United States Environmental Protection Agency

Chemical Safety for Sustainability: EPA Research to Meet 21st-Century Needs

Presentation to the Science Advisory Board

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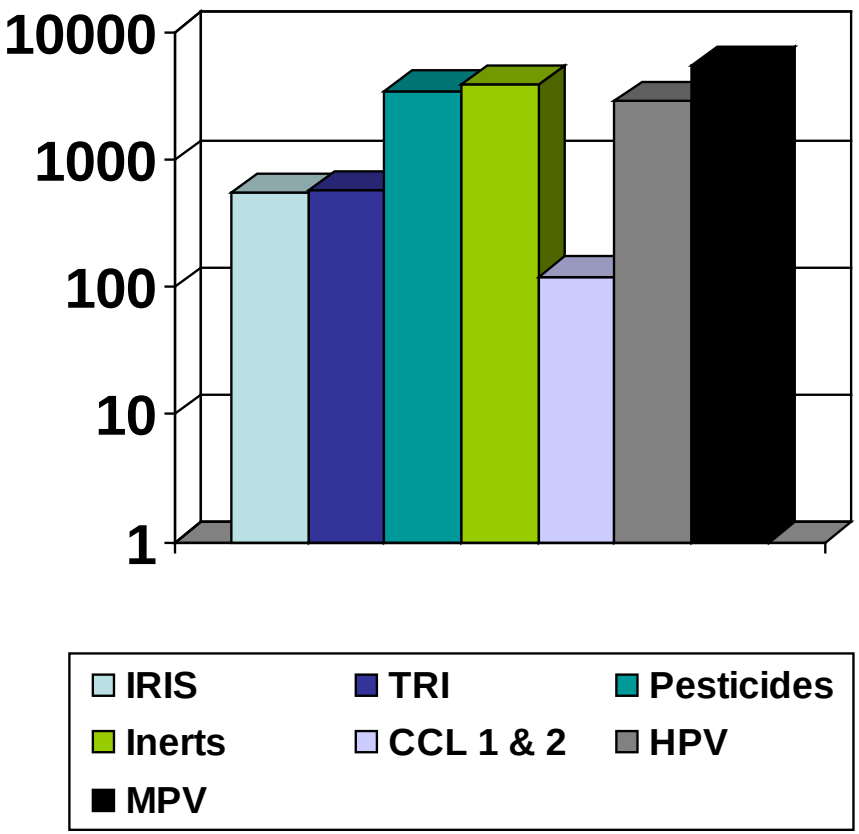
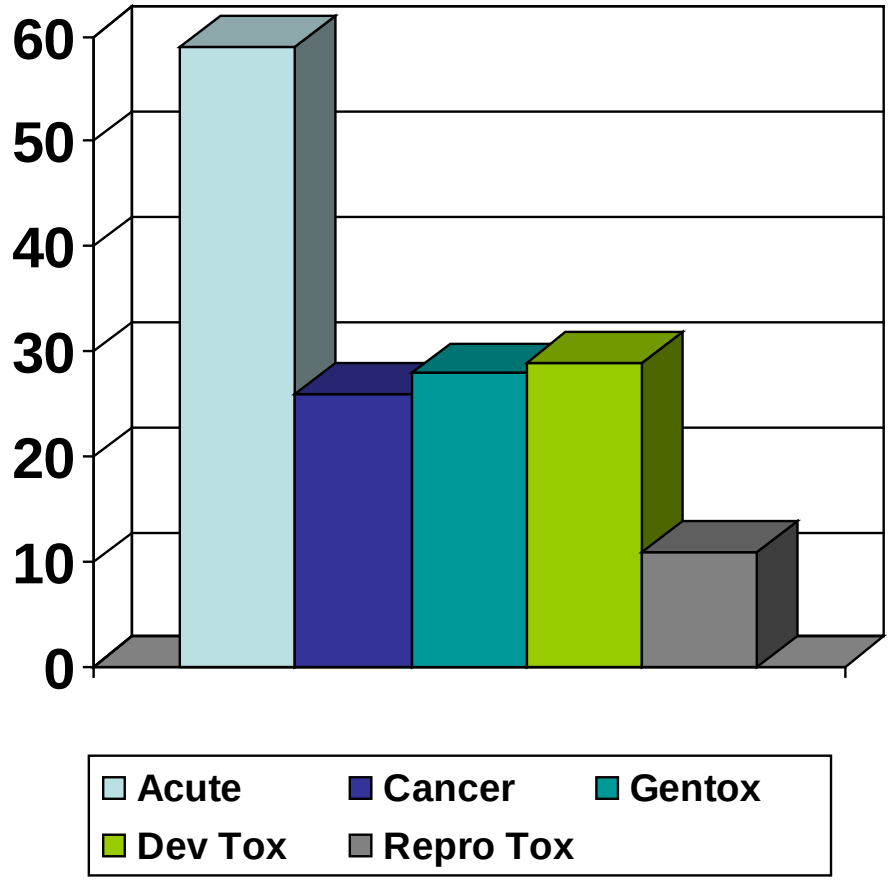
3 March 2011

The Chemicals Situation

Many Chemicals



Little Data (%)



Judson, et al *EHP* (2009)

United States Environmental Protection Agency

Problem Statement

Although chemicals are essential to modern life, we lack innovative, systematic, effective, and efficient approaches and tools to inform decisions that reduce negative environmental and societal impacts of chemicals.

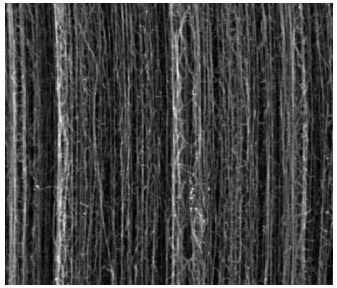
Vision

EPA science will lead the sustainable development, use, and assessment of chemicals by developing and applying integrated chemical evaluation strategies and decision support tools.

Why Is It Time to Change How EPA Conducts Chemicals Research?

Because new technology and greater knowledge give us the opportunity to

. . .introduce new substances, such as carbon nanotubes . . .



Source: NASA

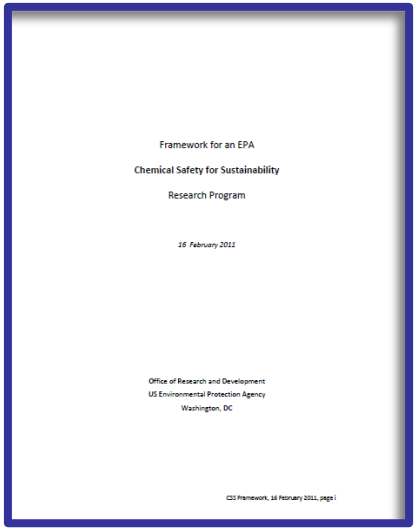
. . . in a more environmentally sustainable way than we were able to do with substances such as asbestos in the 20th century . . .

Source: ATSDR

. . . and provide more efficient tools for assessments.

HTS Robotic Platform

CSS Framework


Framework for an EPA

Chemical Safety for Sustainability

Research Program

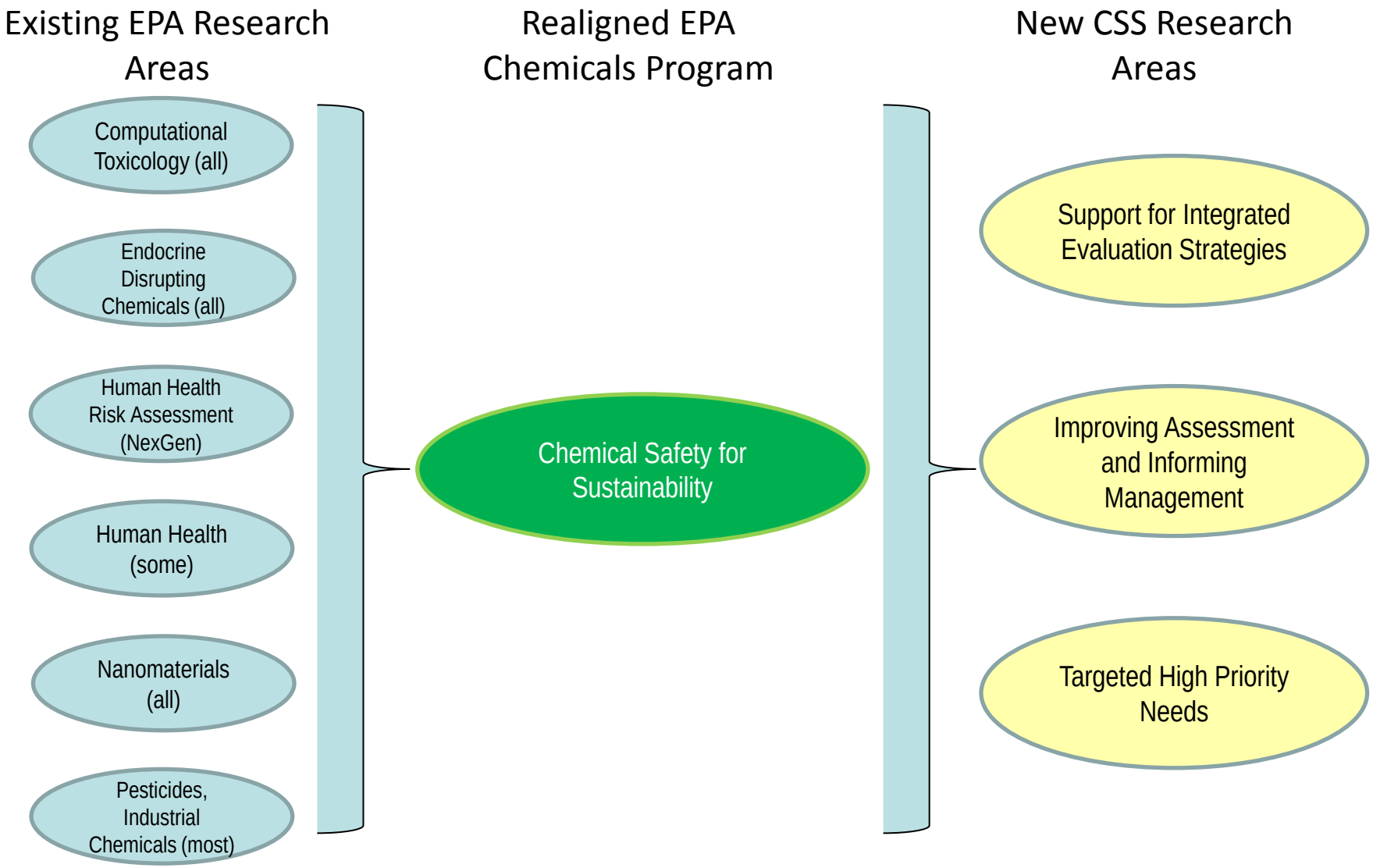
16 February 2011

Office of Research and Development
US Environmental Protection Agency
Washington, DC

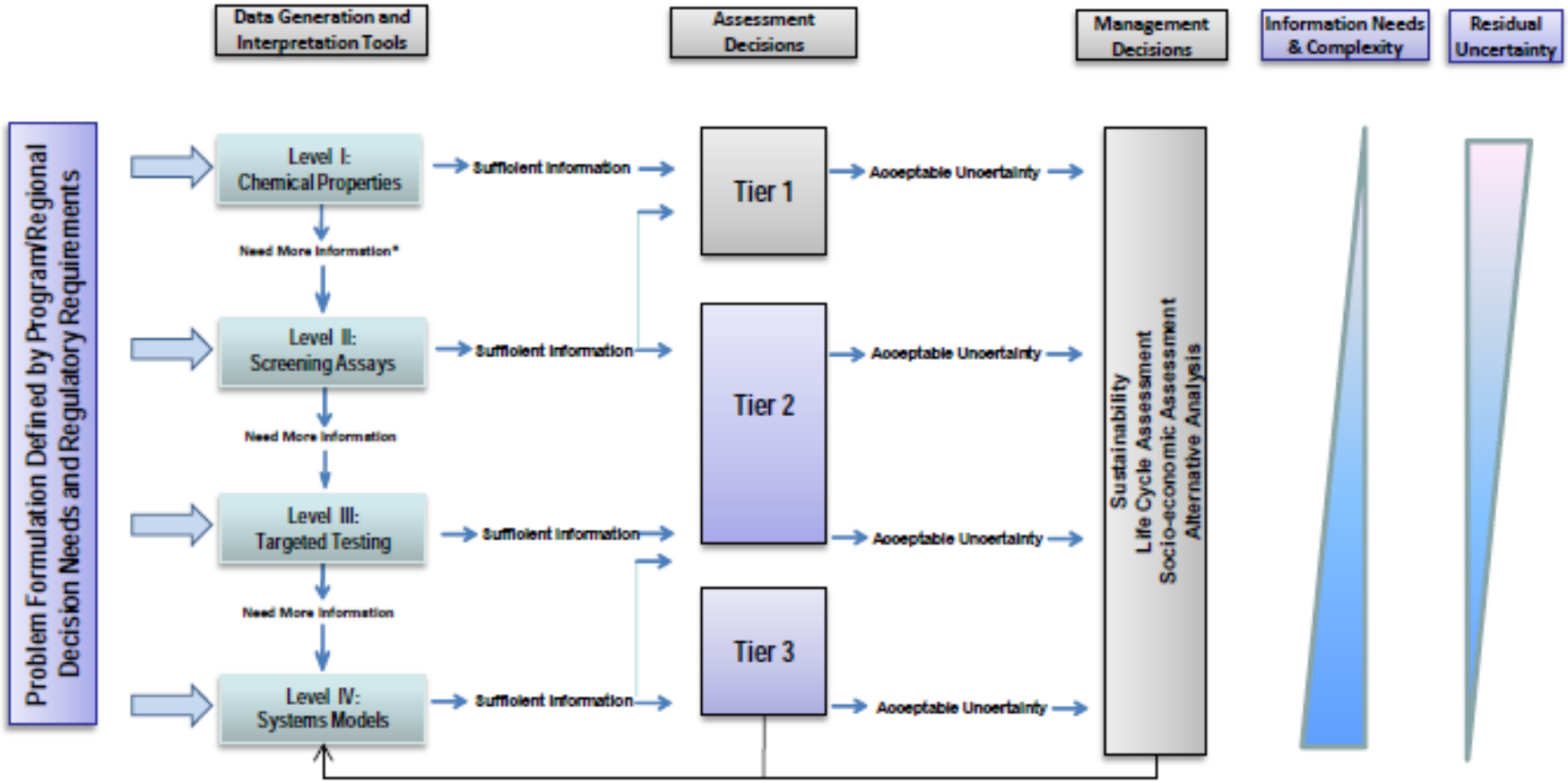
CSS Framework, 16 February 2011, page i

- Developed in consultation with EPA Program Offices and Regions, 3/2010-10/2010
    - Formerly referred to as Safer Products for a Sustainable World
    - Articulates research needs and key science questions to address
- Drivers
    - Broadly applicable and integrative predictive approaches that cover the chemical's life cycle
    - Efficient and effective evaluation assessment and management tools
    - Fulfilling time critical regulatory mandates
- Composed of all or partial elements of 6 current MYPs
    - FY 12 PB: 292 FTEs; $95M
- CSS Implementation Team has been formed to guide Research Action Plan development
- Research Action Teams composed of ORD scientists now developing concepts for integration of activities
- Current portfolio has been mapped to CSS Research Matrix

Aligning EPA's Chemicals Research Activities



CSS Conceptual Model



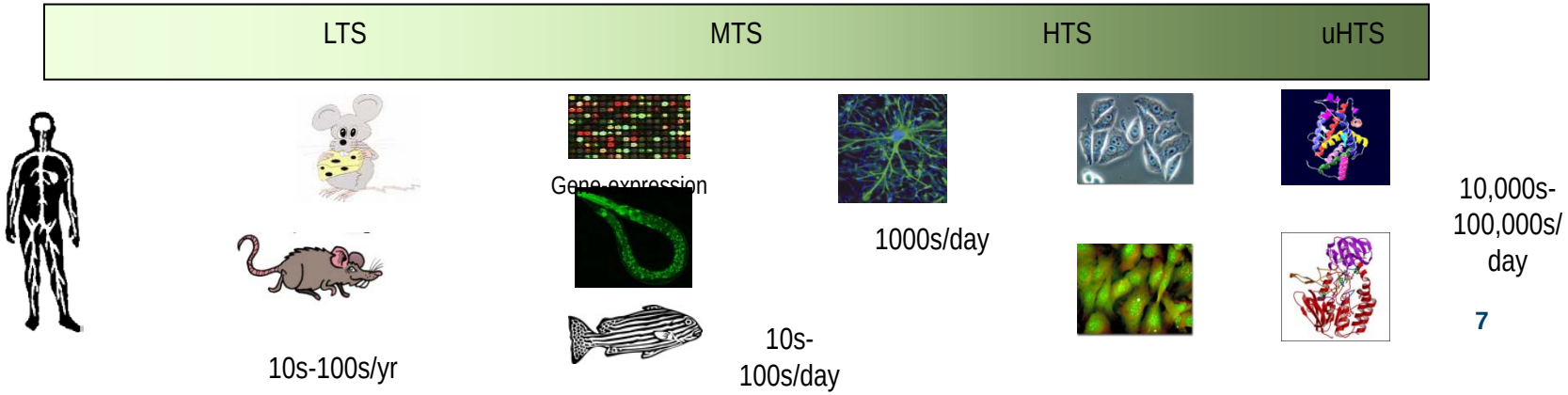
CSS Research Area 1:
Developing the Scientific Knowledge, Tools and Models for Integrated Evaluation Strategies

Problem

- Over 200,000 chemicals registered in European REACH; 75,000 chemicals in TSCA with very few evaluated for safety
- EPA cannot efficiently or effectively assure the safety of all chemicals using currently available evaluation and assessment approaches

Goal

- Develop the tools needed for efficient approaches that allow the integrated evaluation, assessment and management of thousands of chemicals over their life cycle



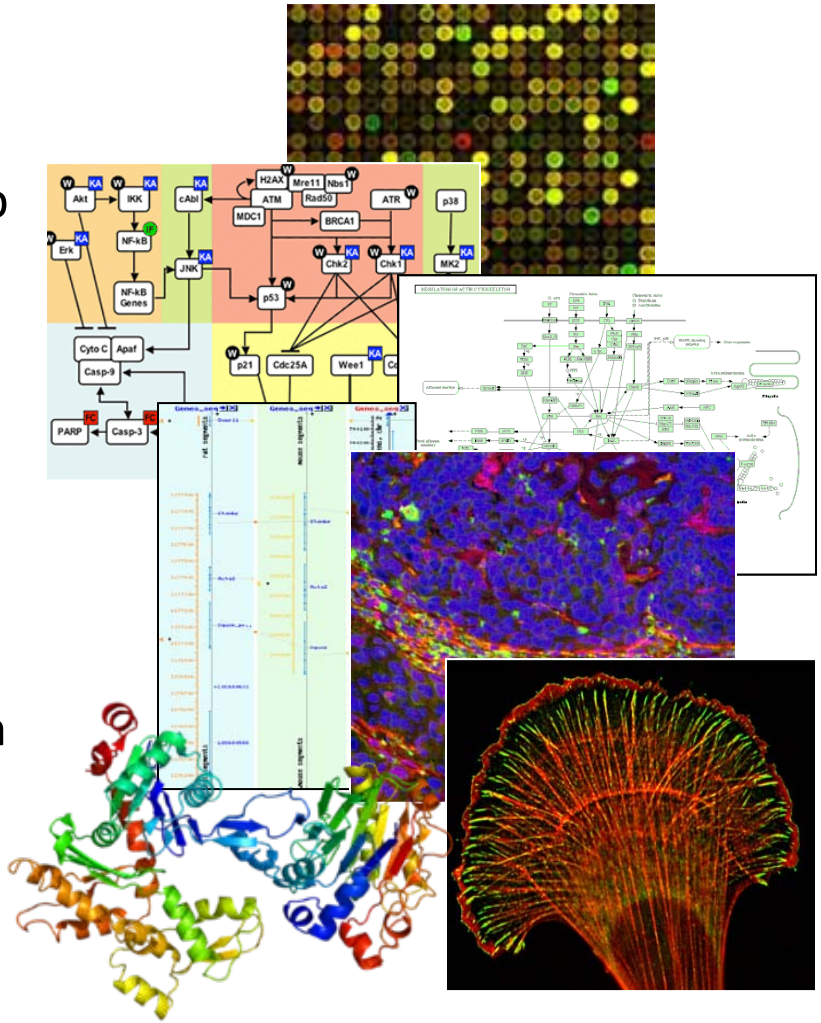
CSS Research Area 2:
Improving the Relevance of Assessment and Management Methods for Chemical Safety

Problem

- Our current assessment and risk management approaches cannot keep up with environmental decision-making needs

Goals

- Integrate next-generation risk assessment approaches across the Agency
- Facilitate management decisions that can be made faster and more efficiently, while reducing uncertainties about risks.



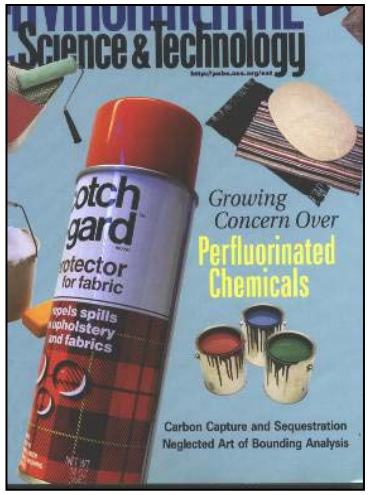
Photos courtesy of MIT Koch Institute

CSS Research Area 3:
Targeting High-Priority Research Needs for Immediate and Focused Attention

Problem. EPA has near-term critical research needs that are essential to fulfilling regulatory mandates.

Goal. A process to ensure that EPA's highest-priority needs are incorporated into the CSS program.

- Needs will be determined by annual (or regular) discussions between the senior managers of the CSS program and those of the EPA program and regional offices, informed by input from EPA stakeholders.



Recent Accomplishments

- Cumulative effects research on EDCs confirmed NAS recommendation that focus of assessments should be on disruption of same health outcome and not pathways that lead to it
- Triclosan-mediated reduction of thyroid function demonstrated following brief exposure of juvenile or weanling rats
- Multi-laboratory application of molecular and systems biology to study effects of EDCs on small fish populations and develop mechanism-based predictive models
- Development and public release of databases such as ACToR and ToxRefDB
- Completion and publishing of ToxCast Phase 1
- Comprehensive environmental assessment case studies for nano TiO2 (final) and silver (external review draft)
- Ongoing collaboration with industry on LCA for nano-enabled Li-ion batteries.

Anticipated Accomplishments

- Completion and Publication of ToxCast Phase II
  - 700 additional chemicals in broader suite of assays; includes ~100 failed pharmaceutical compounds
  - First generation predictive signatures for repro, developmental and cancer outcomes

- Screening 1000 additional chemicals through endocrine related ToxCast assays (e1k)
  - includes large number of reference chemicals to determine relevance of assays

- Development of screens for thyroid disruption and phthalates MOA

- Characterization of wastewater treatment plants as sources of EDCs and persistence of EDCs through land application of biosolids

- PFCs: Methods for characterizing in surface and ground waters and evaluation of molecular signals and pathways altered in mammals by exposure

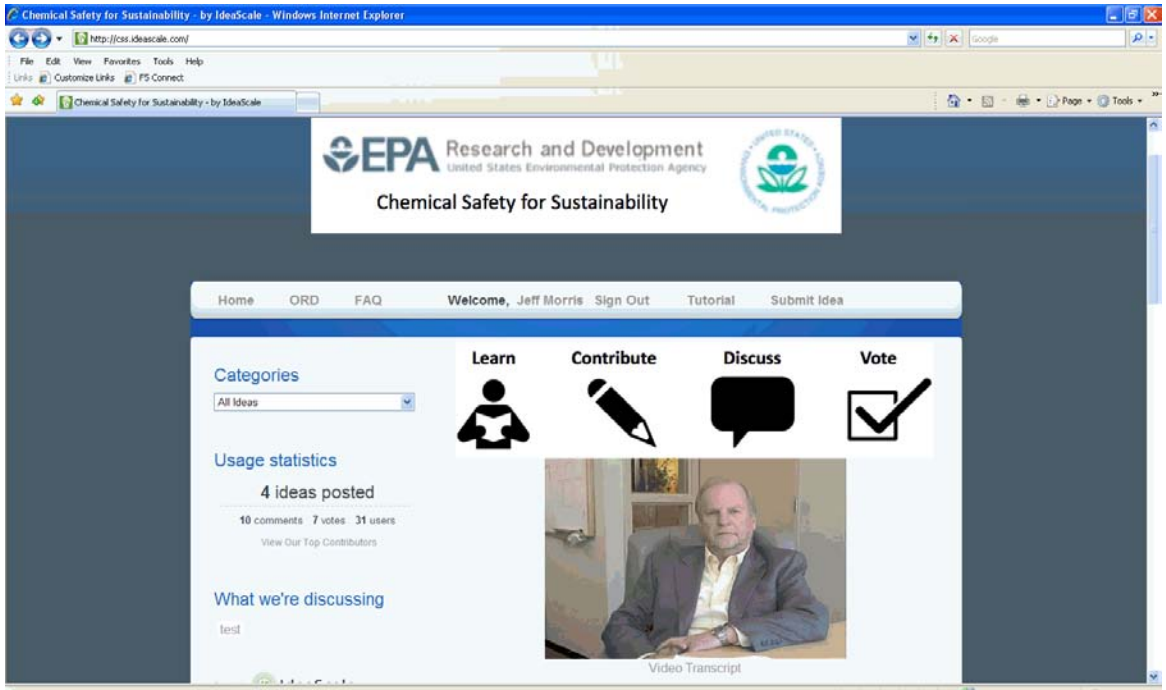
- Source-to-effects evaluation of nano-scale cerium oxide used as diesel fuel additive.

External Stakeholder Input: Providing Comments, Generating Ideas

We have created a web site to serve as a forum for reading, providing and responding to comments on the CSS research program.

css.ideascale.com

- Open February 24- March 24
- Three-fold objective: (1) *inform stakeholders about research framework,*
  (2) solicit input, and
  (3) generate ideas on how to best design, implement, and transparently communicate chemicals research at EPA.



FY 2012 Budget Highlights

Chemical Safety for Sustainability (CSS)

(FY 2010 Enacted $77.8M, FY 2012 PB $95.7M, Change +$17.8M)

- The CSS program focuses on developing enhanced chemical screening and prioritization approaches that enable smarter context-relevant chemical assessment and risk management. Included in this research EPA will:
  - Develop new scientific information and tools to enable green chemistry that will lead to the development of safer chemicals and more sustainable electronic products ($5.4M)
  - Develop next-generation computational toxicology tools to speed and facilitate implementation of the Agency's Endocrine Disruptor Screening Program ($2.0M)
  - Accelerate the latest state of the art technologies to assess and manage environmental endocrine disrupting chemicals (EDCs) by complementing EPA's in-house research effort through STAR grants to academic institutions ($7.0M)
- The completion of biotechnology research for management of insect resistance in genetically modified crops allows for a reduction of $1.4M.
- A $1.5M reduction to human health research on screening assays and predictive approaches reflects a difficult choice that must be made in the face of current fiscal realities.

Potential Game Changers

Nanomaterials - Evaluating the fate/transport, exposure and hazard potential before they are introduced into the environment by

- Determining what material properties drive hazard and/or exposure; applying green chemistry approaches to reduce potential impact and developing cellular and non-cellular in vitro assays to target in-depth testing

Computational Toxicology – Employing state of the science approaches to construct predictive signatures of toxicity

- Providing basis for more intelligent testing approaches that reduces reliance on use of animals, prioritizes chemicals for evaluation and allow s chemicals to be evaluated for those endpoints that appear to be most likely to be induced while maintaining adequate safeguards of human health and the environment

Life Stage Susceptibility to Chemical Exposure - Recognizing that infants can be more vulnerable to toxicants, and realizing that reducing exposure can save lives,

- Develop and apply new scientific tools that link chemical properties to biological activities, translate the impact on biological activities to diseases of children such as birth defects, infant mortality and morbidity, and asthma; and provide knowledge to design safer alternative chemicals.

United States
Environmental Protection
Agency

Example of a **CSS Problem**: Life Stage Impacts from Chemicals

Agarwal, et al. *"The average country-level decreases in various categories of TRI concentrations saved an excess of 13,800 infant lives from 1989 to 2002."**

Yet every year, hundreds of millions of pounds of toxicants continue to be emitted into the nation's air, water, and land.**

A CSS Challenge:

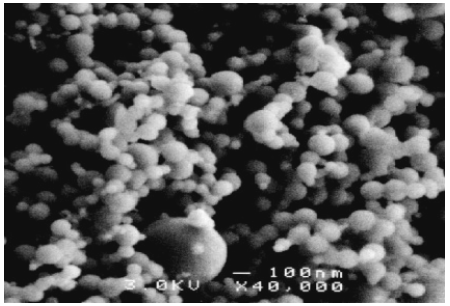
- Recognizing that infants are more vulnerable to toxicants,
- and realizing that reducing exposure can save lives,
- how to develop and apply new scientific tools that identify: (1) what chemicals/chemical properties are causing the most impact, (2) how those impacts can best be addressed to reduce environmentally induced infant mortality and morbidity, and (3) what factors should be considered in designing safer alternative chemicals.

*Nikhil Agarwal, Chanont Banternghansa, and Linda T.M. Bui,"Toxic Exposure in America: Estimating fetal and infant health outcomes from 14 years of TRI reporting," *Journal of Health Economics* 29 (2010) 557-574.
**US PIRG Report, executive summary (22 January 2003).

Example of **CSS Progress**: An Integrated, Multi-tier Health Effects Testing Approach for Nanomaterials

1. Physicochemical Characterization

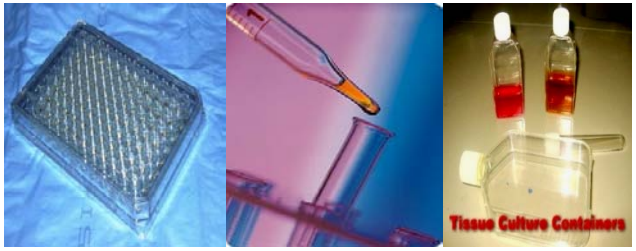
Selected specific nanoparticle types based on EPA and international (OECD) priorities



Well-characterized manufactured nanomaterials (vertical and horizontal testing)

2. Alternative Test Methods

(Non-Cellular and Cellular Based Assays)

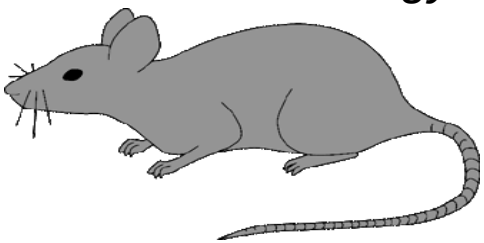


Collaborations
(NCCT; NTP; OECD)

-Screen/Rank
-Design *In Vivo* Testing

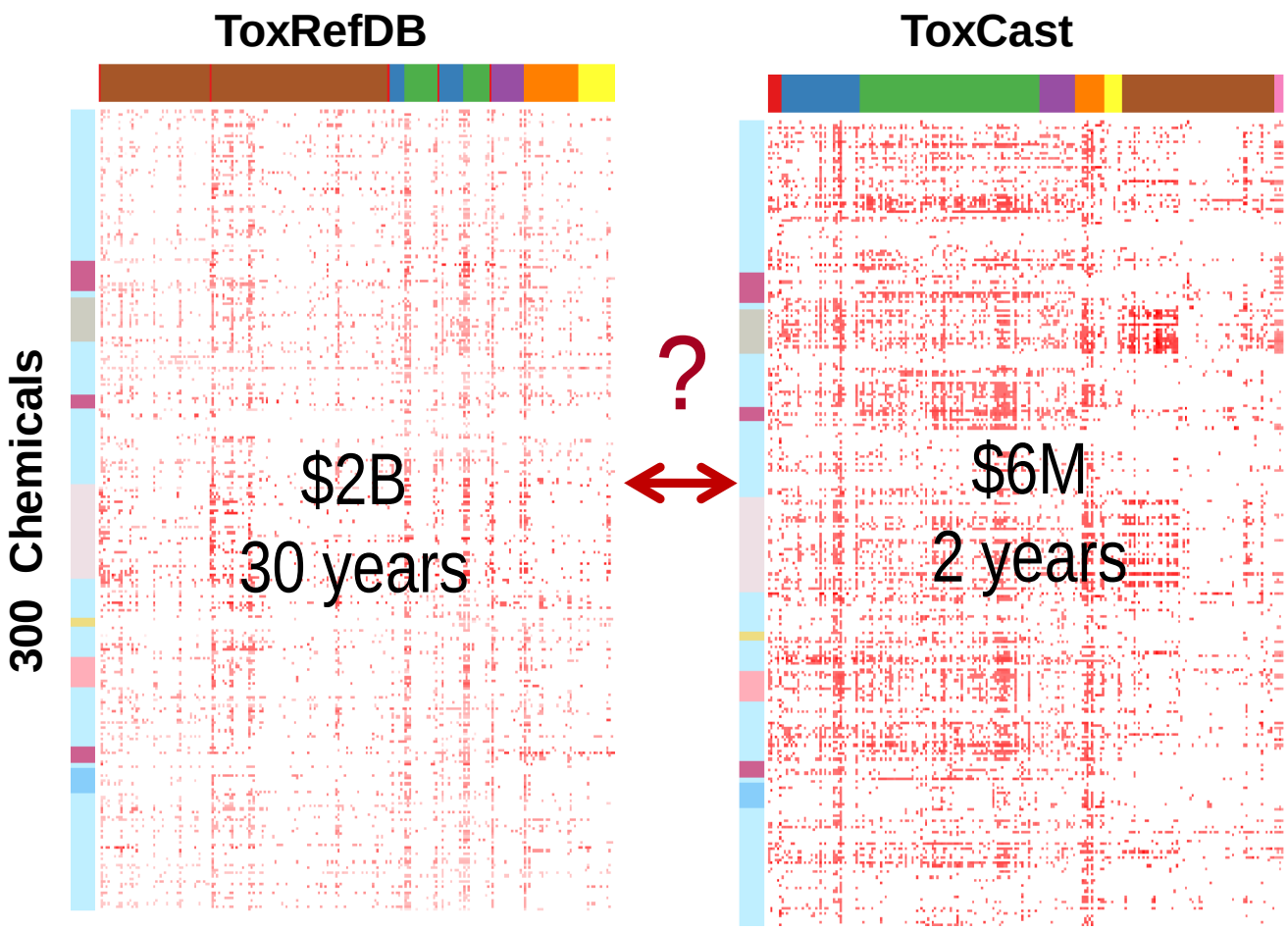
-Identify and Validate Alternative *In Vitro* Tests Predictive of *In Vivo* Toxicity

3. In Vivo Toxicology



Collaborations
(NCCT; NTP; OECD)

Example of **CSS Potential**: ToxCast enabling more chemical assessments using less resources



Traditional Toxicology

Computational Toxicology