Chemical Safety for Sustainability Research Program

U.S. EPA Office of Research and Development
Presentation to the CSS BoSC Subcommittee
October 6, 2015

Tina Bahadori, Sc.D.
National Program Director

Overview

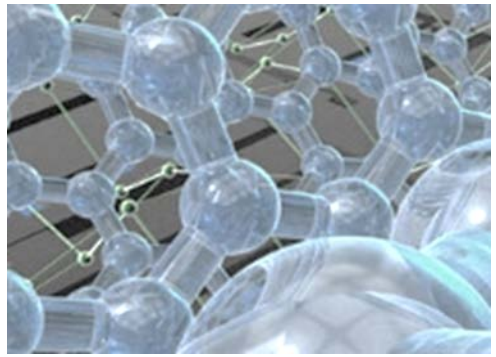
- **Overview of Office of Research and Development**
- **Chemical Safety for Sustainability (CSS) Research Program**
  - Who are we, and what do we do?
- **CSS Fiscal Year 2016-2019 Strategic Research Action Plan**

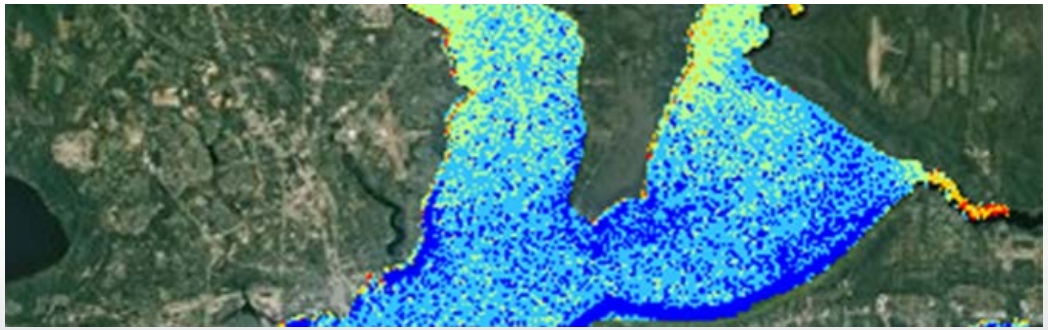
21st Century Environmental Challenges

- Climate change
- Changing energy landscape
- Multi-pollutant exposure
- Increasing nitrogen and phosphorus impair water quality
- Susceptibility & environmental justice
- Thousands of new industrial chemicals and pesticides each year
- Chemical, biological, radiological-based terrorism

Scientific Challenges

- Generate information to advance understanding of complex relationships between human activities and impacts to health and the environment
- Revolutionize assessment of potential for risks to humans and the environment
- Predict adverse outcomes of societal choices over time and space
- Promote innovative and sustainable solutions to 21st environmental challenges

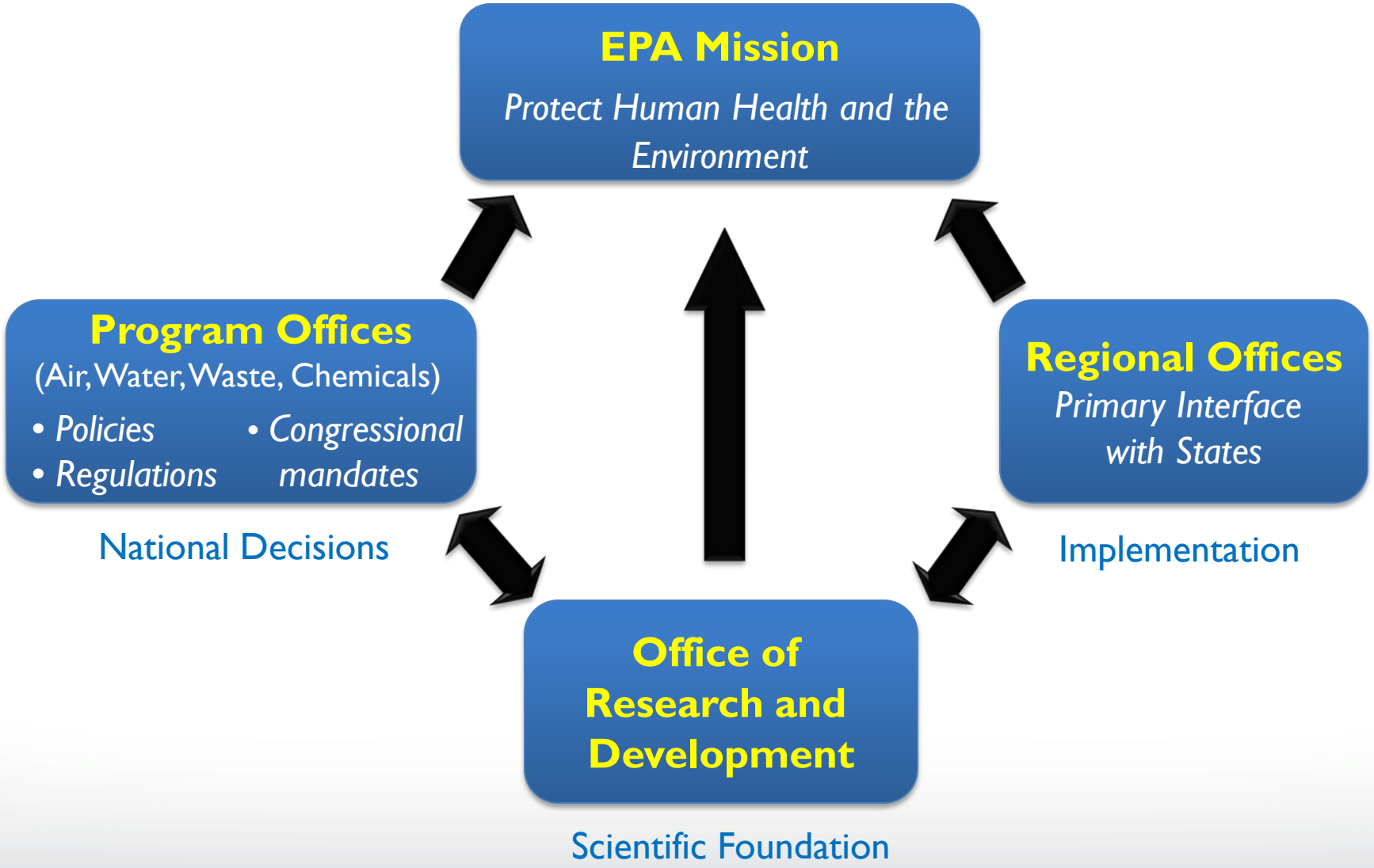




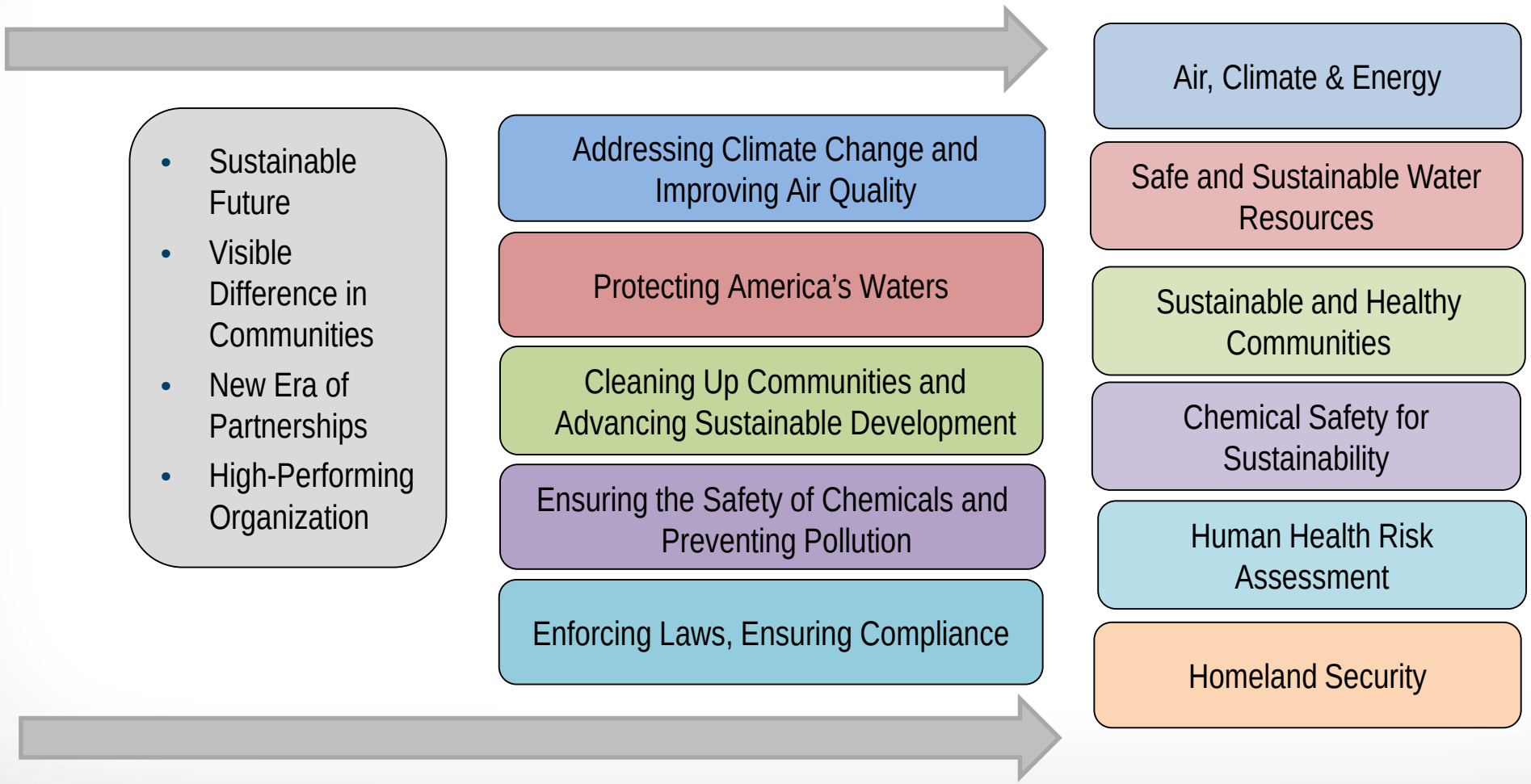
Research that prepares us for these challenges

- **Innovative** – foster creativity and stimulate transformational change
- **Integrative** – work collaboratively across disciplines
  - Across ORD labs and centers
  - Engage EPA and outside stakeholders
- **Solution–oriented** – emphasis on developing sustainable solutions
- **Responsive** – provide relevant and timely results to inform environmental policy decisions
- **Translational** – end users receive the necessary information to utilize ORD products

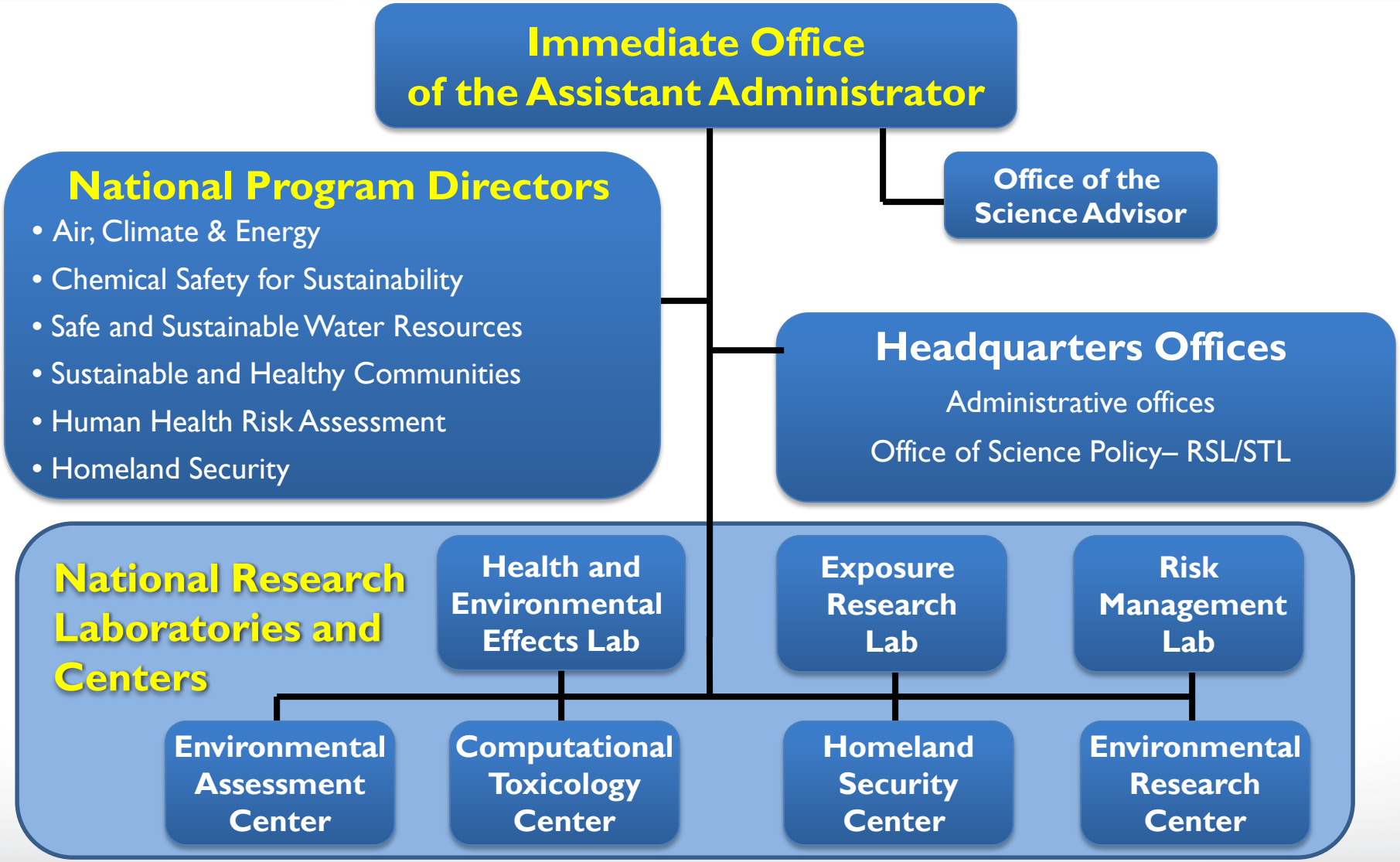
Science to Support EPA's Mission



Aligning Research with EPA Strategic Goals



ORD Organizational Chart

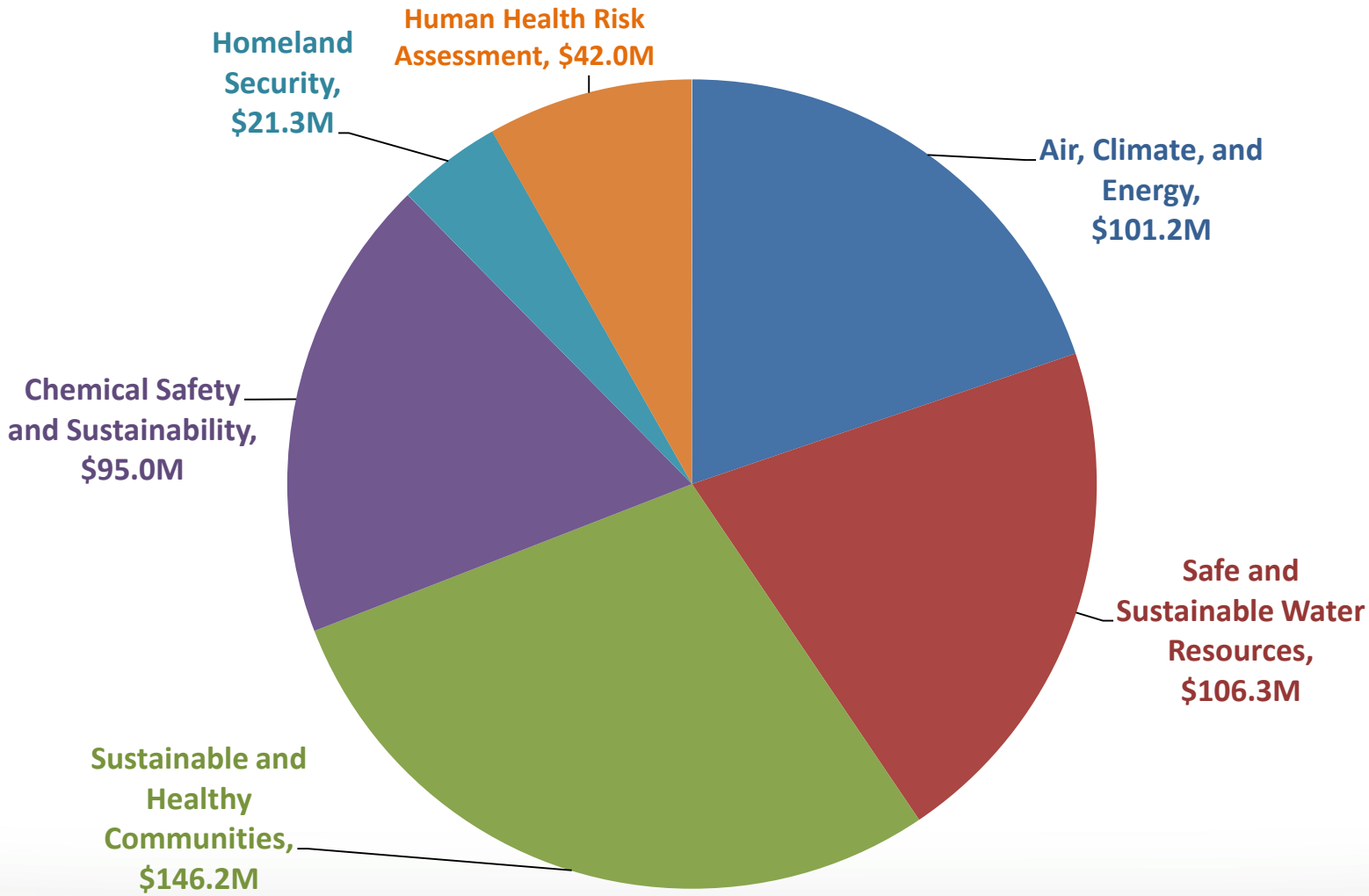


Connections: ORD National Research Programs and Cross Cutting Roadmaps

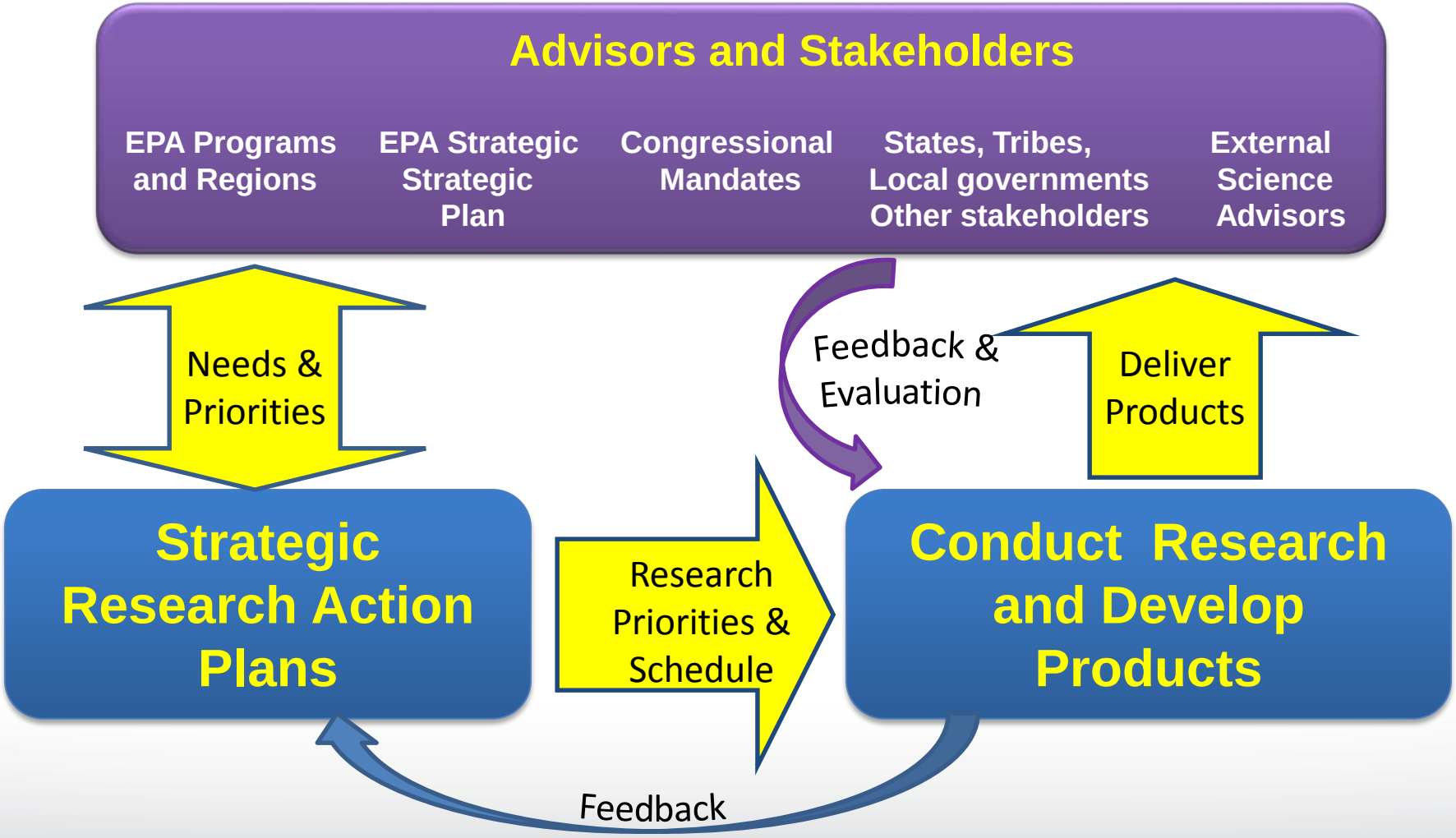
- **Six Strategic Research Action Plans (StRAP):**
  - Describes our research program for internal and external audiences
  - Serves as our guide for resource planning activities
  - First generation covered 2012-2016
  - Current (2nd) generation 2016-2019
  - Developed in consultation with advisors (Science Advisory Board and Board of Scientific Counselors), EPA partner offices, other stakeholders

NOTE: Final StRAPs and 2 Roadmaps (Nitrogen & Co-pollutants, Children's Environmental Health) are completed and available at http://www2.epa.gov/research/strategic-research-action-plans-2016-2019. Revised draft roadmaps for Climate Change and EJ being reviewed by the BoSC EC.

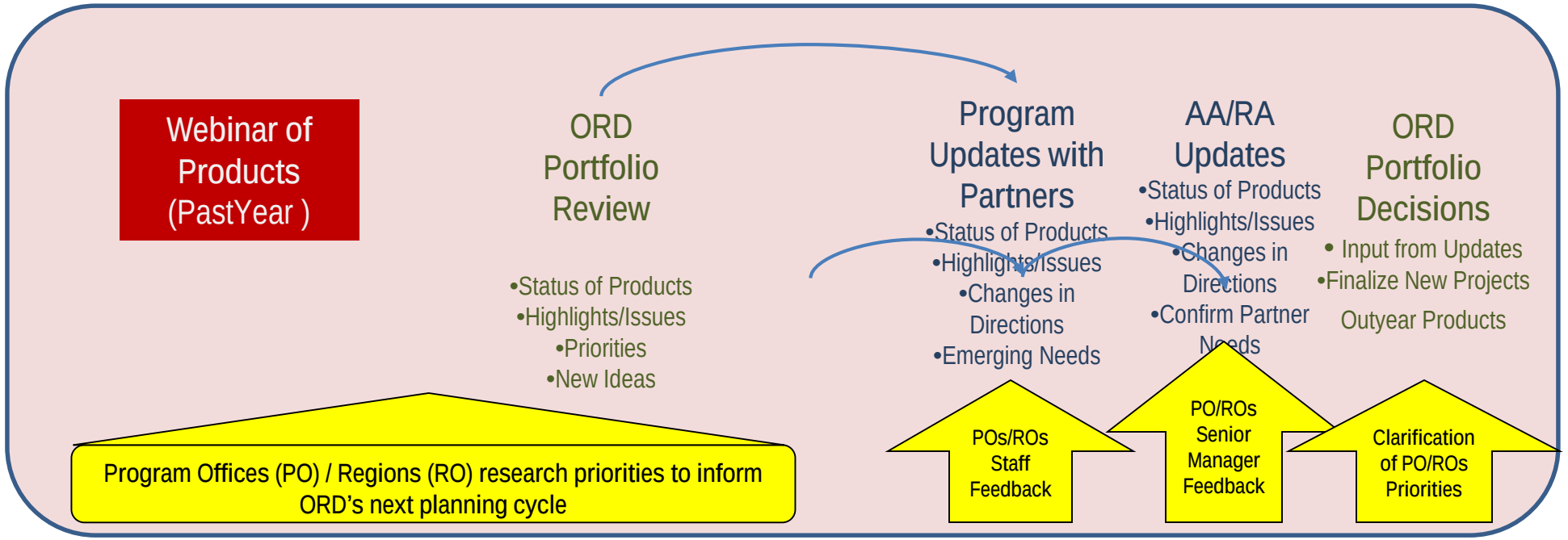
ORD's FY 2017 Budget by Research Program Projects



Research Planning to Research Results

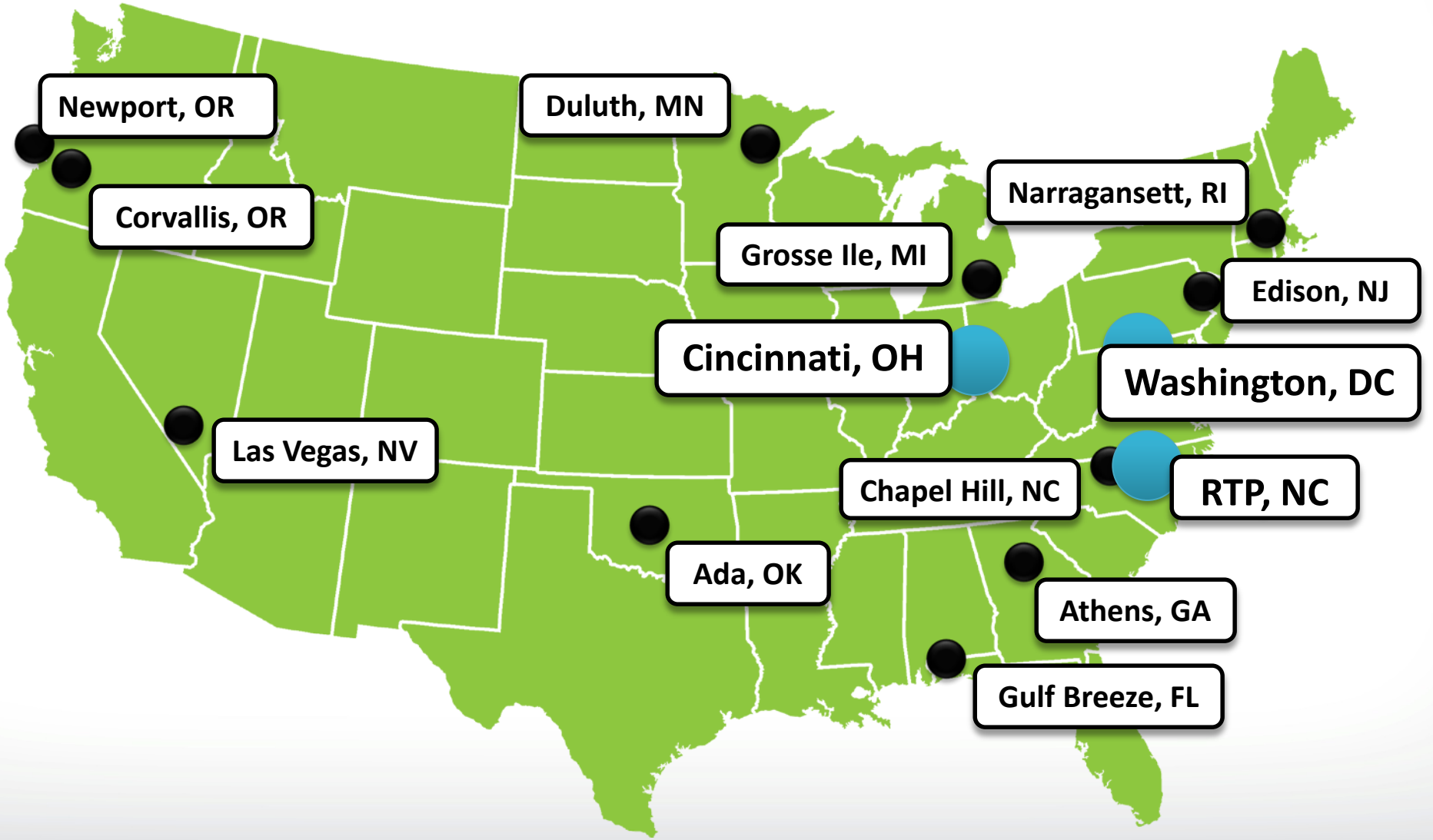


Extensive Interaction with EPA Partners



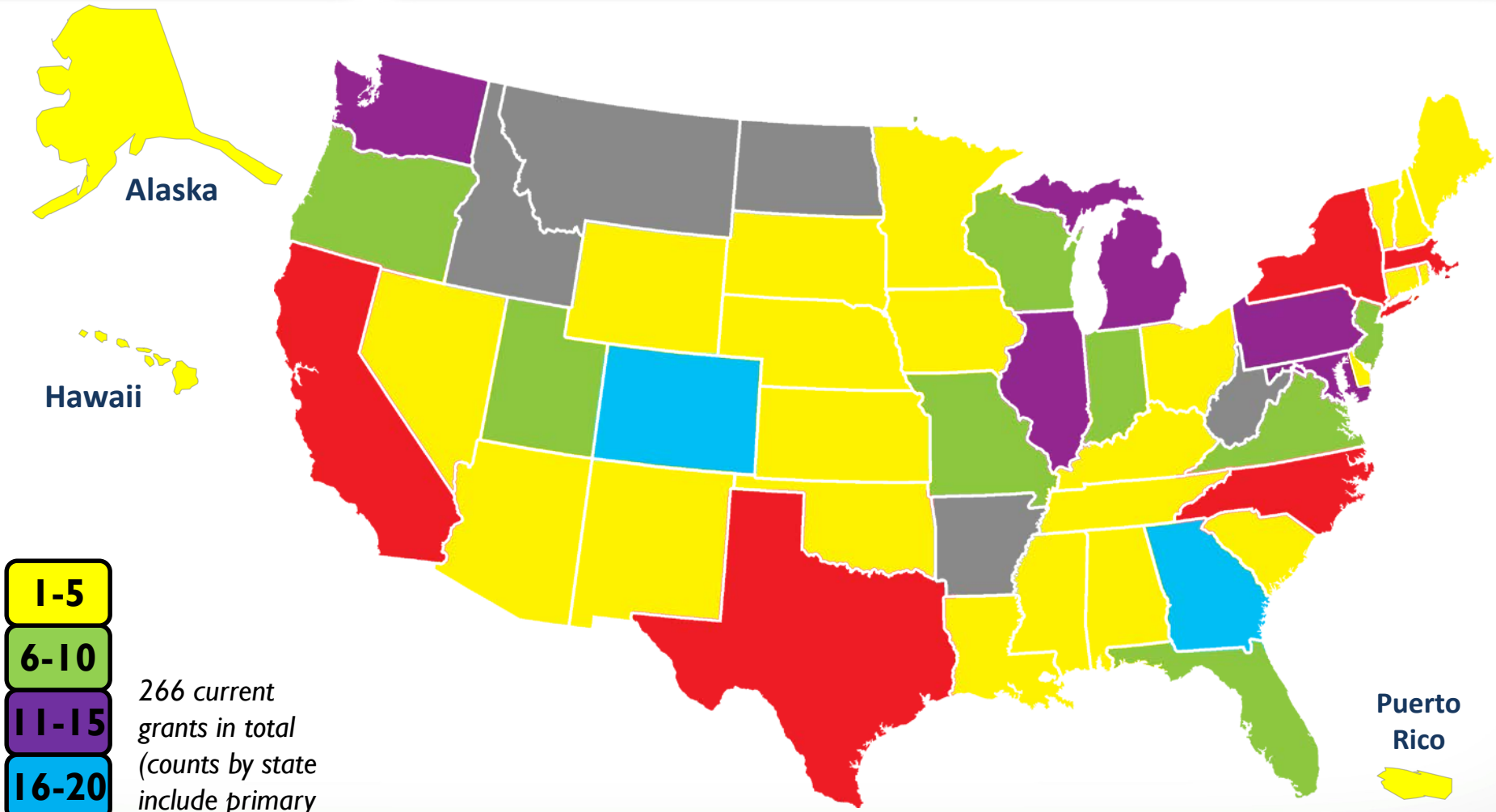
← Regular Meetings/Updates, Targeted Discussions →
The developing role of Project Advocates

ORD Research Facilities



EPA Research Grants to Universities

STAR Research Grants by State



266 current grants in total (counts by state include primary and secondary Institutions)

$52 million extramural research grants + $9 million fellowships
(FY 2014 Enacted Budget)

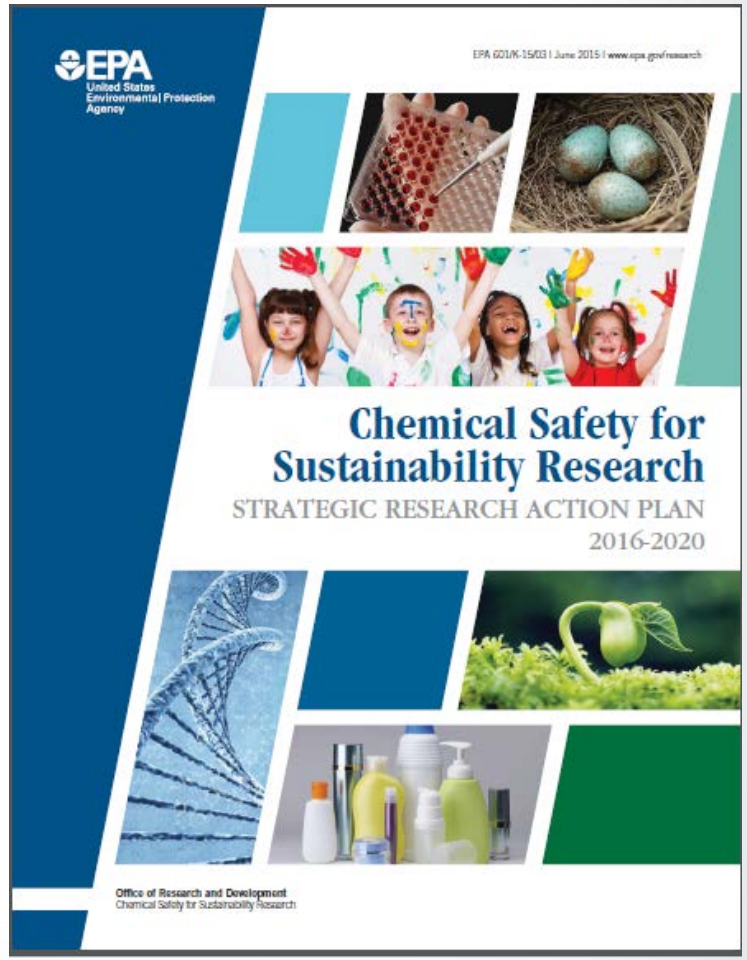
Problem Statement

Chemicals are a lynchpin of innovation in the American economy. Moving toward sustainable innovation requires designing, producing, and using chemicals in safer ways.

- Information and methods are needed to make better-informed, more-timely decisions about chemicals, many of which have not been thoroughly evaluated for potential risks to human health and the environment.
- Scientific understanding is required to anticipate potential for adverse impacts on human health or wildlife populations based on knowledge from data rich chemicals.
- The EPA's Chemical Safety for Sustainability Research Program (CSS) is designed to meet this challenge.

CSS 2016-2019 Strategic Research Action Plan (StRAP)

- **Build Knowledge Infrastructure**
  - Make information publicly accessible.
  - Combine different types of data in new ways to characterize impacts of chemicals across their life cycle to human health and the environment
- **Develop Tools for Chemical Evaluation**
  - Develop and apply rapid, efficient, and effective chemical safety evaluation methods
- **Promote Complex Systems Understanding**
  - Investigate emergent properties in complex chemical-biological systems by probing how disturbances and changes in one part affect the others and the system as a whole
- **Translate and Actively Deliver**
  - Demonstrate application of CSS science and tools to anticipate, minimize, and solve environmental health problems



https://www.epa.gov/research/chemical-safety-sustainability-strategic-research-action-plan-2016-2019

The CSS Vision

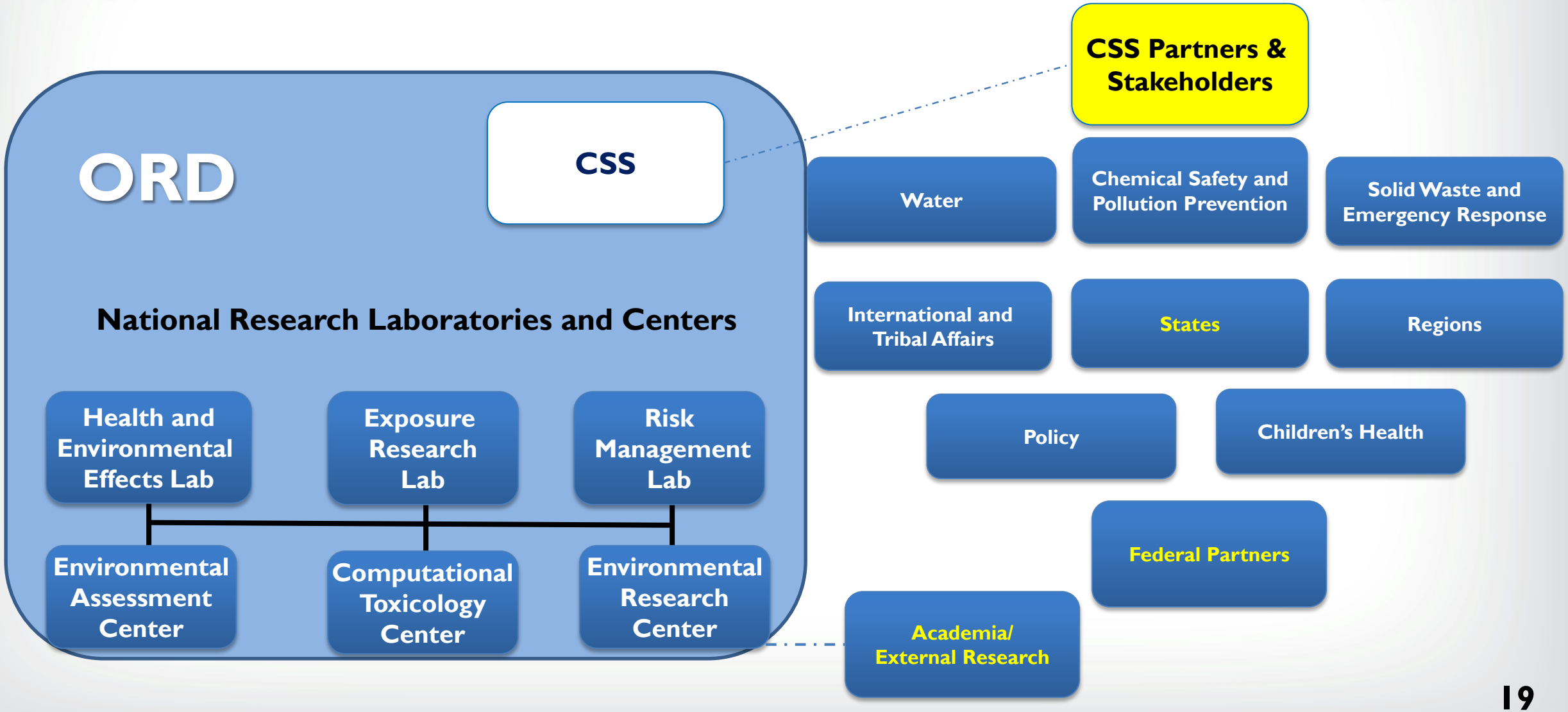
Vision

CSS will lead development of innovative science to support safe, sustainable use of chemicals and materials required to promote ecological wellbeing, including human and environmental health, as well as to protect vulnerable species and populations.

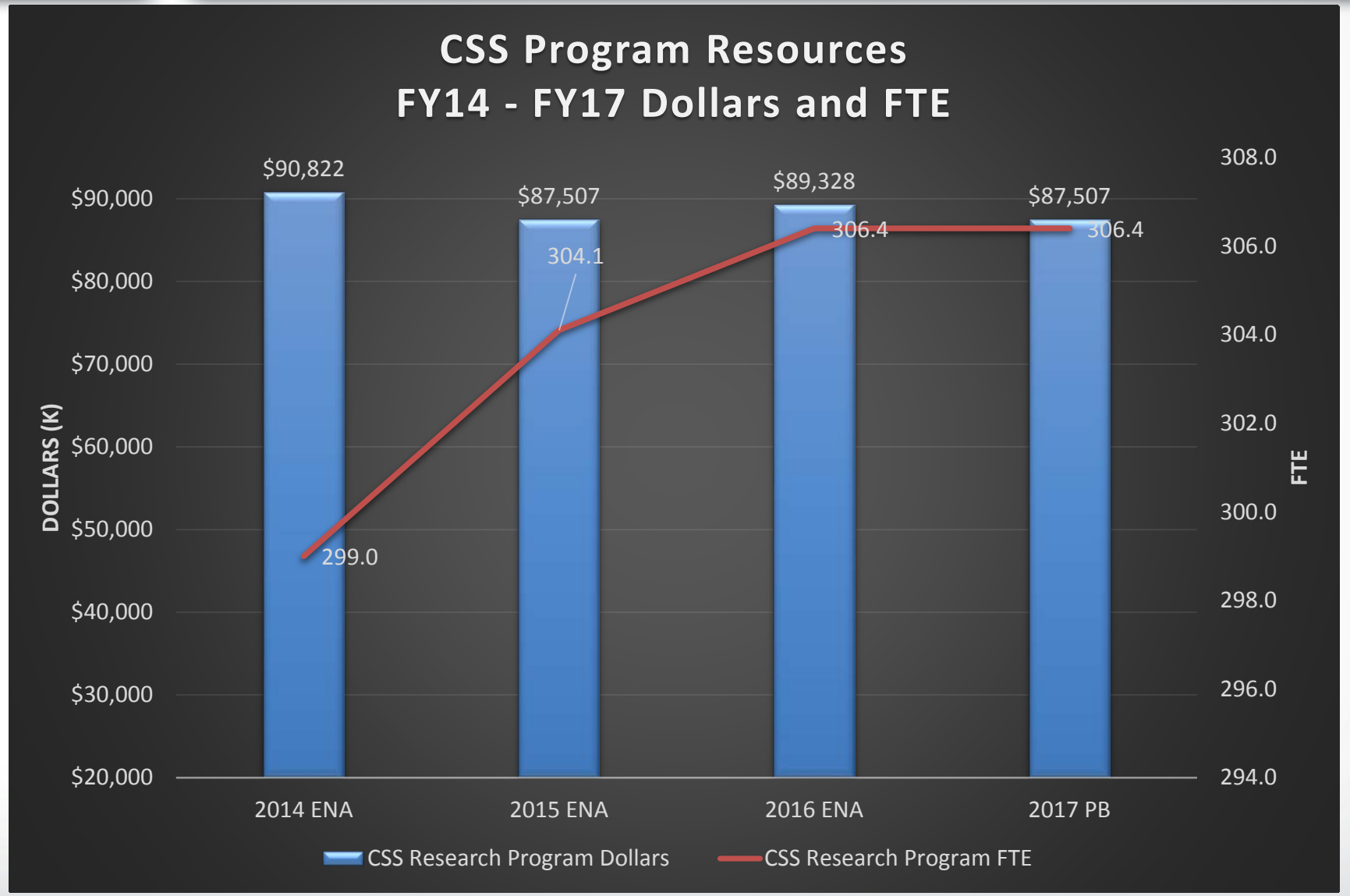
Overarching Research Priorities

- Address impact of existing chemicals, materials/products across the lifecycle.
- Anticipate impacts of new chemicals, materials/products across the lifecycle.
- Enable consideration and evaluation of complex interactions of chemical and biological systems to support Agency decisions.

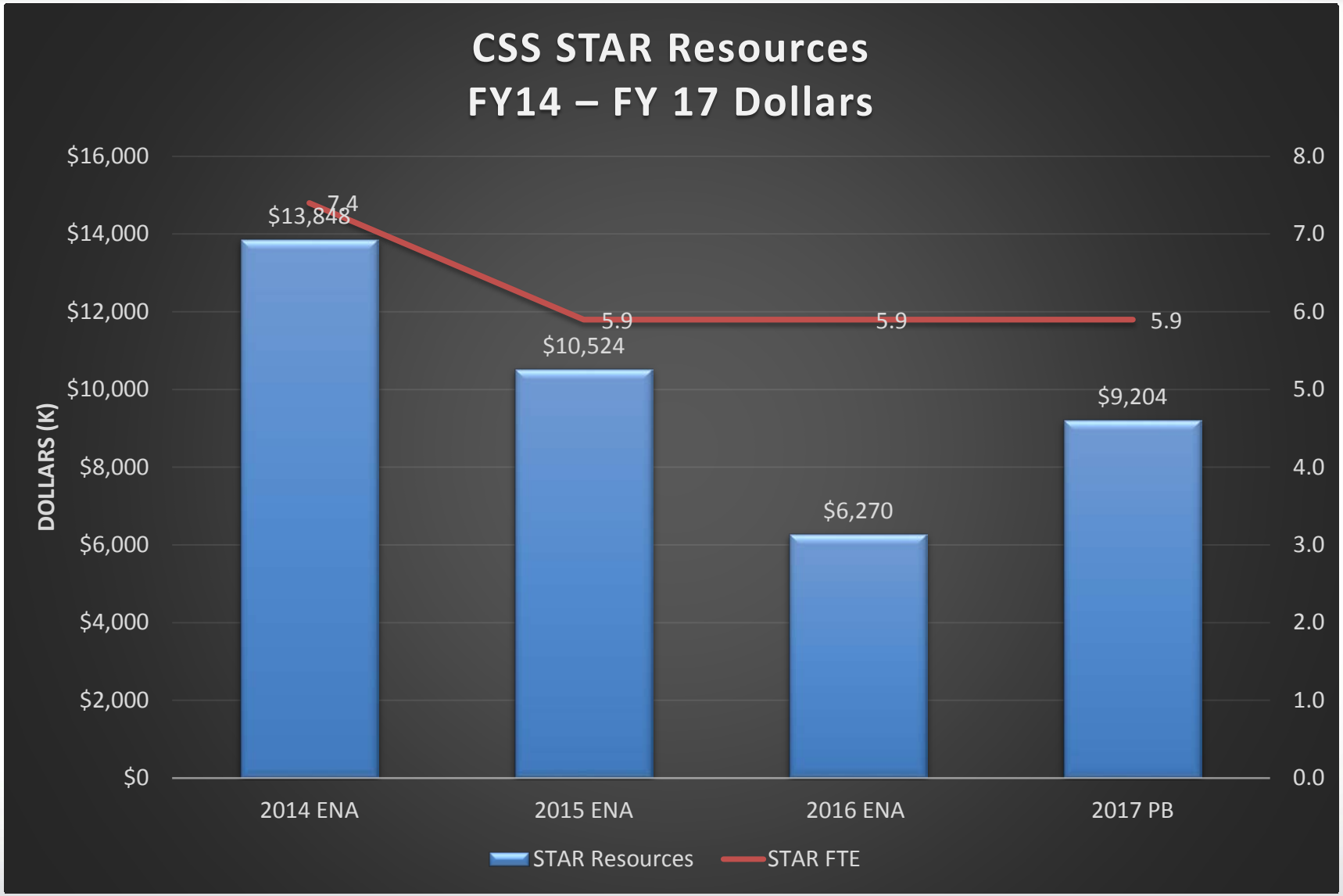
How We Do It


ORD
CSS
National Research Laboratories and Centers
Health and Environmental Effects Lab
Exposure Research Lab
Risk Management Lab
Environmental Assessment Center
Computational Toxicology Center
Environmental Research Center
CSS Partners & Stakeholders
Water
Chemical Safety and Pollution Prevention
Solid Waste and Emergency Response
International and Tribal Affairs
States
Regions
Policy
Children's Health
Federal Partners
Academia/ External Research

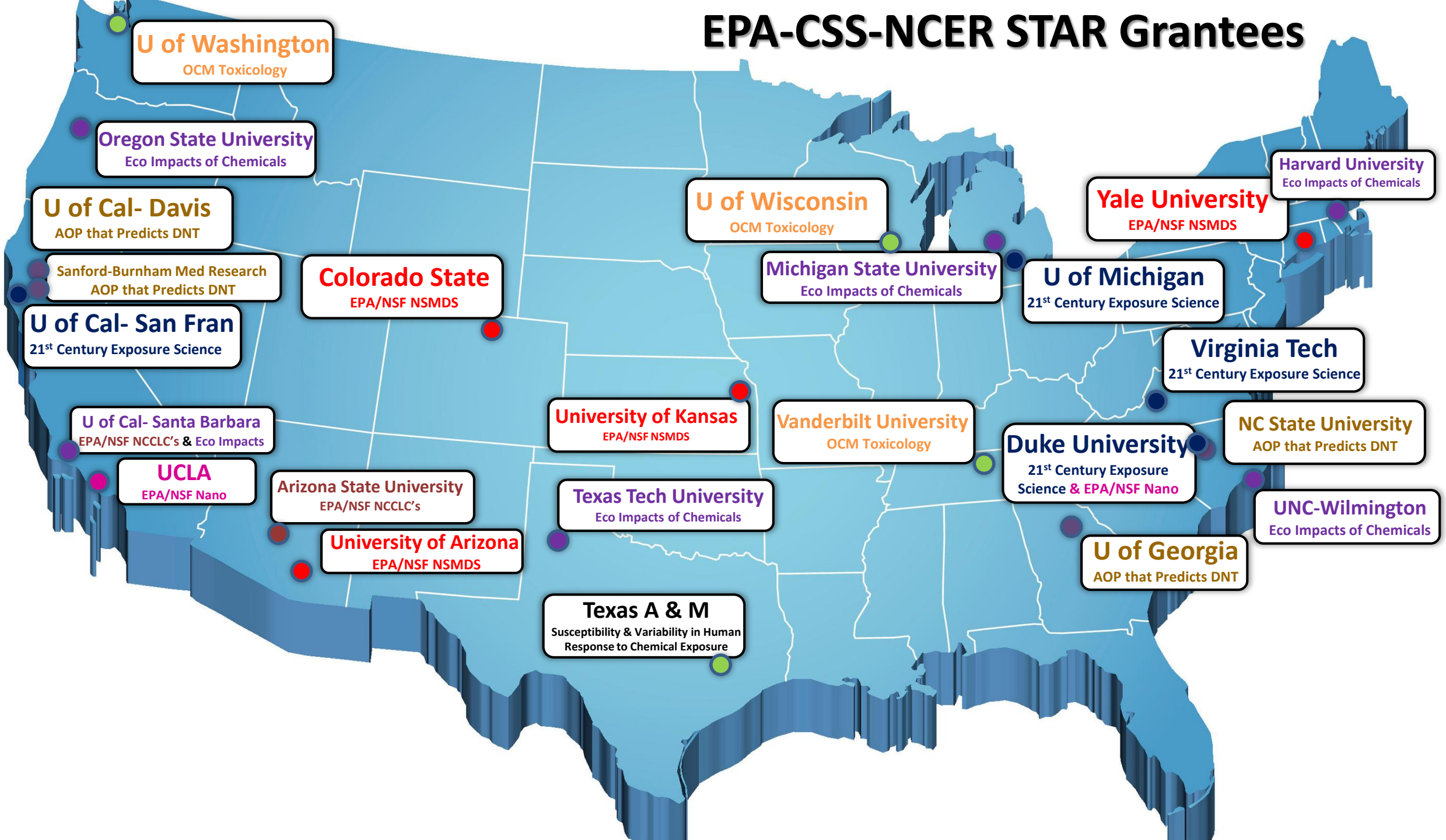
Resource Trends



STAR Grant Resources

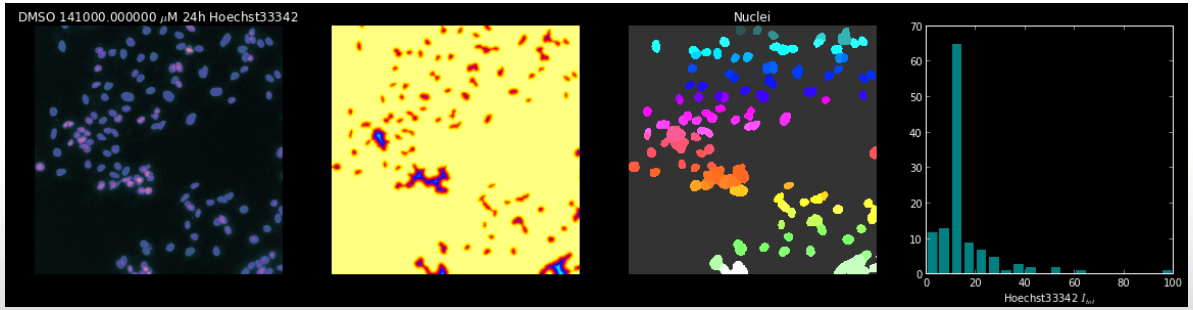


EPA-CSS-NCER STAR Grantees

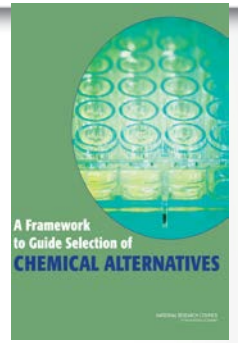


Shift in Perspective

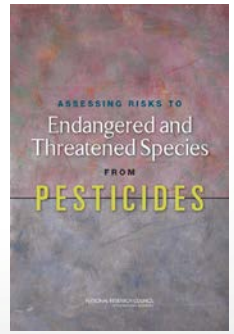
- **Increase Predictive Capacity -- adopt the AOP framework**
  - Organize what we know and utilize that knowledge to support risk-based decision-making
  - Evaluate effects of cumulative exposures and cumulative risk
- **Exploit complex systems modeling to advance mechanistic understanding**
  - Integrate understanding of exposures-dose-effects across levels of biological organization
  - Predict early 'tipping-points'
- **Impose a life cycle perspective**
  - Evaluate safety of chemicals and materials in the context of how these are designed and used in society
  - Includes engineered nanomaterials, sustainable chemistry, alternatives
- **Increase focus on developmental health, vulnerable and susceptible populations**
- **Explore higher-throughput approaches with wider coverage of chemistry and biology**



Scientific Guidance



- **Relevant NAS Studies:**
  - **Integrating 21st Century Science into Risk-Based Decisions**
    - Multi-agency funded NAS Study as a follow up to NRC's Toxicity Testing in the 21st Century
    - Incorporates Exposure Science in the 21st Century.
    - Seeking advice on whether the types of data CSS generates are ready to be applied; if so, under what circumstances; and what other steps are needed to increase confidence in the data and models that are being generated (committee being assembled)
  - **Unraveling Low Dose Toxicity: Case Studies of Systematic Review of Evidence**
  - **Microbiome of Built Environments;**
  - **Advancing Understanding of the Implication of Environmental-Chemical Interactions with the Human Microbiomes**
  - **Design and Evaluation of Safer Chemical Substitutions**
    - Consideration of novel data streams in a framework to guide selection of alternatives
  - **Assessing Risks to Threatened and Endangered Species**



- **SAB and BoSC: BoSC Subcommittee Meeting: November 16-18, 2016**

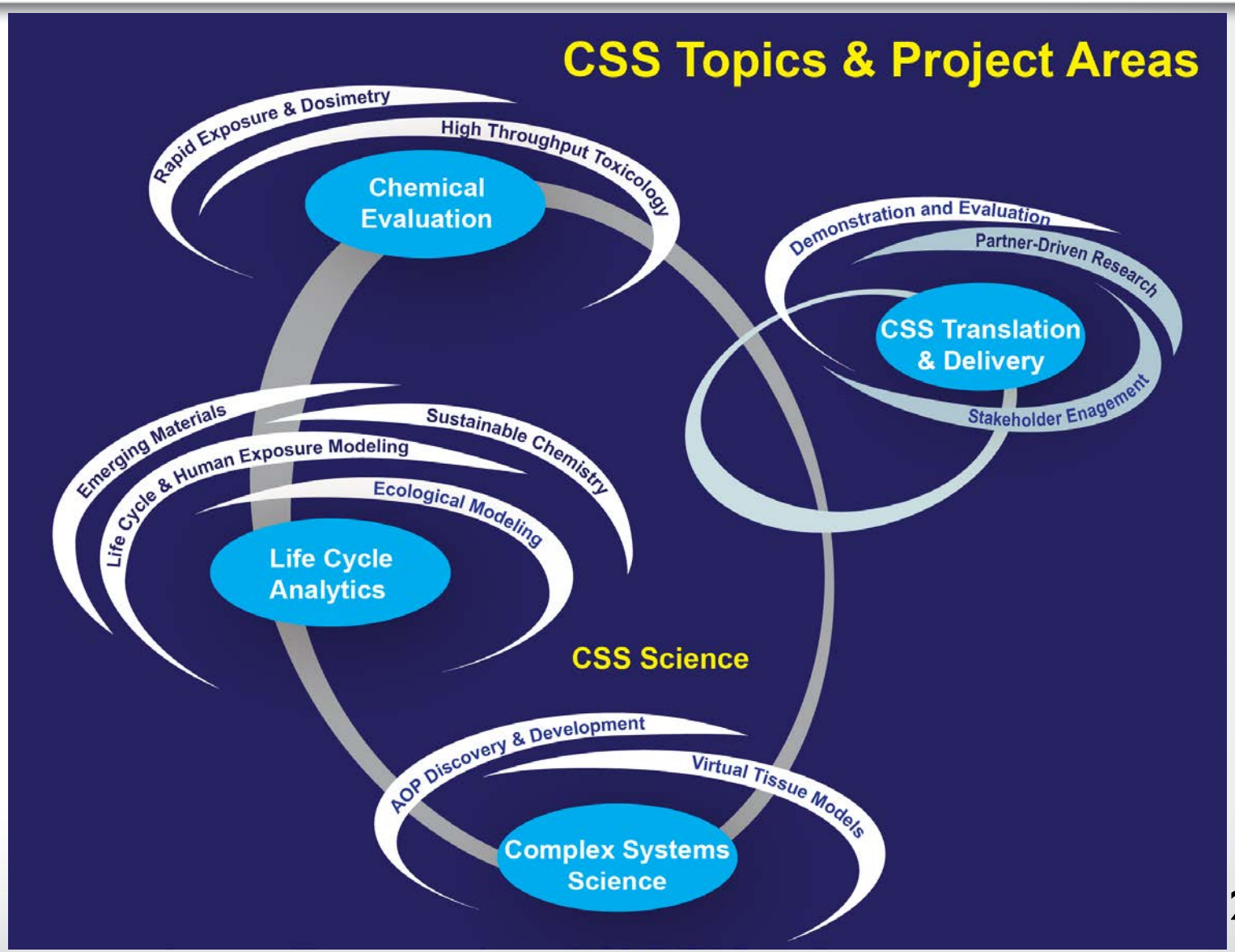
CSS Program Design

Three Research Topics

- Chemical evaluation
- Life cycle analytics
- Complex systems

One Translation Topic

- Solutions-Based Translation and Knowledge Delivery



CSS Research Topics

- **Chemical Evaluation:**
  - Advance cutting-edge methods for chemical prioritization, screening & testing
  - Provide the data for risk-based evaluation of existing chemicals and emerging materials.

  Project areas: High-throughput Toxicology, Rapid Exposure and Dosimetry
- **Lifecycle Analytics**
  - Address critical gaps in accessible tools and metrics for quantifying risks to human and ecological health across the life cycle of chemicals, materials, products.
  - Advance methods to efficiently evaluate alternatives and support sustainable chemical design and use.

  Project areas: Lifecycle and Human Exposure Modeling, Sustainable Chemistry, Emerging Materials, Ecological Modeling
- **Complex Systems Science**
  - Adopt a systems-based approach to examine the complex interactions among exposures and biological effects
  - Predict adverse outcomes resulting from exposures to chemicals

  Project areas: Adverse Outcome Pathways Discovery and Development, Virtual Tissues

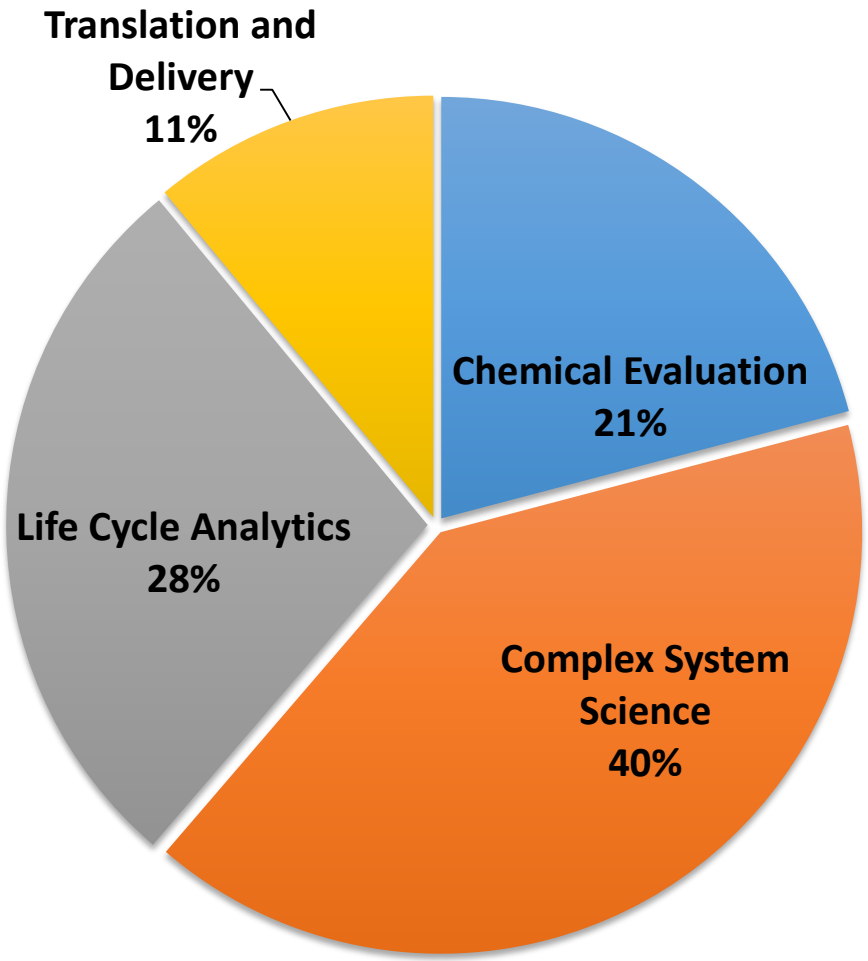
CSS Translation Topic

- **Solutions-based Translation and Knowledge Delivery:**
  - Actively translate the results of CSS research, from data to information to knowledge to application
  - Integral to developing solutions to meet the needs of the Agency and its partner and stakeholder communities,

  Project area: Demonstration and Evaluation for Risk-Based Decisions

  - **Other Related Activities:**
    - Partner-Driven
      - Respond to short-term high priority science needs for CSS partners
    - Stakeholder Engagement
      - Allow for active and strategic engagement of the stakeholder community

CSS Budget by Topics



CSS Topics:
FY17PB RAP$ and FTE

The Case Study Approach

- **The CSS StRAP is designed to drive the longer term science vision for the program.**
- **Within each CSS project, specific case studies are being developed in collaboration with program and regional partners to reflect EPA's near-term priorities.**
- **This case study approach ensures that the purpose and the application of CSS science is clearly defined upfront in collaboration with the partners and that the product developed is fit for the intended purpose.**
- **The poster sessions will present these case studies.**

FY16-19 Case Studies I

Chemical Evaluation

- **HTT 1:** ***Annotation of ToxCast Assays Supporting the EDSP***
- **HTT 2:** ***Screening for Disruptor of Thyroid Hormone Synthesis***
- **RED 1:** ***Approximating Cumulative Risk of Endocrine Disrupters***
- **RED 2:** ***Quantitative Domains of Applicability of Prediction Methods for EDSP21***

Complex Systems Science

- **AOPDD 1:** ***Putative Adverse Outcome Pathway (AOP) Development to Support the Use of High Throughput and Pathway-Based Toxicology Data for Hazard Identification and Prioritization***
- **AOPDD 2:** ***Application of Adverse Outcome Pathways (AOPs) to Environmental Surveillance and Monitoring—Use of Pathway-based Data to Link Exposures to Chemical Mixtures in Surface Water with Predicted Biological Effects***
- **AOPDD 3:** ***A Strategy and Workflow for Incorporating Exposure and Pharmacokinetic Considerations into Chemical-Specific Applications of the AOP Framework***
- **VTM 1:** ***Computational and in Vitro Models of Valvulo-Septal Morphogenesis***
- **VTM 2:** ***Computational and in Vitro Models of Embryonic Morphogenetic Fusion***
- **VTM 3:** ***Human Physiome and Cellular Systems Models for Thyrotrophic Neurodevelopment***

FY16-19 Case Studies II

Lifecycle Analytics

- **SustChem 1:** ***Sustainability Dashboard: Comparison of Flame Retardant Alternatives***
- **SustChem 2:** ***Applying Sustainable Chemistry Tools to Identify Structural Analogs, Predict Transformation Products, and Estimate Human Health and Ecological Hazards: A Case Study of Carbamate and OP Pesticides***
- **EM 1:** ***Silver Nanoparticles***
- **EM 2:** ***Carbon Nanotubes and Graphene Family Nanomaterials***
- **EM 3:** ***Copper and Cerium Dioxide Nanomaterials Case Study***
- **LC & HEM 1:** ***Building Article Case Study for Demonstration and Evaluation of a Life Cycle-Human Exposure Modeling (LC-HEM) Framework***
- **EcoMod 1:** ***Integrated Probabilistic Modeling for Assessment of Chemical Risks to Birds***
- **EcoMod 2:** ***Chemical Risk Assessment for Aquatic Ecological Systems: Methods and Data to Establish Persistence, Bioaccumulation and Toxicity for Low Solubility Organic Chemicals***
- **EcoMod 3:** ***Pesticide Impacts to Aquatic Endangered Species***

Translation and Knowledge Delivery

- **D&E 1:** ***Combining in vitro Estrogen Receptor with Guideline in vivo Data to Make a Case for EDSP Chemical Prioritization and Replacement of a Subset of Tier 1 Tests***
- **D&E 2:** ***Development of Point-of-Departure Database for Predictive Toxicology***

Transformation Builds on Knowledge

- **Increase Predictive Capacity**
  - Organize what we know and utilize that knowledge to support risk-based decision-making
  - Evaluate effects of cumulative exposures and cumulative risk
- **Exploit complex systems modeling to advance mechanistic understanding**
  - Integrate understanding of exposures-dose-effects across levels of biological organization
  - Predict early 'tipping-points'

—**Consider exposures that matter: focus on developmental health, vulnerable and susceptible populations and lifestages**

—**Focus on Lifestage: Account for early life exposures with life long health implications**

—**Provide a new vantage point on Cumulative Exposure and Cumulative Risk Assessment**

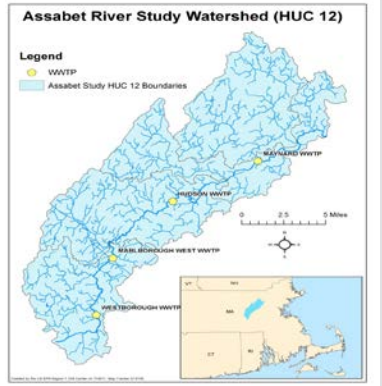
—**Enable environmental (and public) health protection**

Strategic Partnerships and Collaborations

- **Proposing a paradigm shift in how existing and emerging chemicals and products are evaluated for safety**
  - Significant focus on predictive capacity and agile responses
  - Moving from a knowledge poor management posture to one that is proactive, sustainable, and fostering innovation
- **To advance and apply research results, heavy reliance on strategic partnerships including:**
  - Tox21: trans-federal partnership for advancing toxicity testing in the 21st Century
  - Collaborations with the European Commission and Canada
  - OECD: coordination and international harmonization
  - NNI: trans-federal partnership for nanomaterials
  - openLCA
  - Engagement with the private sector and (E)NGO's
  - Active engagement with CSS stakeholders, including Regions and States
  - Academia through STAR Grants

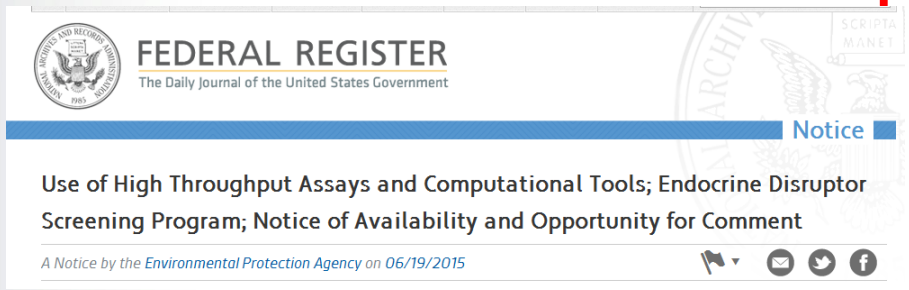
Examples of Regional Collaborations to Translate and Apply CSS Research

- **Region 1, 9, 10:** Exploring ways to use CSS Sustainable Chemistry and LifeCycle Analytics tools to inform design of safer new products.
- **Region 9:** Applications of CSS Science to incorporating ESA requirements into pesticide risk assessments.
- **Region 5:** Pollution Prevention Program training academic and industry partners on using CSS developed tool Program to Assist the Replacement of Industrial Solvents (PARIS III) to inform decisions about safer solvent substitutions.
- **Region 5, 8:** (through Great Lakes National Program with OW): Collaborating to develop AOP-informed biological effects–based tools for monitoring impacted surface waters in the great lakes.
- **Region 8:** Collaborating in the development of 'high throughput toxicity values' through application of CSS tools/models to data poor chemicals.



Regulatory Applications

EPA Endocrine Disruptor Screening Program
http://www.epa.gov/endo/

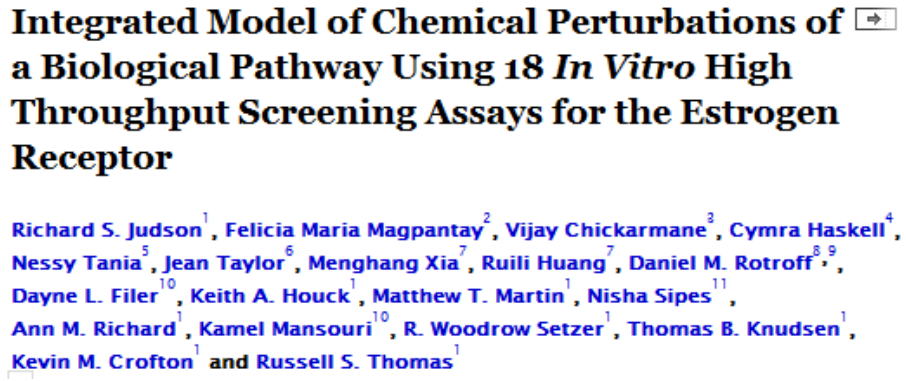


FEDERAL REGISTER
The Daily Journal of the United States Government

Notice

Use of High Throughput Assays and Computational Tools; Endocrine Disruptor Screening Program; Notice of Availability and Opportunity for Comment

A Notice by the Environmental Protection Agency on 06/19/2015



Integrated Model of Chemical Perturbations of a Biological Pathway Using 18 *In Vitro* High Throughput Screening Assays for the Estrogen Receptor

Richard S. Judson[1], Felicia Maria Magpantay[2], Vijay Chickarmane[3], Cymra Haskell[4], Nessy Tania[5], Jean Taylor[6], Menghang Xia[7], Ruili Huang[7], Daniel M. Rotroff[8,9], Dayne L. Filer[10], Keith A. Houck[1], Matthew T. Martin[1], Nisha Sipes[11], Ann M. Richard[1], Kamel Mansouri[10], R. Woodrow Setzer[1], Thomas B. Knudsen[1], Kevin M. Crofton[1] and Russell S. Thomas[1]

Environmental Science & Technology

Article

pubs.acs.org/est

Screening Chemicals for Estrogen Receptor Bioactivity Using a Computational Model

Patience Browne,*[,†] Richard S. Judson,[‡] Warren M. Casey,[§] Nicole C. Kleinstreuer,[∥] and Russell S. Thomas[‡]

Environmental Science & Technology

Article

pubs.acs.org/est

High Throughput Heuristics for Prioritizing Human Exposure to Environmental Chemicals

John F. Wambaugh,*[,†] Anran Wang,[†,§,∥] Kathie L. Dionisio,[‡] Alicia Frame,[†,∥] Peter Egeghy,[‡] Richard Judson,[†] and R. Woodrow Setzer[†]

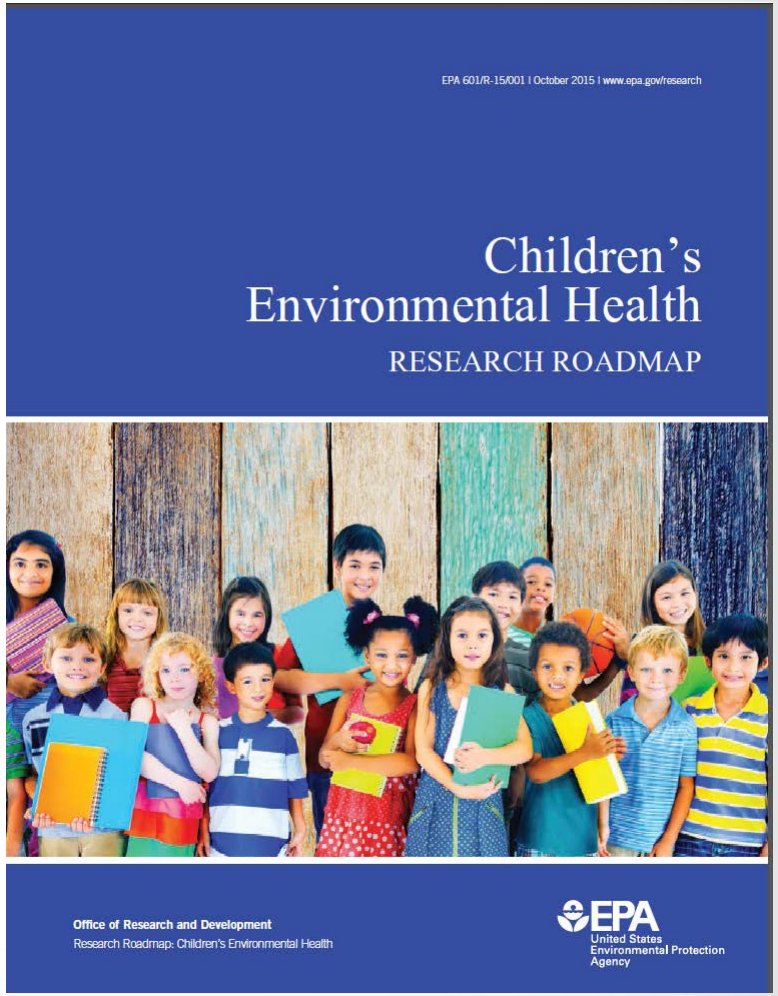
New Chemical Legislation

- The Frank R. Lautenberg Chemical Safety for the 21st Century Act
  - Modernizing the Toxic Substances Control Act (TSCA)
  - Signed into law June 22, 2016
- Health-based Safety Standard
- Vulnerable populations are explicitly considered
- Focus on Exposure
- Implementation of alternative testing methods not based on vertebrate animals

Children's Environmental Health

Preventing Disease Through Healthy Environments

- ORD is investing heavily in Children's Environmental Health research – intramural, extramural, and through strategic partnerships
- This roadmap helps connect the dots among these efforts and focuses on areas where EPA can play a significant leadership role
- This roadmap will build stronger bridges to EPA partners and stakeholders who care about Children's Environmental Health issues
- Resulting research will provide the science required for EPA actions to promote Children's Environmental Health and Wellbeing
- CEH Implementation Working Group
- First Annual Report in 2016



BoSC Meetings So Far

- 2015: CSS BoSC Subcommittee met to evaluate plans to implement CSS StRAP.
  - Meeting was held jointly with HHRA.
  - Report Available
- 2016: Deeper Dive into CSS projects
- BoSC Executive Committee 'owns' the cross-cutting research roadmaps, including Children's Environmental Health.
  - First Annual Report will be reviewed by the BoSC EC in November 2016

Charge Questions

- **The Charge Questions for the 2016 CSS BoSC Subcommittee meeting will address two categories of questions:**
  - **Science: Are we doing the right science right? Are we missing anything big?**
  - **Integration: We have highlighted critical areas of integration within and between projects. Is our approach right? Are there other areas we should be enriching?**