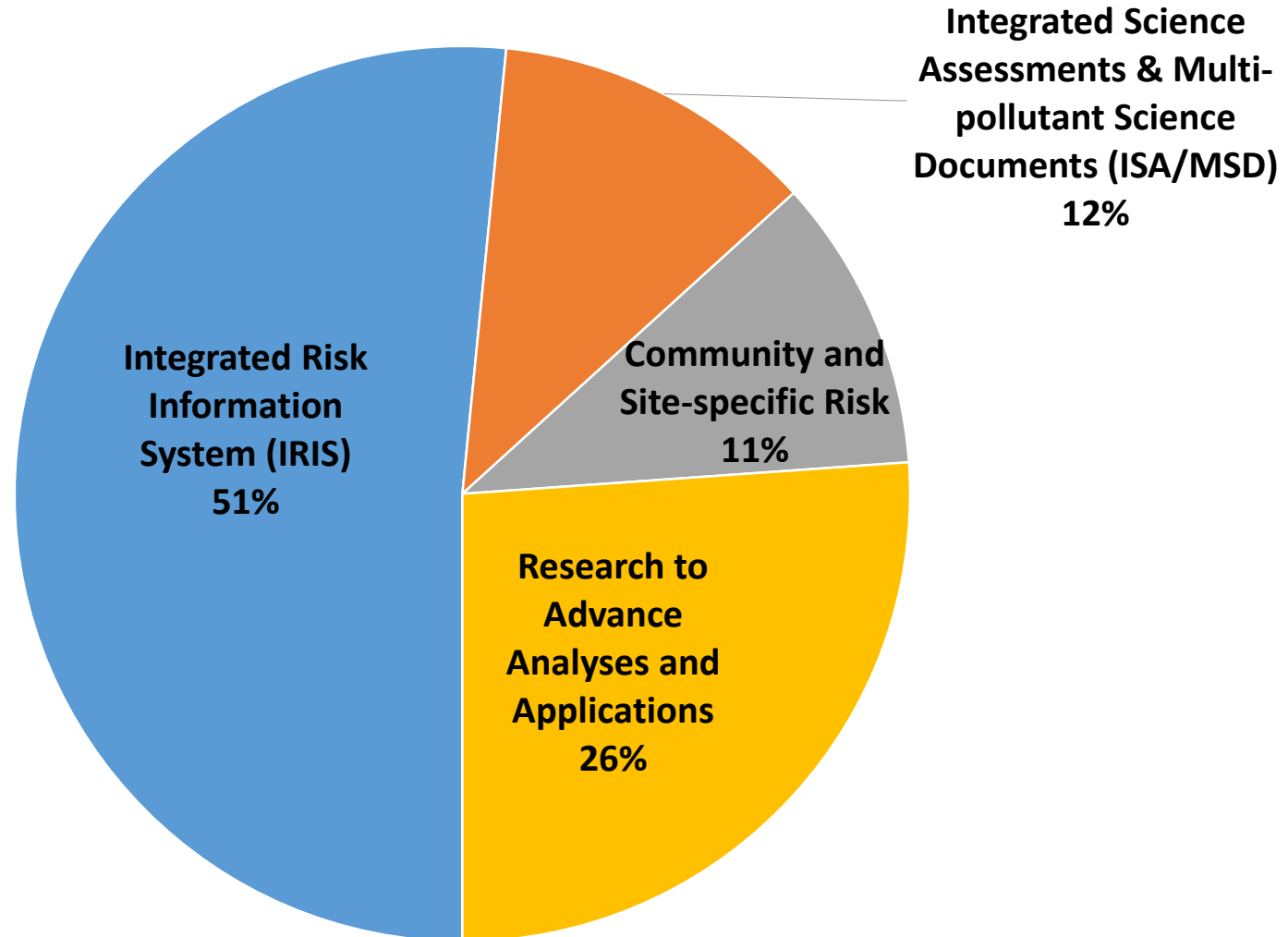


ORD's FY 2016 Budget by Research Program Projects



HHRA Budget by Topics

**HHRA Topics
FY16PB \$**





HHRA Budget by Projects

HHRA Projects
FY16PB \$

