Chemical Safety for Sustainability Research Program Overview

U.S. EPA Office of Research and Development

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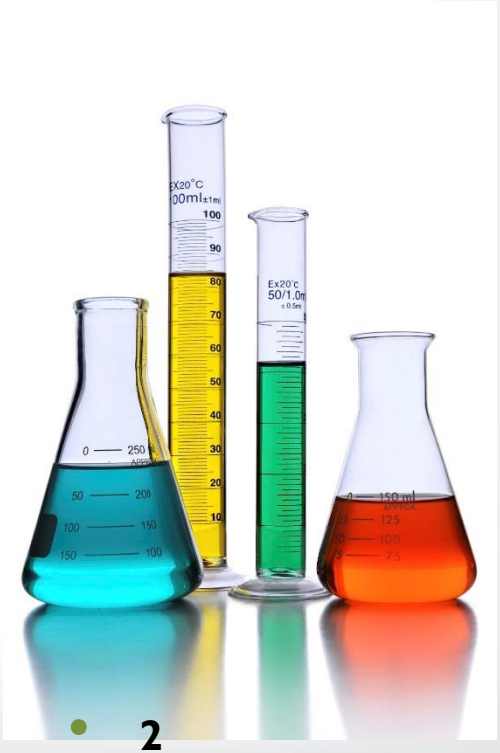
Problem Statement

- **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.**

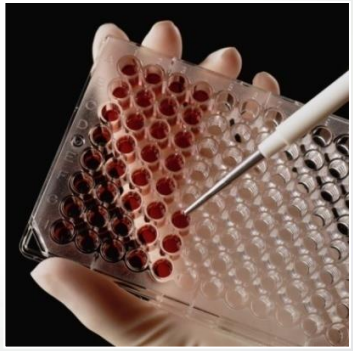


CSS Vision and Goals

- **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.**

- **The 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.



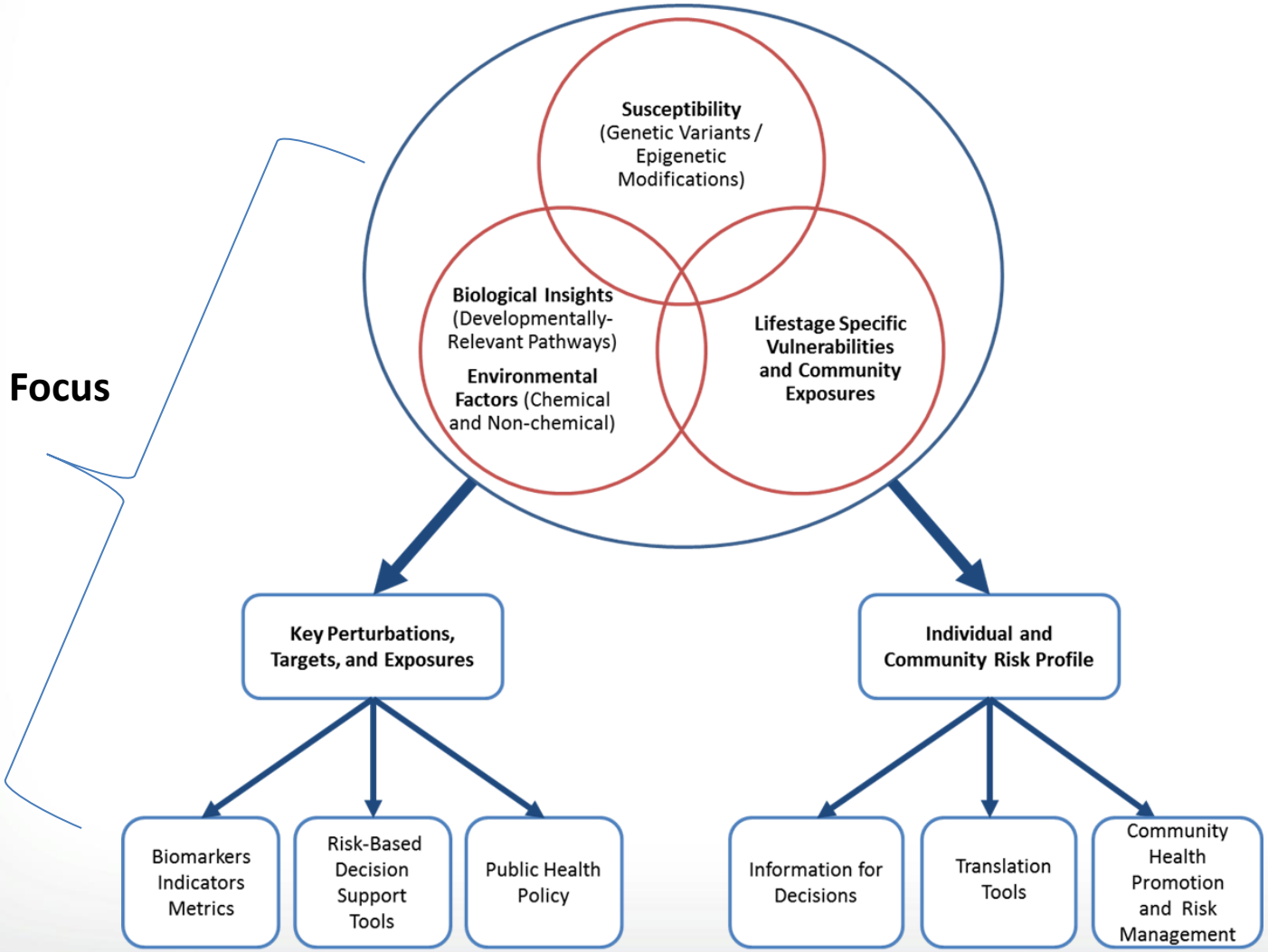



EPA Priorities

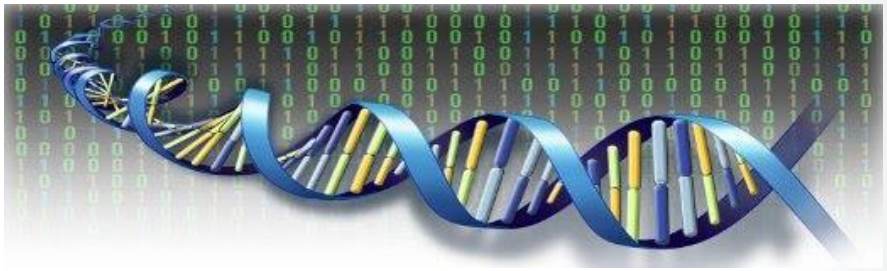
- **<u>EPA Strategic Plan, Goal 4: Ensure Chemical Safety</u>. Reduce the risk and increase the safety of chemicals that enter our products, our environment, and our bodies.**
- **Innovative research will provide the tools to:**
  - Assess safety of high-priority chemicals and advance understanding of potential risks from exposure to multiple chemicals
  - Enhance chemical screening and testing approaches for priority setting and context-relevant chemical assessment and management
  - Inform Agency actions and help local decision makers manage and mitigate exposures to contaminants of greatest concern
  - Promote innovations in chemistry to encourage development and use of safer chemicals
  - Evaluate human health and ecological risks associated with new chemical substitutes
  - Provide systems understanding needed to protect children and other vulnerable groups

Environmental Health Research Translation Framework

CSS Focus



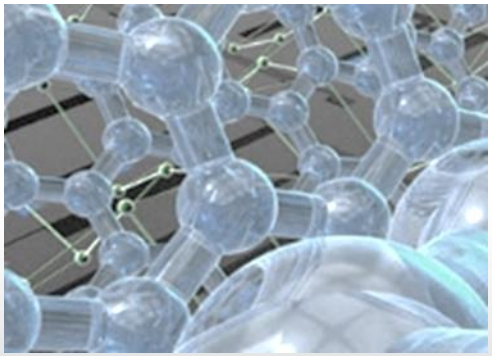
CSS Program Objectives



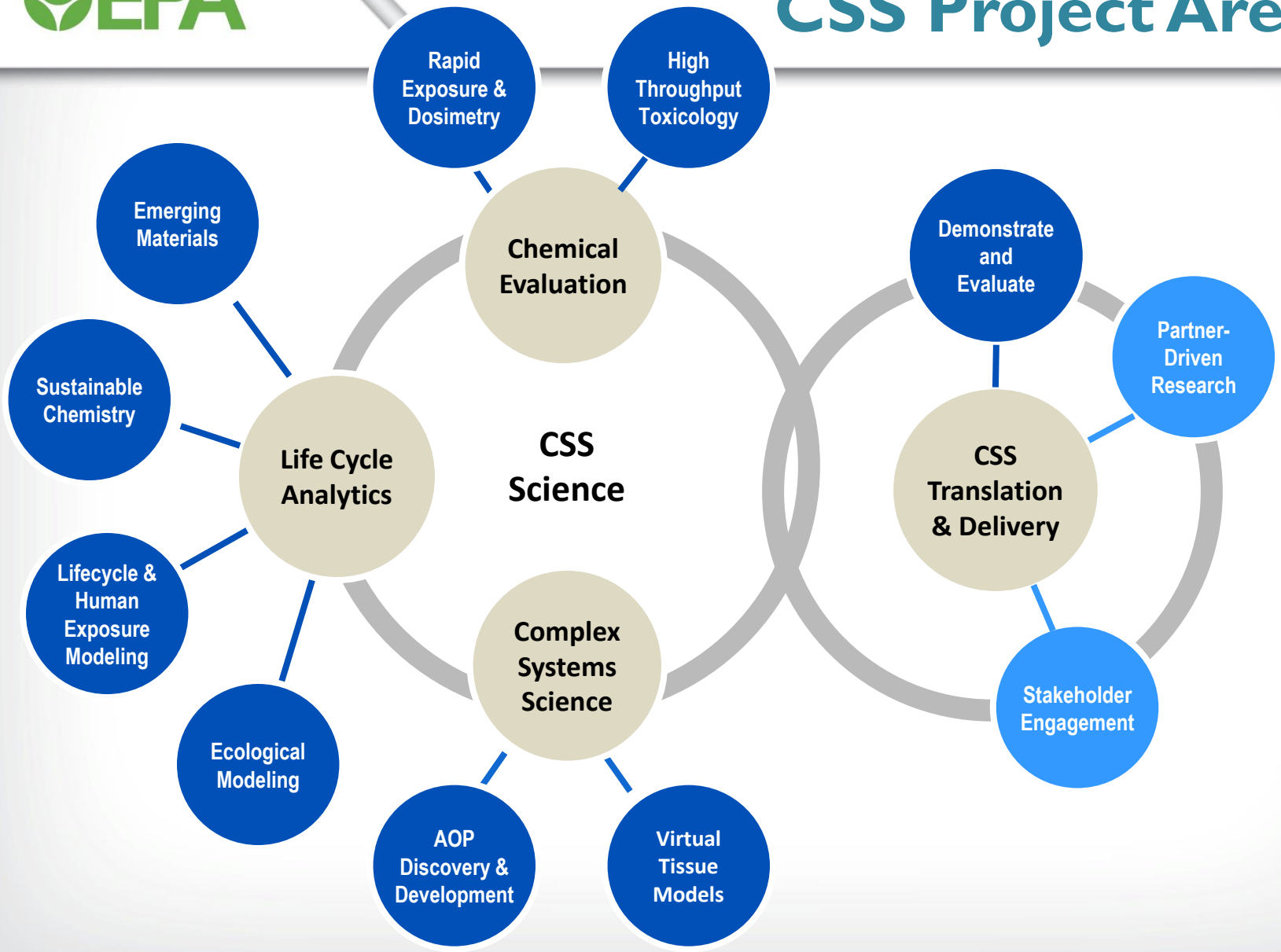
- **<u>Build Knowledge Infrastructure</u>.** Make information publicly accessible. Combine different types of data in new ways to characterize impacts of chemicals to human health and the environment
- **<u>Develop Tools for Chemical Evaluation</u>.** Develop and apply rapid, efficient, and effective chemical safety evaluation methods
- **<u>Promote Complex Systems Understanding</u>.** 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
- **<u>Translate and Actively Deliver</u>.** Demonstrate application of CSS science and tools to anticipate, minimize, and solve environmental health problems

CSS Research Topics

- **Chemical Evaluation:** Advance cutting-edge methods and provide data for risk-based evaluation of existing chemicals and emerging materials.
- **Lifecycle Analytics:** Addresses critical gaps and weaknesses in accessible tools and metrics for quantifying risks to human and ecological health across the lifecycle of manufactured chemicals and products.
- **Complex Systems Science:** Adopt a systems based approach to examine complex chemical-biological interactions and predict potential for adverse outcomes resulting from exposures to chemicals.
- **Solutions-based Translation and Knowledge Delivery:** (1) Promote web-based tools, data, and applications focused on tailored solutions to support chemical safety evaluations and related decisions, (2) Respond to short-term high priority science needs for CSS partners, (3) Allow for active and strategic engagement of the stakeholder community.



CSS Project Areas



Science Challenges and Outputs

Chemical Evaluation

High Throughput Toxicology

Challenges

- Expand coverage in HTP toxicity screening schemes for high priority biological areas such as endocrine disruption and adverse outcomes such as developmental toxicity
- Incorporate xenobiotic metabolism into HTP test methods

Outputs

- Guidance for evaluating technical performance and biological domain of high-throughput assays including lists of reference chemicals for specific toxicity endpoints
- New medium- and high-throughput assays and development of models (signatures) to cover important areas of biological space/high priority adverse outcomes
- Approaches for incorporation of xenobiotic metabolism and challenging chemical classes into high-throughput test method

Rapid Exposure and Dosimetry

Challenges

- Rapidly characterize potential for real-world exposure to chemicals, including those associated with consumer product use
- Develop critical HTP data required to forecast exposure and dose for thousands of chemicals of interest to Agency

Outputs

- High-throughput pharmacokinetic (HTPK) data and models for risk-based prioritization
- High-throughput exposure data and models for risk-based prioritization

Science Challenges and Outputs

Lifecycle Analytics

Sustainable Chemistry

Challenges

- Exploit advances in HTP screening, mechanistic toxicology, and computational chemistry to identify influential chemical determinants of adverse biological impacts

Outputs

- Chemical feature sets and models for use with selected AOPs
- Strategies to evaluate potential for environmental and human health impacts of new and alternative chemicals to support safer chemical design and chemical screening

Emerging Materials

Challenges

- Identify critical intermediate properties of ENMs that are predictive of potential risks
- Understand and efficiently predict interactions between ENMs and biological or other complex media

Outputs

- Protocols for evaluating engineered nanomaterials in complex biological or environmental systems
- Tools to efficiently screen for potential toxicity and exposure based on features of ENMs

Science Challenges and Outputs

Lifecycle Analytics

Lifecycle and Human Exposure Modeling

Challenges

- Integrate chemical exposure and lifecycle knowledge to model and assesses human health and ecological impacts of alternatives
- Develop approaches to rapidly evaluate environmental and human health impacts and metrics to quantify trade offs between risks and other sustainability factors

Outputs

- Life Cycle Harmonization Tool that will allow greater interoperability of Life Cycle and Exposure databases and tools
- Case study evaluation of a chemical/product Life Cycle/Human Exposure Modeling framework
- LC-HEM Tool for evaluating chemical/product impacts in a life cycle assessment framework

Ecological Modeling

Challenges

- Rapidly evaluate ecological impacts associated with use of manufactured chemicals with limited data
- Capture spatial and temporal dynamics to target critical experimental measurement required to understand chemical impacts on populations of vulnerable ecological species

Outputs

- Demonstration of ERA tools that reduce uncertainty for high priority and methodologically challenging chemicals, comparing ecologically relevant risk assessments to those based on limited data
- Decision framework for using models of various complexities, data requirements, and levels of ecological realism for differing ERA requirements or fit-for-purpose

Science Challenges and Outputs

Complex Systems Science

AOP Discovery and Development

Challenges

- Application of AOP framework in concert with new data streams to predict potential impacts of chemicals on ecological and human health to support risk-based decision-making

Outputs

- An Adverse Outcome Pathway knowledgebase that enhances the utility of pathway-based data for risk-based decision-making
- Case studies demonstrating relevant application of adverse outcome pathway knowledge to risk-based decision-making

Virtual Tissue Models

Challenges

- Assemble pathway data and biological knowledge into dynamic systems models for assessing developmental toxicity
- Capture system dynamics in a platform of experimental and computational models for predictive toxicology to support hypothesis development and targeted study to improve understanding of chemical impacts on biological organisms

Outputs

- Integrated predictive system to assemble pathway data, information and knowledge of embryological systems into dynamical VTMs for assessing prenatal developmental toxicity
- Integrated predictive system to assemble pathway data, information and knowledge into dynamical VTMs for assessing neuro-developmental toxicity linked to thyroid disruption

Science Challenges and Outputs

Translation and Delivery

Demonstration and Evaluation

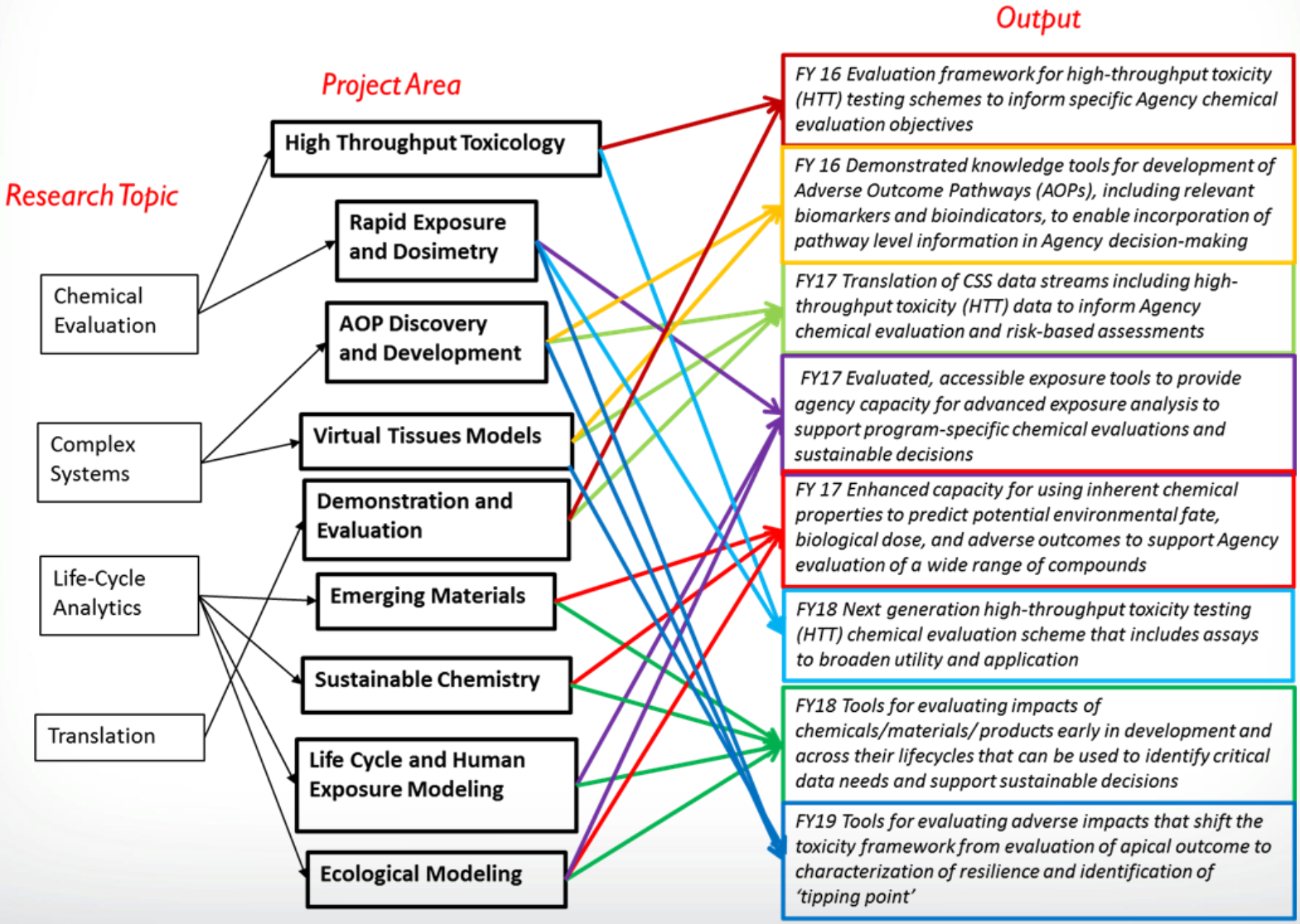
Challenges

- Integrate new information with existing methods and infrastructure to develop qualitative and quantitative approaches that support specific Agency science-based decisions
- Systematically evaluate new information and approaches to determine when these can be applied "fit-for-purpose" for EPA decisions
- Develop measures of confidence and uncertainty to support use of new approaches "fit-for-purpose" by EPA decision makers

Outputs

- Develop and evaluate a process to produce rapid points of departure (POD) for use in evaluating and managing data-poor chemicals
- Develop a framework(s) to evaluate novel groups of assays, methods and models for hazard ID and/or screening and prioritization

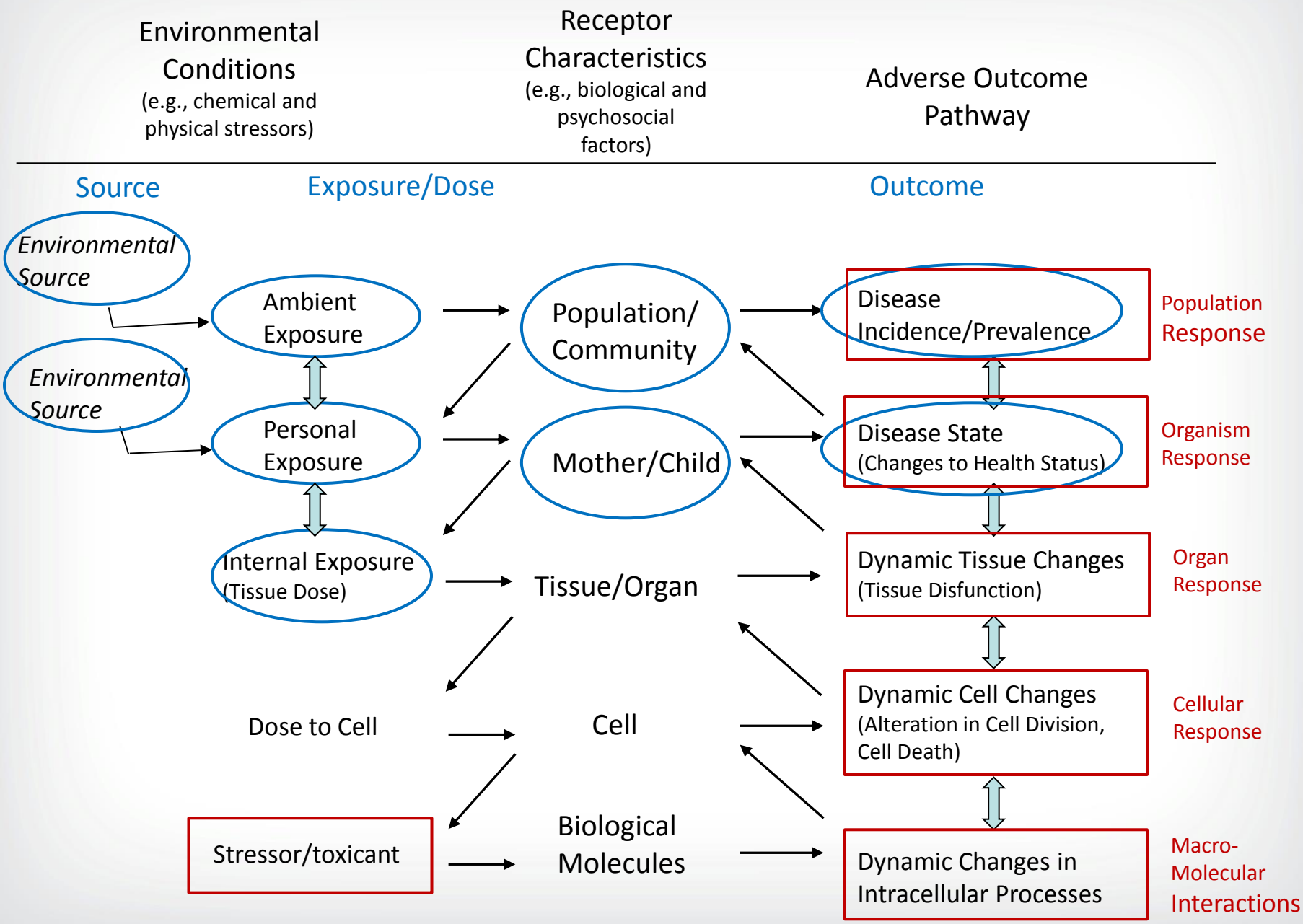
Anticipated Accomplishments (Outputs)



Transformation Builds on 2012-16

- **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**

Concept for Integrated CEH Research: Addressing Complexity



Anticipated Impacts (Outcomes)

- **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.
- **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