Chemical Safety for Sustainability Research Program

U.S. EPA Office of Research and Development

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National Program Director
SAB Pre-meeting, July 3, 2014

Overview

- **Chemical Safety for Sustainability Research Program**
  - Who are we, and what do we do?
  - Examples of recent accomplishments
- **Fiscal Year 2016-2019 Strategic Research Action Plan**
  - Priorities and mandates
  - Translation
- **Integration, collaboration and partnerships**

ORD Research Programs

Air, Climate & Energy

Sustainable & Healthy Communities

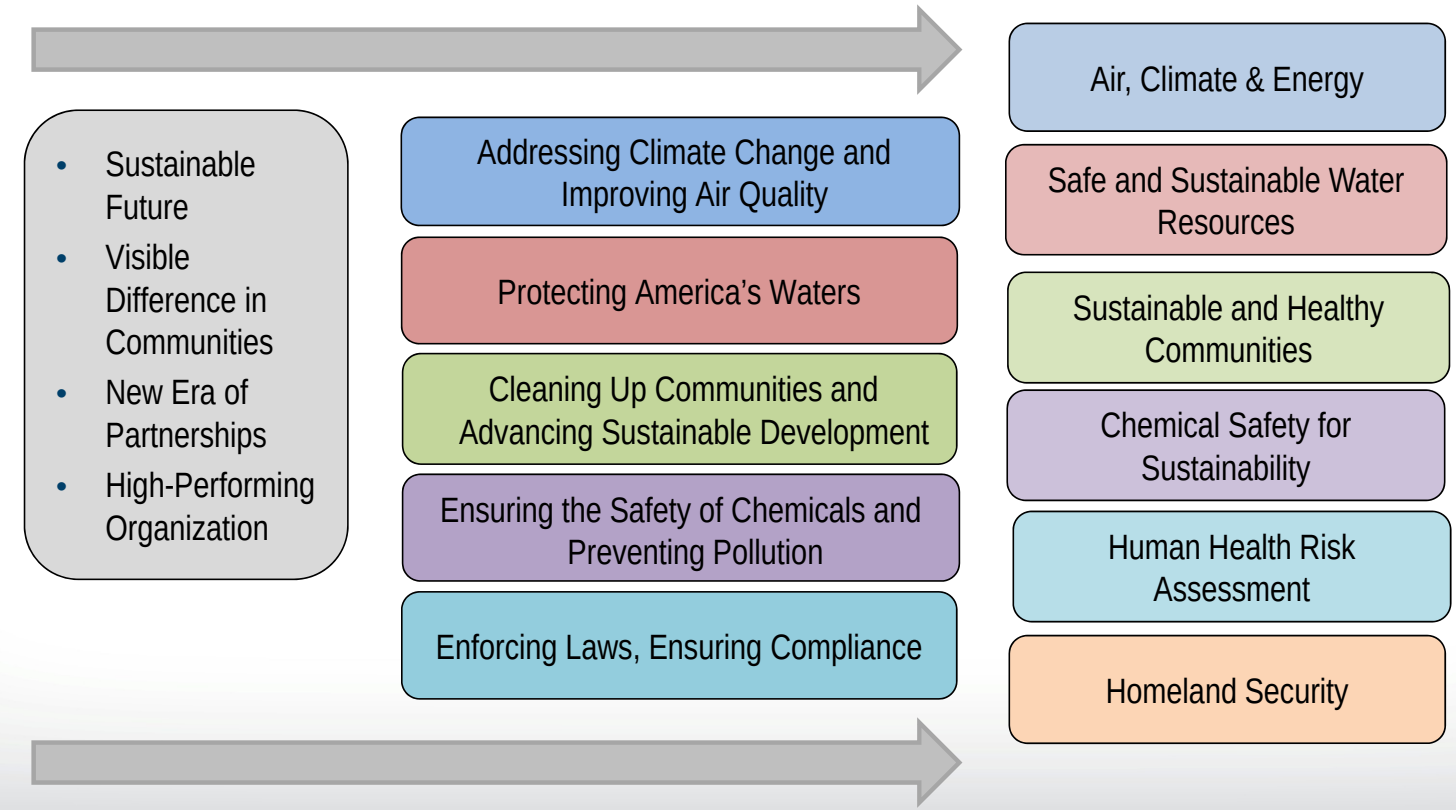
Homeland Security

Chemical Safety for Sustainability

Human Health Risk Assessment

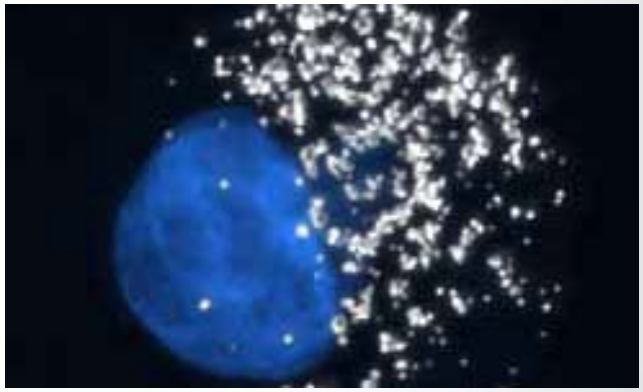
Safe & Sustainable Water Resources

Aligning Research with EPA Strategic Goals



Problem Statement

- **Chemicals are a lynchpin of innovation in the American economy**
- **Sustainable innovation requires designing, producing, and using chemicals in safer and more sustainable 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.**
- **CSS is designed to meet this challenge.**

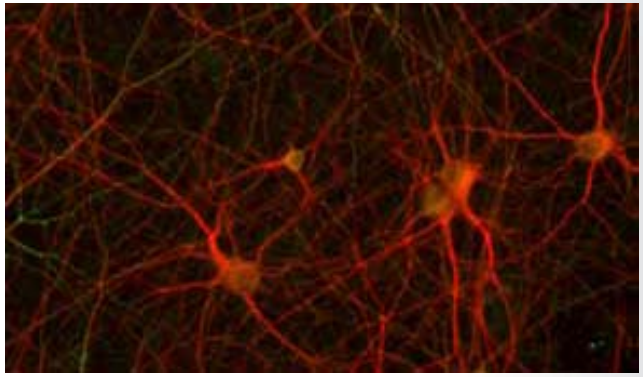


CSS Vision

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.

CSS Overarching Priorities

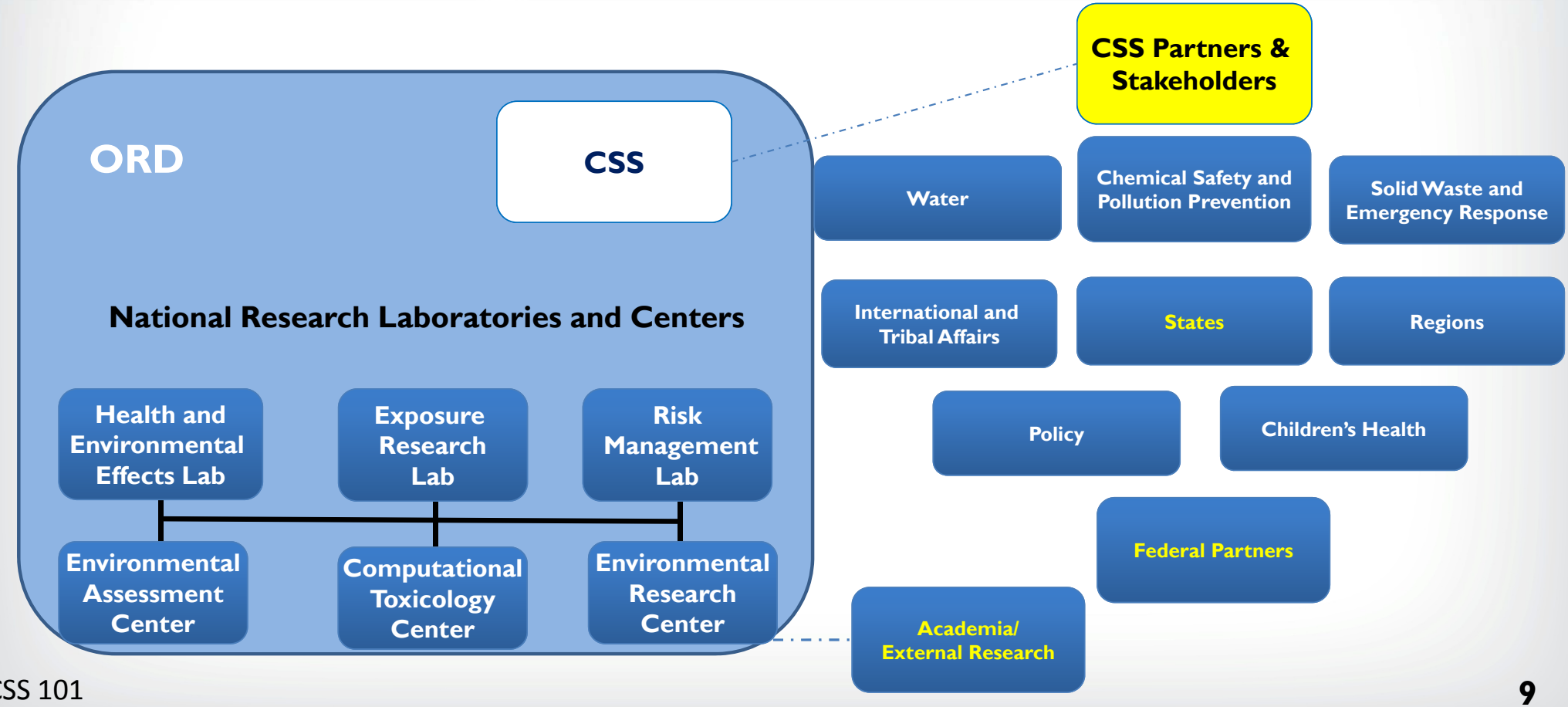
- **CSS overarching priorities are to enable EPA to:**
  - **Address impact of existing chemicals, materials/products across the lifecycle.**
  - **Anticipate impacts of new chemicals, materials/products across the lifecycle.**
  - **Enable consideration and evaluation of complex interactions of chemical and biological systems to support Agency decisions.**



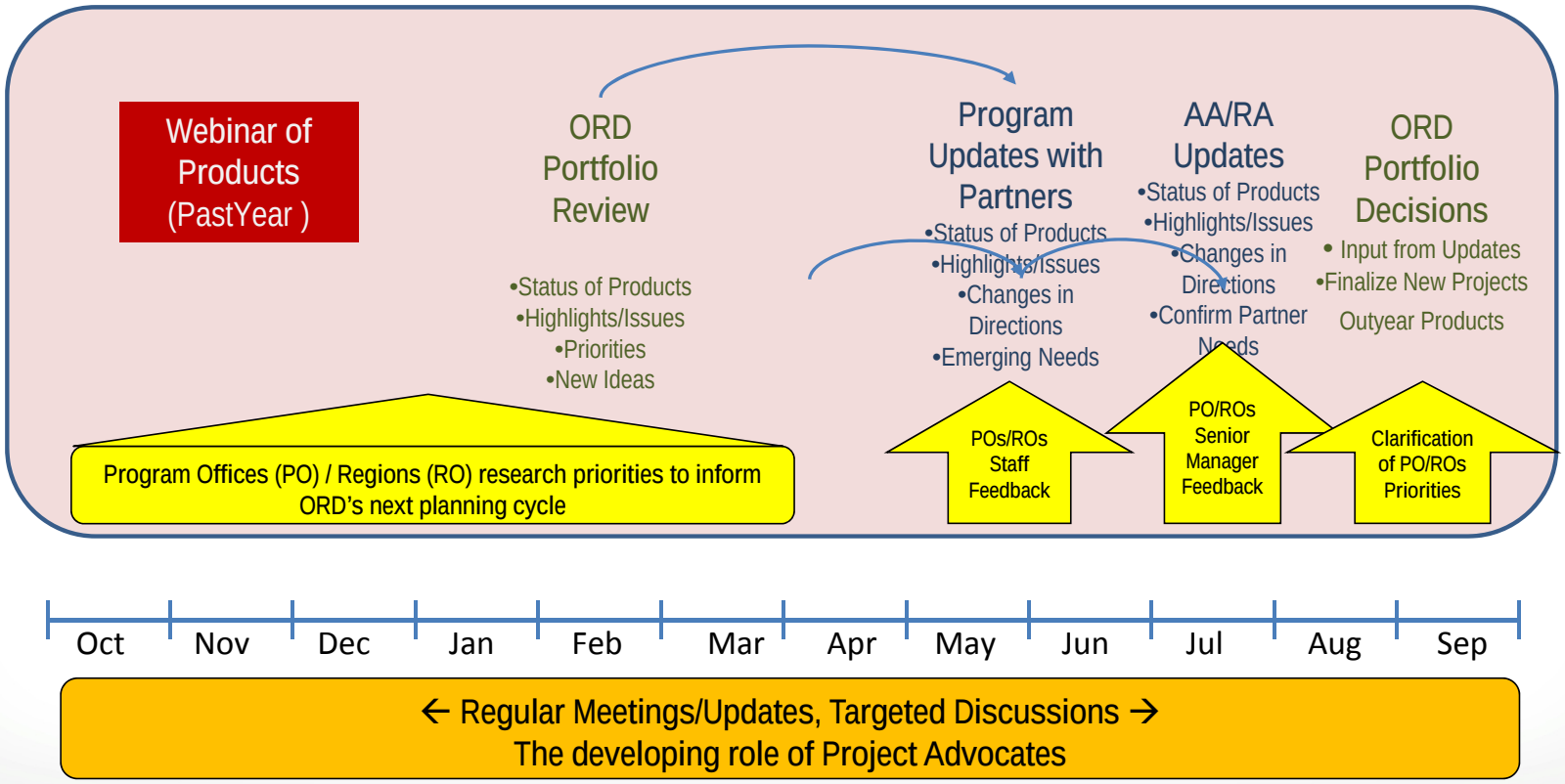
What We Do

- **Build Knowledge Infrastructure**
  - Combine different types of data in new ways to characterize impacts of chemicals 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

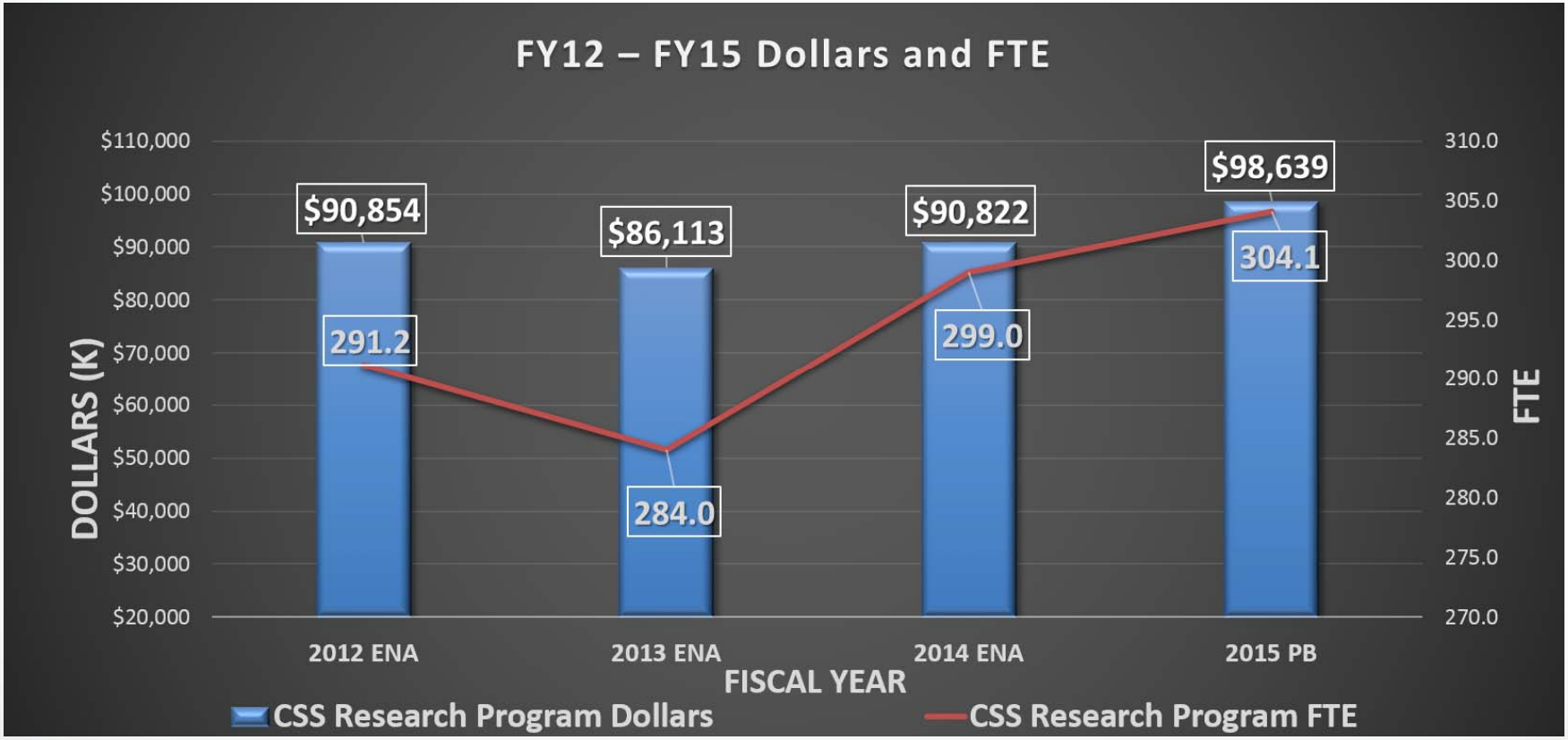
How We Do It


CSS Partners & Stakeholders
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
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

Extensive Interaction with EPA Partners

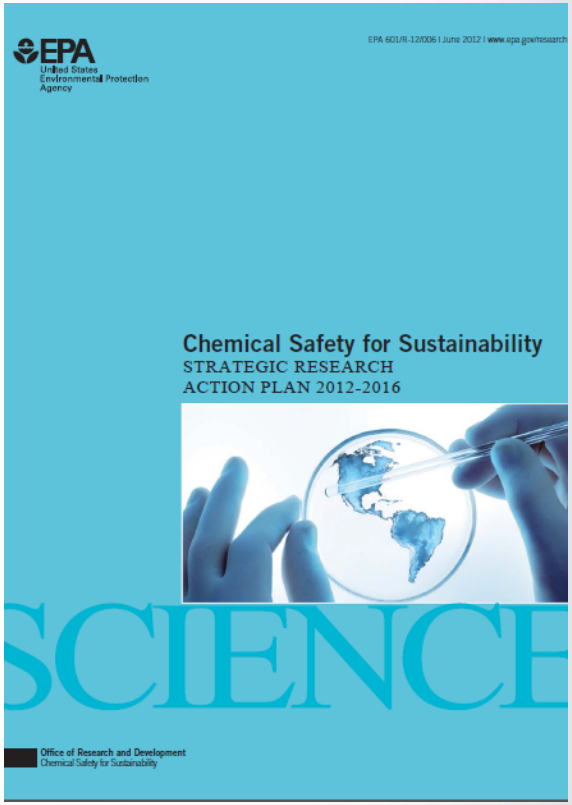


Resource Trends



Strategic Planning

- **What is a Strategic Research Action Plan (StRAP)?**
  - Describes research program for internal and external audiences
  - Developed in consultation with advisors (SAB and BOSC), EPA partner offices, other stakeholders
  - Serves as our planning document; guides allocation of ($ and people) resources
- **Early Input from SAB and BOSC**
  - Preliminary Draft: just beginning 2016-2019 StRAP updates
  - Kicks off the year long process with EPA partners and stakeholders
  - High level strategic plan; are we heading in the right direction?



Fiscal Year 2016-2019 Strategic Planning

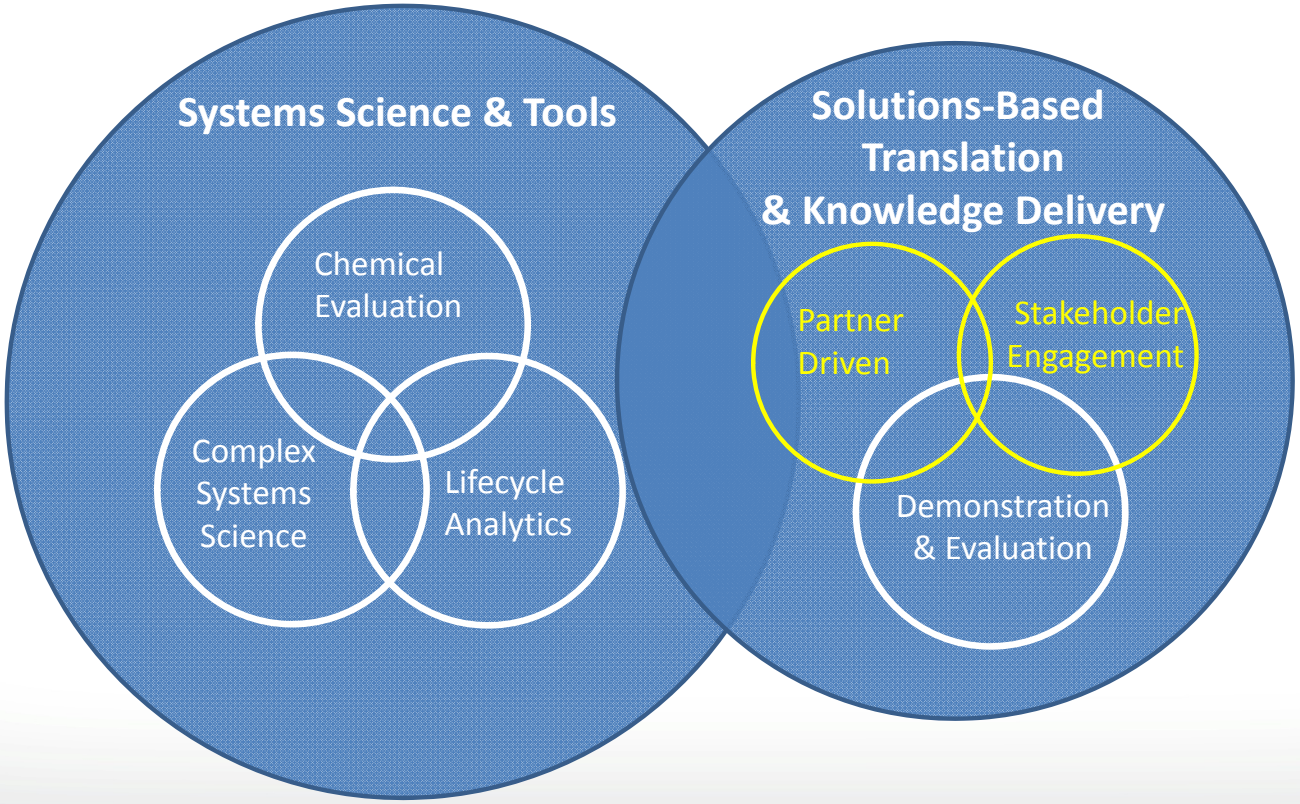
- **8 Themes reduced to 4 Research Topics**
- **21 Projects reduced to proposed 9 project areas**
- **Integrated, transdisciplinary, high impact**
- **Promotes and fosters innovation**
- **Through research translation and knowledge delivery**
  - Increase transparency; enhanced access to CSS science
  - Develop tailored solutions; partner-driven and partner-focused
  - Strategic engagement of the stakeholder community; democratizing science

2016-2019 CSS Topics

- **Three Research Topics in Systems Science and Tools**
  - Chemical evaluation
  - Complex systems
  - Life cycle analytics
    - Topic is designed to provide the science and tools needed to look at chemicals and materials (including nano) in the context of how these are designed and used in our society.
    - Considers green chemical design, lifecycle impacts, and sustainable use.
- **One Translation Topic**
  - Solutions-Based Translation and Knowledge Delivery

CSS Program Design

Chemical Safety for Sustainability



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.

  Examples of project areas: High-throughput Toxicology, Rapid Exposure and Dosimetry
- **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

  Examples of project areas: Adverse Outcome Pathways Discovery and Development, Virtual Tissues
- **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.

  Examples of project areas: Lifecycle and Human Exposure Modeling, Ecological Modeling, Emerging Materials, Sustainable Chemistry

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,

  Example of project area: Demonstration and Evaluation for Risk-Based Decisions

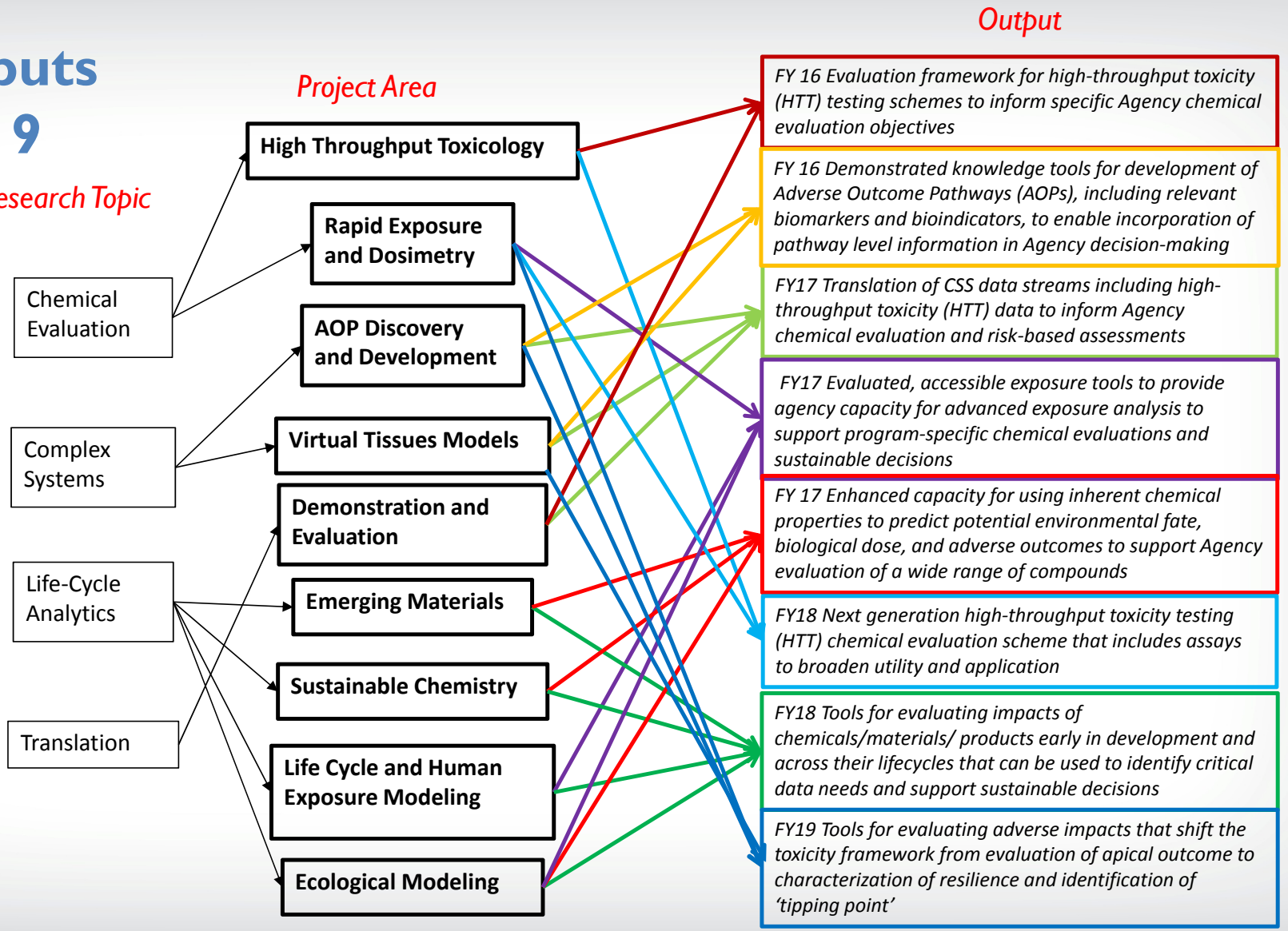
  - **Other Related Activities:**
    - Partner-Driven
      - Respond to short-term high priority science needs for CSS partners
    - Stakeholder Engagement
      - Allow for active and strategic engagement of the stakeholder community

Transformative not Incremental Science

A central challenge for CSS is to anticipate potential for adverse impacts on human health or wildlife populations based on knowledge from data rich chemicals. In the new StRAP:

- Adopt the AOP framework to help us
  - organize what we know and utilize that knowledge to support risk-based decision-making
  - Evaluate effects of cumulative exposures and cumulative risk (Effect Based Biomonitoring)
- Using complex systems modeling, advance the mechanistic understanding of how chemical disruption of cell lineage, fate and behavior propagates to higher levels of biological organization and adverse developmental outcomes.
  - Examine dose-response effects
  - Predict early 'tipping-points'
- Account for exposure information; Integrate our understanding of human and ecological exposures and effects
- Impose a life cycle perspective: to look at chemicals and materials in the context of how these are designed and used in our society; includes engineered nanomaterials, sustainable chemistry, and alternatives
- Narrow focus on developmental health and vulnerable and susceptible populations
- Explore Higher throughput approaches to cover broader swath of the chemistry and biology spaces

CSS Outputs FY 16-19



Integration: Amplifying Resources

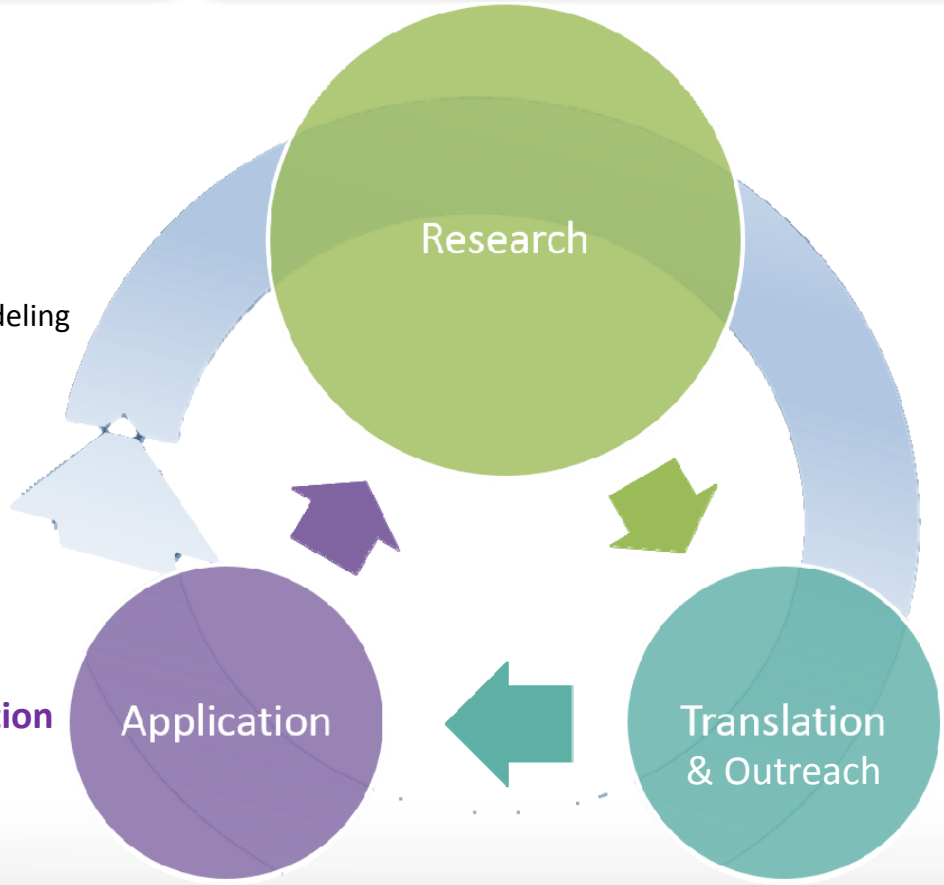
- **CSS integration across National Research Programs (NRPs) primarily through ORD cross-cutting research roadmaps.**
  - CSS led the development of the Children's Environmental Health Research Roadmap that describes integration with SHC (including EPA-NIEHS Children's Centers), ACE, HHRA, and SSWR.

- **Through preliminary FY 16-19 StRAP planning, identified additional integration opportunities**
  - ACE: Advancing Development of high(er)-throughput approaches to evaluate volatiles and other air pollutants [results of two successful Pathfinder Innovation Projects (PIP)]
  - ACE, SSWR, and SHC: Advancing development of higher throughput lifecycle assessments
  - SSWR: Effect-based monitoring; advancing multi-pollutant/mixtures chemical evaluations
  - SHC: Accessible exposure information
  - HSR: Rapid screening tools
  - HHRA: use of new CSS data in NCEA assessments

Bench to Application Translation

CSS FY 16-19 Example Project Areas

- High Throughput Toxicology
- Rapid Exposure & Dosimetry
- AOP Discovery & Development
- Virtual Tissues Models
- Ecological Modeling
- Lifecycle & Human Exposure Modeling
- Sustainable Chemistry
- Emerging Materials (nano)
- Demonstration & Evaluation



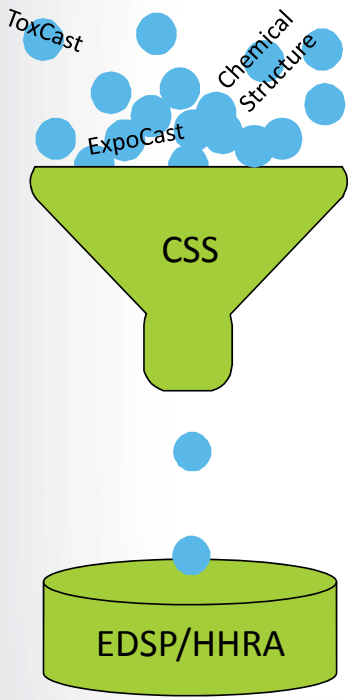
High-throughput Toxicology
Rapid Exposure & Dosimetry

Demonstration & Evaluation

Stakeholder workshops/training
iCSS Dashboard
RapidTox

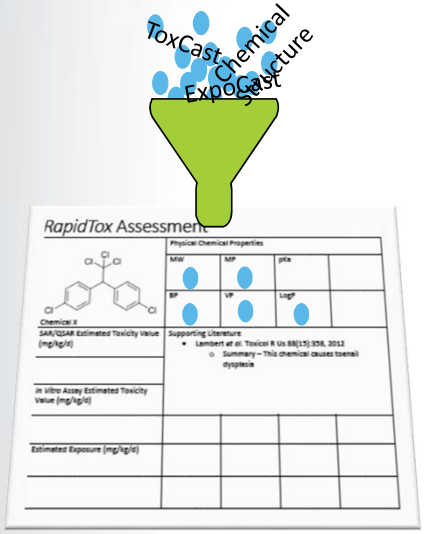
- **EDSP21 Rapid Prioritization**
- **HHRA (OSWER/Regions)**

Examples of Solutions-Based Data Integration



- **Endocrine Disruptor Screening Program**
  - Integrate high-throughput in vitro screening data, QSAR, and high-throughput exposure data
  - For ER, 18 in vitro assays and ~20 QSAR/docking models
  - Benchmark in vitro ER activity with current in vivo models
  - High-throughput exposure models based on use profiles and calibration against human biomonitoring data
- **High-Throughput Toxicity Values**
  - Develop points-of-departure (PODs) from SAR/QSAR, high-throughput *in vitro* screening (with RTK), and short-term *in vivo* transcriptomics
  - Enhance ToxRefDB to include full dose-response data
  - Evaluate alternative PODs against traditional PODs based on apical effects identified from animal studies (e.g., IRIS, OPP, NTP, PPRTV, ATSDR, etc.)

Examples of Outreach, Translation, & Application



Tox PI

Estrogen Receptor

- **Stakeholder Engagement and Training**
  - ToxCast data workshops (January 14 and April 2, 2014)
  - Monthly Communities of Practice webinars
- **Endocrine Disruptor Screening Program (CSS – OCSPP/OSCP)**
  - Prioritize chemicals for Tier 1 screening
  - Undergoing 2 SAP reviews in 2014
- **High-Throughput Toxicity Values (CSS – HHRA)**
  - Quantitate uncertainty using Bayesian evaluation framework
  - Demonstrate potential for application as first order screening level toxicity values
  - Develop lower tier assessment product
  - Work with program partners to ensure fit-for-purpose

Incorporating Stakeholder Feedback

- **Greater Transparency**
  - Releasing ToxCast "Owners Manual"
    - Chemical procurement and QC
    - Data analysis pipeline
    - Assay annotation
  - Performing 3rd Party QC Audit on ToxCast data
- **Address Critical Weaknesses**
  - Redouble effort to address metabolic competence issue in HTS assays
  - Fill assay data gaps (e.g., thyroid)
- **Move Towards "Validation"**
  - Implement modified validation framework

Strategic Partnerships and Collaborations

- **CSS proposes a significant paradigm shift in how existing and emerging chemicals and products can be 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 ~~achieve this, it relies~~ heavily reliance on strategic partnerships including:**
  - Tox21: trans-federal partnership for advancing toxicity testing in the 21st Century
    - Additional collaborations with the European Commission, Canada, as well as with the private sector and public health advocacy groups.
    - OECD: international collaboration for advancing the Adverse Outcome Pathway Framework
  - Active engagement of CSS stakeholders
  - NNI: trans-federal partnership for advancing sustainable development and evaluation of nanomaterials
  - Strategic collaborations with industry

Leading Edge of Science - STAR

- **CSS leads and fosters application of emerging science, including advances in biology, bioengineering, chemistry, informatics, sensor technologies, to engender and nurture linkages with issues relevant to environmental health.**
- **Through Science to Achieve Results (STAR), CSS funds anticipatory (high risk, high return) RfAs that take advantage of significant science investments made by other Agencies such as NSF and NIH and by international funding organizations.**
- **Additional engagement opportunities**
  - Small Business Research (SBIR), for example to develop sustainable alternatives (through chemistry or engineering design) to flame retardants
  - ORD's Innovation Program, supporting and advancing nuclear and nascent innovation research with transformative promise

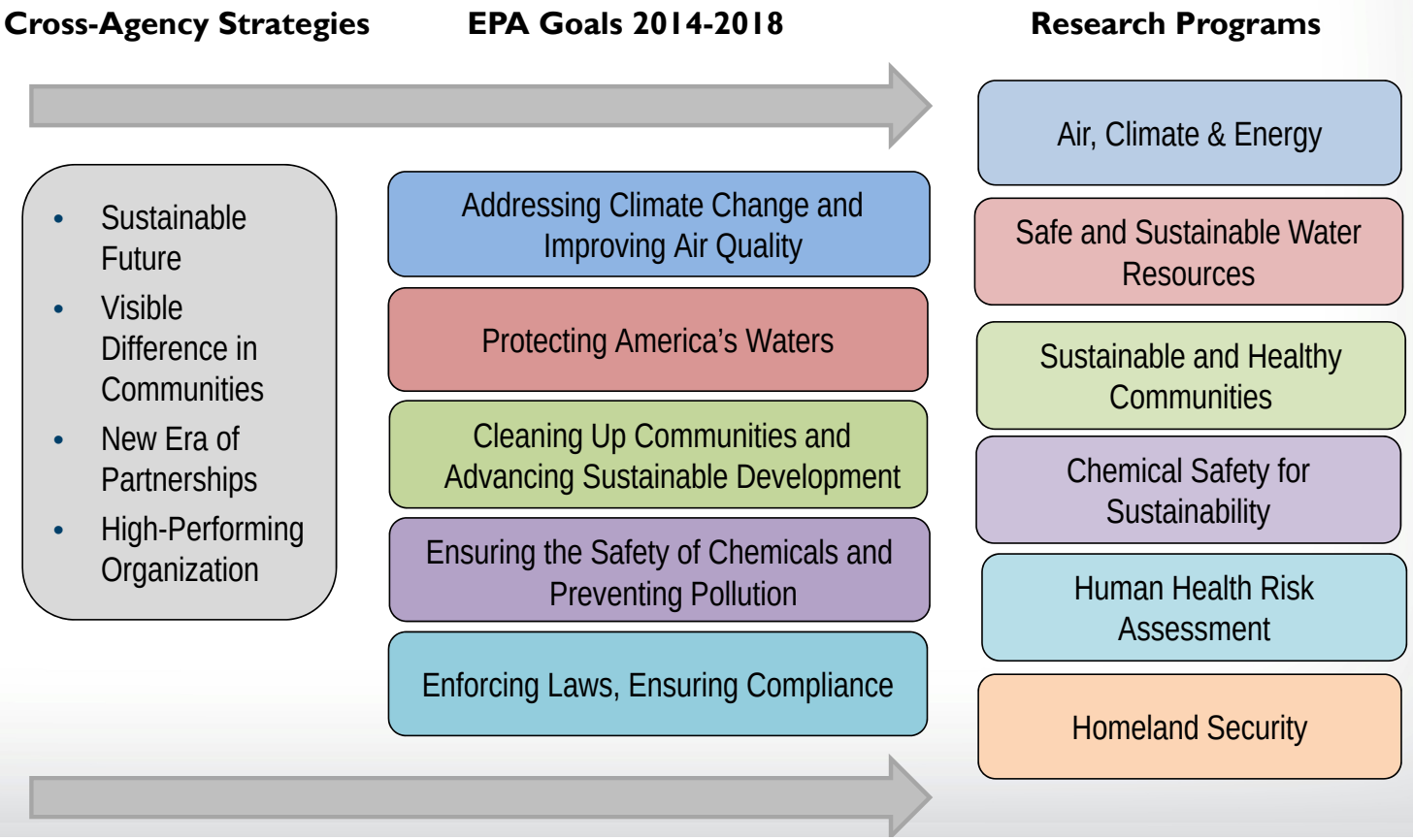
Anticipated Research Accomplishments

- **Accelerate the pace of data-driven chemical safety evaluations:**
  - Information on human and ecological exposure and impacts is incorporated into ORD integrated applications to provide accessible data and tools to support Agency program- and decision-specific needs for chemical safety evaluation.
- **Enable the Agency to use 21st Century Science to make sustainable and public-health protective decisions:**
  - Evaluated, efficient chemical evaluation methods are developed to provide and enhance agency capacity for advanced analysis to support program-specific environmental health evaluations and sustainable decisions.
- **Begin to shift the paradigm of toxicity characterization from apical endpoints to 'tipping points':**
  - Complex systems information across all levels of organization associated with adverse outcomes is incorporated into predictive modeling to inform Agency risk-based assessments.
- **Apply CSS tools to support sustainable innovation and evaluation of chemicals and emerging materials:**
  - Tools are developed and applied to incorporate emerging and HTP exposure and toxicology data streams to evaluate impacts of agency decisions on safe and sustainable innovation and use of manufactured chemicals and materials across the product lifecycle.

CSS Advancing EPA's Mission

CSS:
Science to support Agency's Strategic Goals

Science to prepare the Agency to meet its mid-Century Goals




Questions?

Examples of Recent Accomplishments

- **Accelerated pace of chemical screening**
  - Public release of ToxCast Data on 1,800 chemicals available via iCSS Dashboard; two stakeholder training workshops
- **Transformative advances in high throughput and computational exposure science**
  - Further development of the ExpoCast high-throughput exposure evaluations for application to prioritization in EPA's EDSP21 program; FIFRA SAP to evaluate this approach July 2014
  - Development of Chemical Product Category database CpCAT that provides product use categories ~44,000 chemicals
- **Novel application of tools to evaluate ecological impacts of chemical exposures to non-target species and populations**
  - Homology/AOP tools: Pollinator (non-target) sensitivity to pesticide formulations; vertebrae sensitivity to pharmaceuticals in water (reproductive toxicity)
  - Predictive nest productivity models to incorporate impacts of pesticides applications to reproductive health of wildlife species into ecological risk assessments.
- **Engagement in international efforts to harmonize green purchasing practices**
  - Application of EPA's life cycle assessment tools to provide clear, comparable information about the environmental impacts of different products evaluated internationally in the development of Product Category Rules (PCRs).
- **Incorporation of fate and transport models to evaluate environmental health and safety of nanomaterials**
  - Characterizing the surface properties of silver nanoparticles and how these properties affect their fate in containment systems; developing high-throughput methods for characterizing nanoparticle transport through soils and sediments.

CSS Partner-Driven High-Priority Focus

Emerging and methodologically challenging compounds

- Minimal data requirements for assessing potential hazard and exposure to new chemicals resulting from consumer use of manufactured chemicals/products
- Efficient methods and testing protocols for measuring and estimating persistence, bioaccumulation and important chemical/material properties for new and/or methodologically challenging chemicals and material

Endocrine disruption (includes thyroid focus)

- Focus on EDC relevant AOPs to help prioritize AOP research and selection of chemicals evaluation strategies.

Children's environmental health

- Information on early life stage exposure and hazard are incorporated into ORD integrated applications to provide accessible data and tools that support Agency program- and decision-specific needs
- Pathway level information associated with developmental health outcomes is incorporated into predictive exposure and hazard modeling