EPA
United States
Environmental Protection
Agency

# Chemical Safety for Sustainability Research Program: Overview and Perspectives on 21st Century Science

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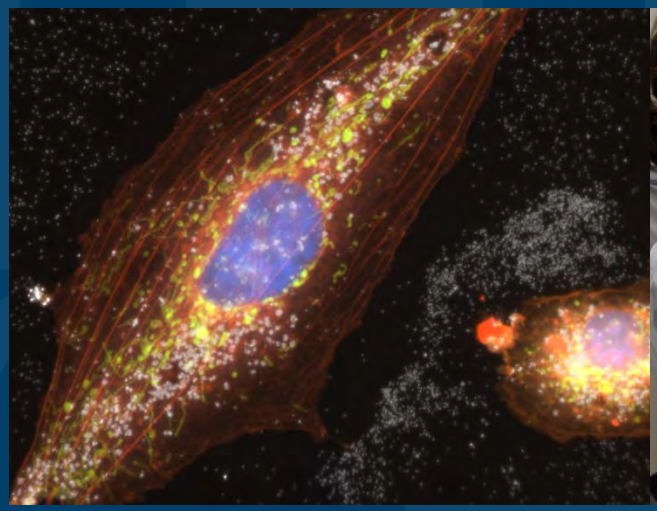
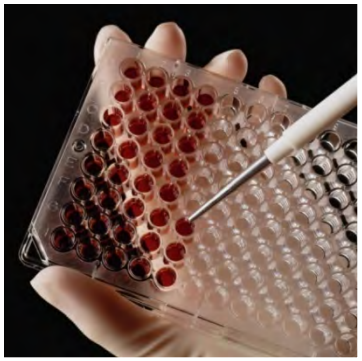
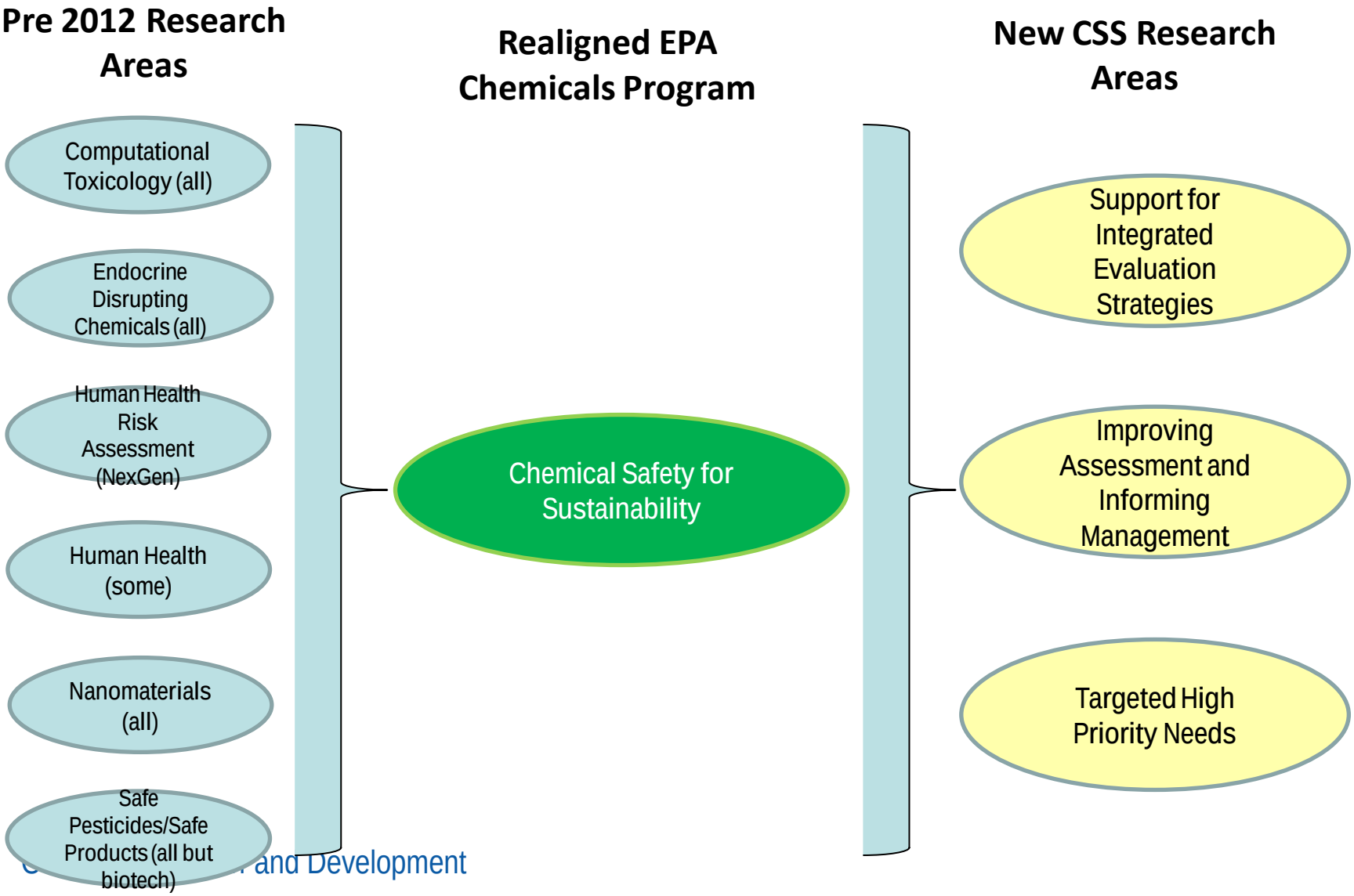


# CSS Vision and Goals

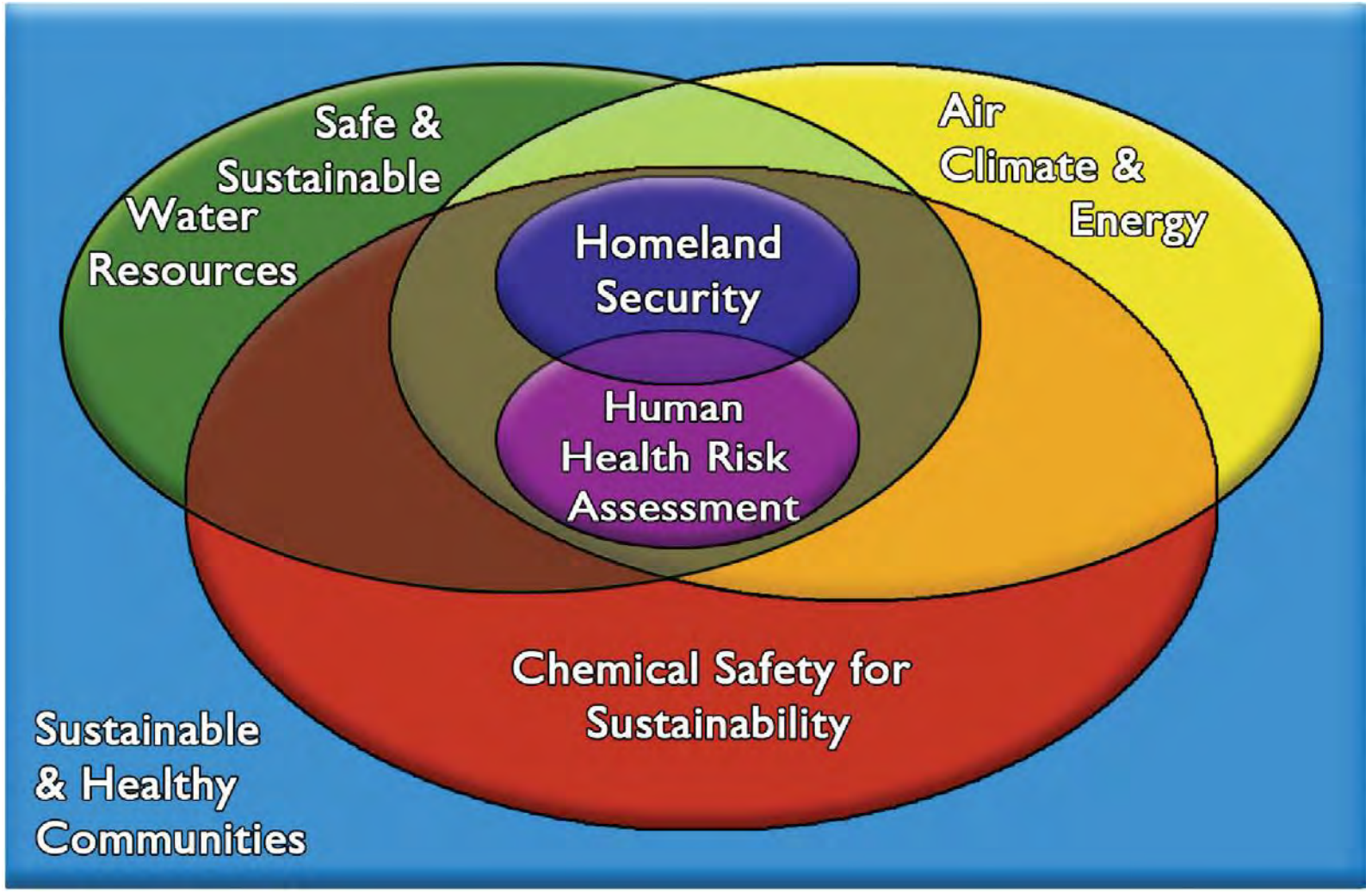


- CSS will lead development of innovative science to ***support safe, sustainable use of chemicals/materials*** required to ***promote ecological wellbeing***, including human and environmental health, as well as to ***protect vulnerable species and populations***.
- The CSS overarching priorities are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

# Aligning EPA's Chemicals Research Activities



# Integrated National Programs

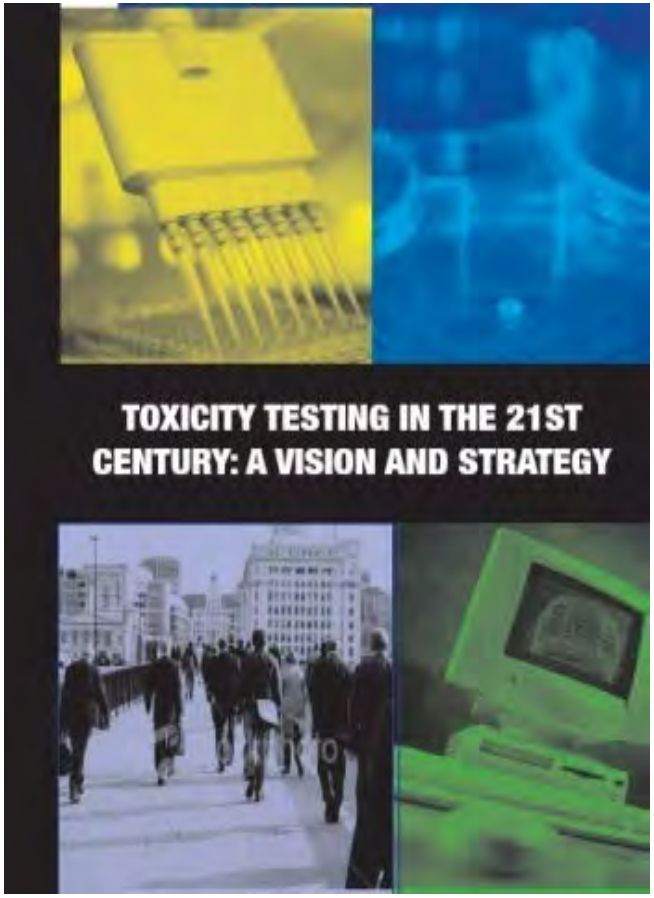


# Environmental Complexity

- A host of emerging drivers - from climate change, to children's health, to green chemistry, to urbanization - demand better information for better environmental and public health decisions.

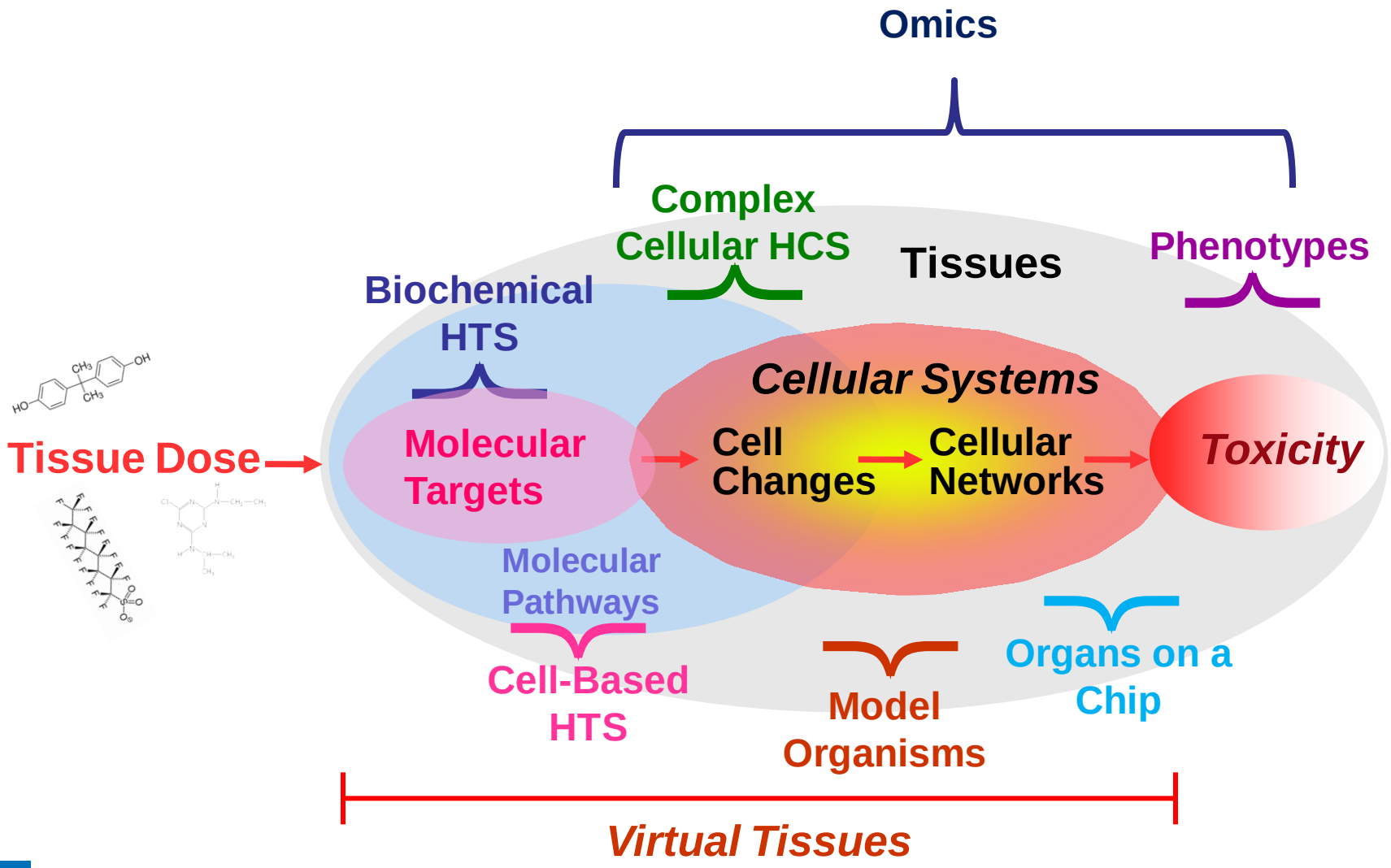
- (Applied) environmental science needs to be agile, adaptive, responsive, and anticipatory/predictive, delivering knowledge that is impactful, timely, and relevant to current and future environmental health challenges.

# National Academy Report (2007)




**Design a 'modern' toxicity testing program to assess potential human risks posed by exposures to environmental agents over a broad range of doses and compounds and to be in a position to use this information in quantitative human health risk assessment.**

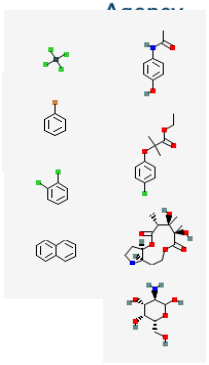
# Predicting Human Toxicity: A Grand Challenge



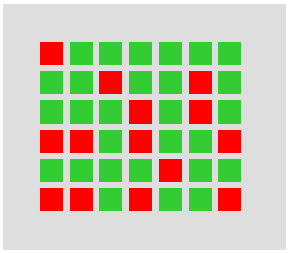
# The Pieces of the Puzzle

- Chemical Space
- Biological Space
- “Validation”
- Prioritization Tools
- Predictive Signatures
- Reverse Toxicokinetics
- High Throughput Risk Assessment
- Exposure Assessment
- Systems Models

# CSS CompTox Research

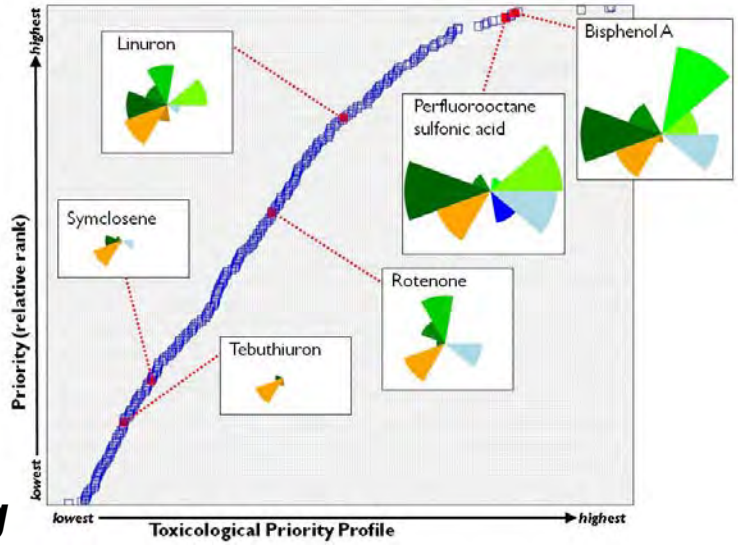


***Thousands of chemicals***



***High throughput biology and chemistry***

***Bioinformatics/ machine Learning***




***Predictive toxicology and exposure science***

**Features:**

-Less expensive
-More chemicals
-Fewer animals
-Solution Oriented

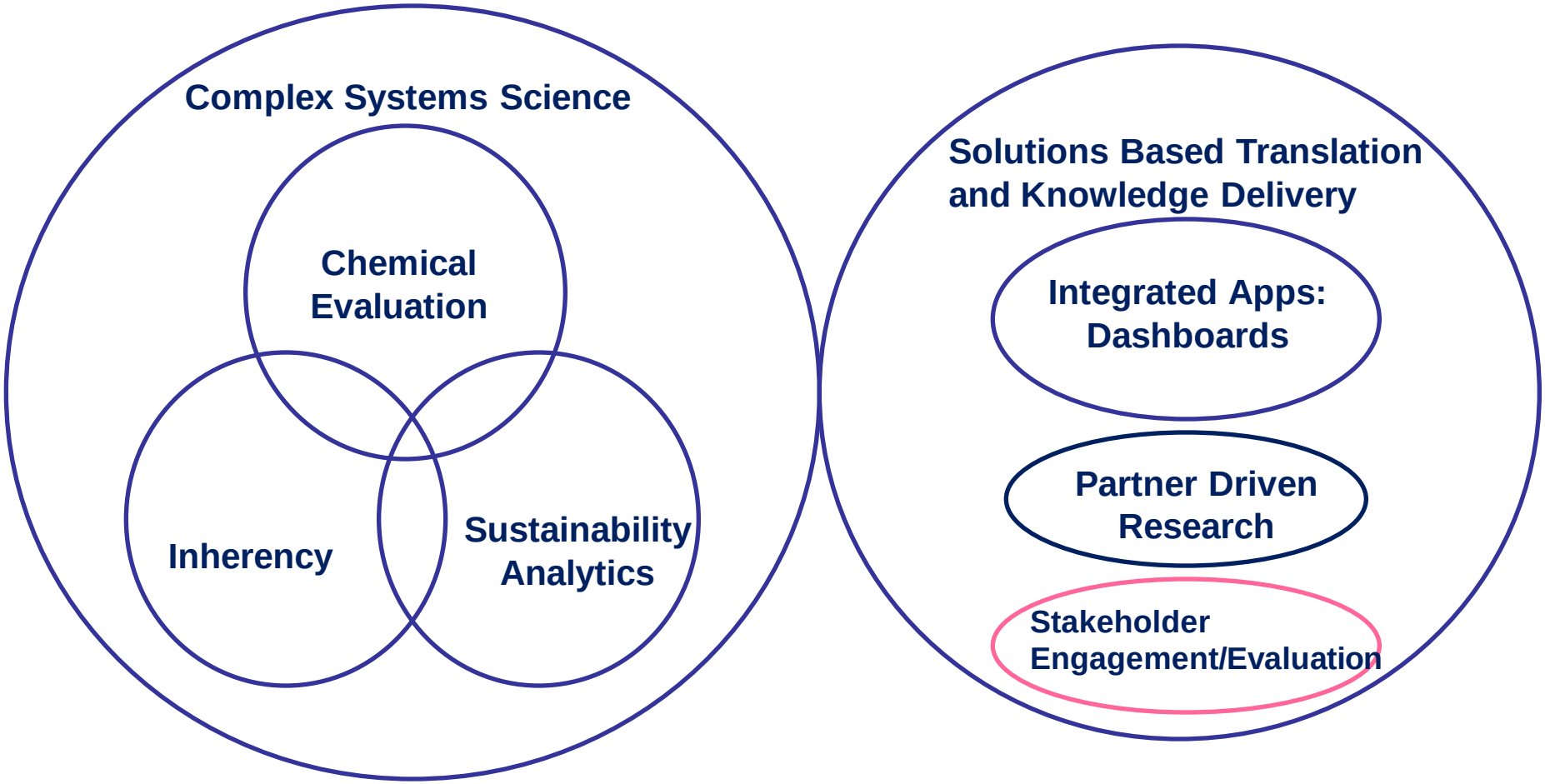
**-Innovative**
**-Multi-disciplinary**
**-Collaborative**
**-Transparent**

# Fast Forward

- Significant progress has been made in high throughput screening thousands of chemicals for potential endocrine hazard
- Predictive toxicology and systems models using a combination of biology, chemistry and statistics are required for risk characterization
- Initial models point the way to real-world applications
  - example EDSP21
- Further research needed:
  - More chemicals, assays, pathways
  - Systems-level models for hazard and exposure
  - Targeted testing approaches to follow up on prioritizations
  - High Throughput Risk Assessment

# CSS Integration Scheme: Research Themes

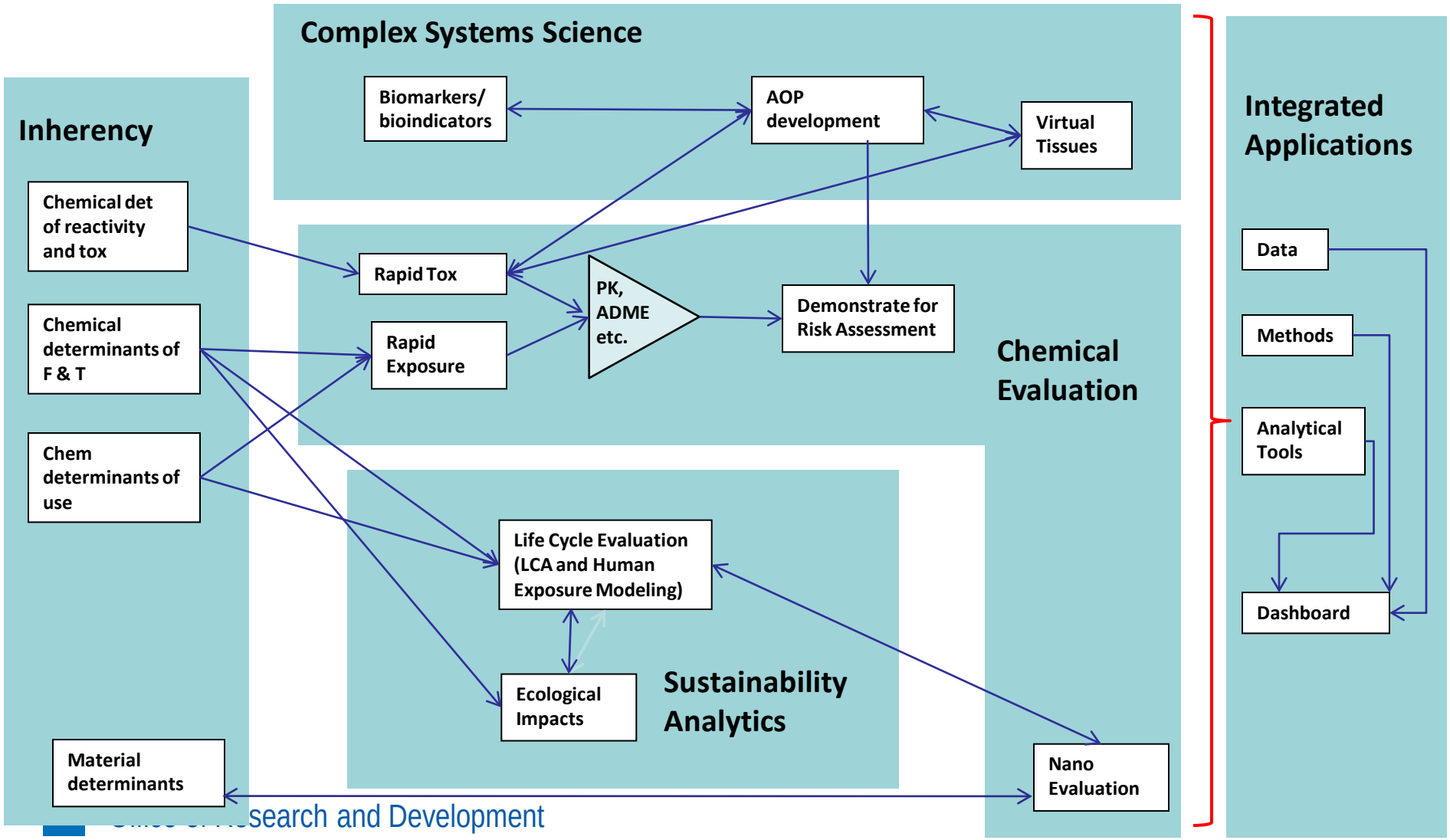
## Safe and Sustainable Chemical Use



# CSS Integrated Research Themes

- **Inherency:** Understand relationships between chemical characteristics and human health & environment impacts
- **Chemical Evaluation:** Improve chemical prioritization, screening & testing
- **Sustainability Analytics:** Develop models & tools to support more sustainable chemical design, manufacture, use & disposal
- **Complex Systems Science:** Predict adverse outcomes resulting from exposures to chemicals
- **Integrated Applications:** Provide accessible chemical information to support chemical safety decisions
- **Partner Driven Research:** Evaluate impacts of high priority chemicals
- **Stakeholder Engagement & Outreach**

# CSS Research Theme Connections



# Critical Tox21 Issues

- Cells don't get disease
- Not all compounds can be screened in HTS
- Need for xenobiotic metabolism
- Need to consider interactions between different cell types
- Need to extrapolate from acute to chronic exposure conditions
- How to measure human variability in sensitivity
- Need to be extrapolate from *in vitro* concentration to *in vivo* dose
- Need to identify human disease-associated pathways and useful assays for those pathways
- Need to integrate multiple data sources (e.g., *in vitro*, animal, human) and endpoints (e.g., HTS, 'omics, disease) into publicly accessible databases with appropriate tools for mining

# Success Depends On

- Well-characterized chemical libraries (identity, purity, concentration, stability)
- Well-characterized assays in terms of reliability and relevance
- Ability to incorporate xenobiotic metabolism
- Informatic tools to integrate and mine robust data from multiple sources
- Understanding the relationships between pathways and disease in animal models and humans
- Making the data freely accessible as quickly as possible
- Scientific outreach and training the next generation

# Validation?

- Performance-based analysis of weight-of-evidence and probabilistic Adverse Outcome Pathways (AOP) models identifying chemical hazard and risk for relevant pathways.

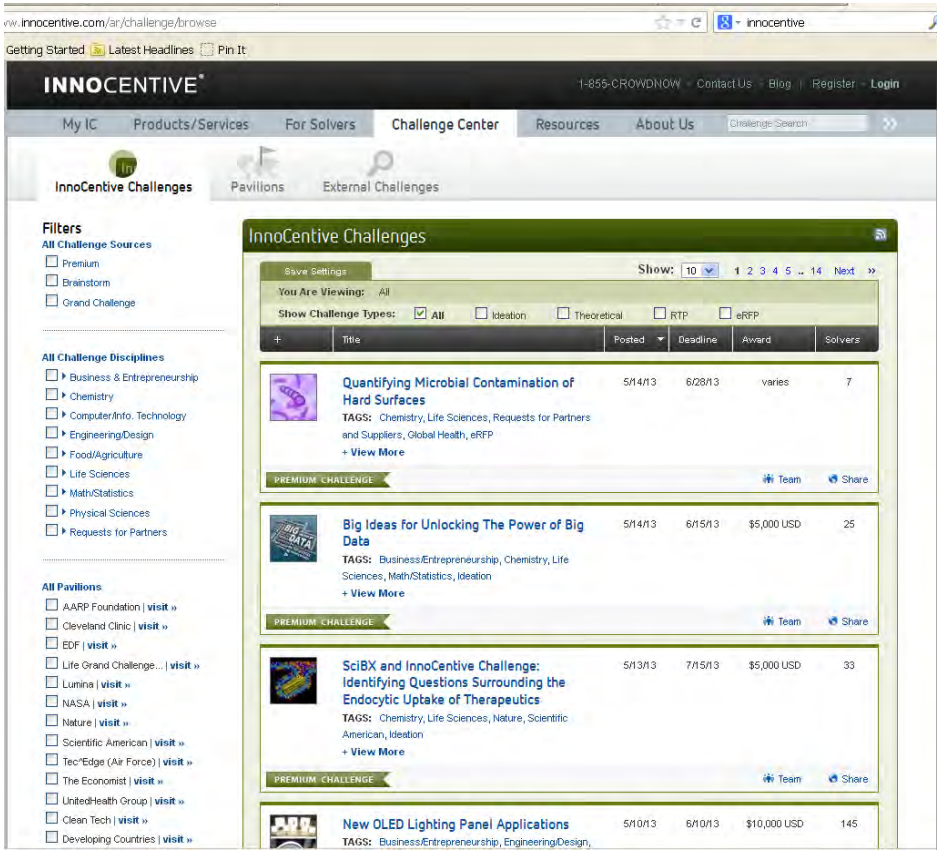
- Identify and incorporate other scientifically relevant information that confirms and improves Adverse Outcome Pathways (AOP) models identifying chemical hazard and risk for those pathways.

# CSS Outreach and Engagement Goals

- Effectively translate new chemical data and models so they are more understandable and usable to stakeholders.
- Increase stakeholder support for the usage of this new approach to prioritize chemicals for risk and to inform policy decisions made about the safety of chemicals.
- Increase stakeholder usage of the new data and models to prioritize chemicals for risk and to inform policy decisions.
- Work with each stakeholder group to determine how to qualify data for use and solicit input on data application.

# Outreach Strategies

- Offering incentives for innovation -- to develop ideas for using new data to inform decisions (TopCoder & Innocentive)
- Working with interested federal partners & external stakeholders to host workshops & trainings
- Promoting through online media, printed materials, news releases, CompTox communities of Practice etc
- EPA hosted trainings (workshops, summits, symposium, etc)
- Stakeholder Feedback & Evaluation- Focus Groups, surveys tracking usage of data, interviews



# Timeline

- September 2013 :Publicly release data through online Chemical Safety for Sustainability Dashboards and solicit feedback about Dashboard usability
- October 2013-February 2014: Workshops hosted by interested external stakeholders how to access data through Dashboards
- September 2013-April 2014: Request stakeholders develop applications for using data to inform chemical risk assessments
- May 2014: EPA Data Summit-Present Computational Toxicology data applications to inform chemical safety risk assessments

***Pictured: 2009 ToxCast Data Summit***

# Chemical Safety for Sustainability: Additional Information and Products

- External web page: http://epa.gov/research/chemicalscience/
- Intranet: http://intranet.ord.epa.gov/nrp/css
- Chemical safety product database: http://intranet.ord.epa.gov/nrp/css/epa-chemical-safety-research-products
- Fact sheets: http://epa.gov/research/priorities/research-factsheets
- Publicly available databases: http://www.epa.gov/research/mmtd/chemsafe.htm
- Chemical safety E-newsletter: http://epa.gov/research/chemicalscience/news.htm