

US EPA ARCHIVE DOCUMENT



The Next Generation of Risk Assessment Program: Overview and Invitation to Engage **Dr. Ila Cote**

U.S. EPA, Office of Research and Development



Advancing the Next Generation of Risk Assessment

Program Overview

Nex  **Gen**



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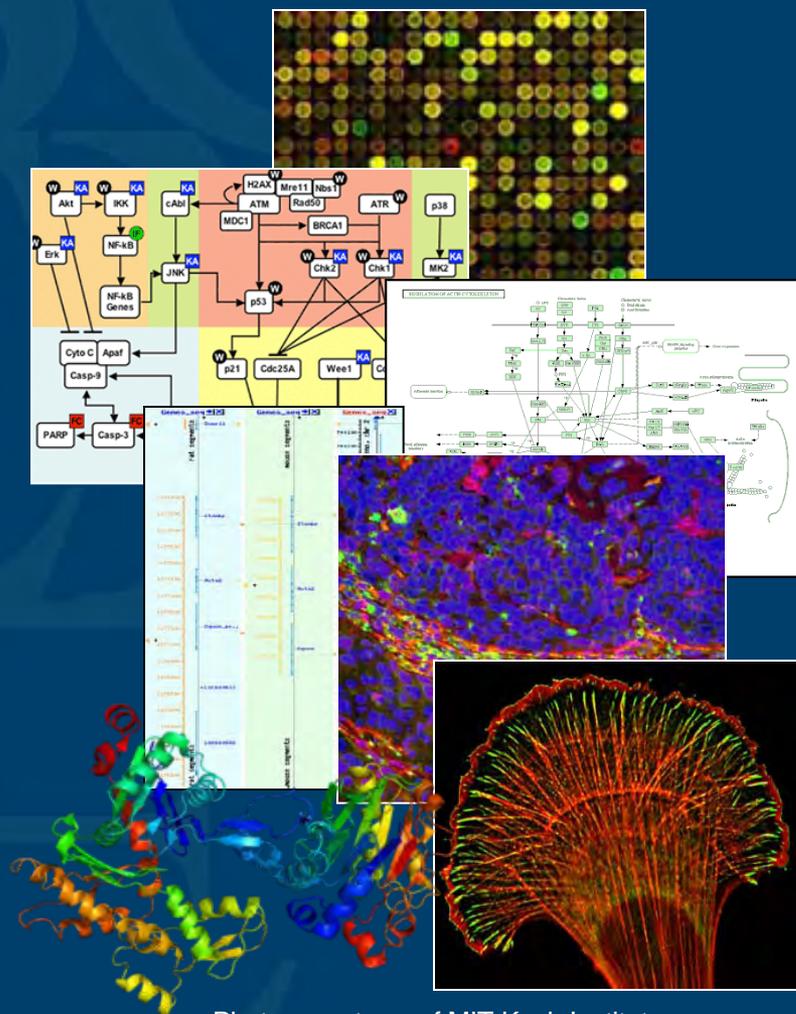
NexGen Partners

- US Environmental Protection Agency, Office of Research and Development
- National Institutes of Environmental Health Sciences & National Toxicology Program
- Centers for Disease Control & Agency for Toxic Substances and Disease Registry
- NIH Chemical Genomics Center
- California's Environmental Protection Agency, Office of Environmental Health Hazard Assessment

What is NexGen??

Program Goal:

To advance risk assessment science via incorporation of recent progress in molecular systems biology



Drivers for Change

- Scientific revolution in biology – most is not used in risk assessment
- In the European Union –
 - REACH ~ 120,000 chemicals
 - Emphasis on “non-standard” data for risk assessment
- In the United States –
 - Several NRC reports and workshops
 - Tox21 – 10,000 chemicals tested in biotech assays the next few years
 - EPA’s Chemical Safety and Sustainability Initiative

Objectives of NexGen

- Pilot a NexGen Framework
- Refine bioinformatics systems for knowledge mining and creation to serve risk assessment.
- Develop prototype health assessments
 - refined through discussions with scientists, risk managers, and stakeholders
 - responsive to the context of risk.

Draft Paradigm - NexGen Risk Assessments

Molecular Biology Informed; Responsive to Risk Context

Tier 1 Assessments

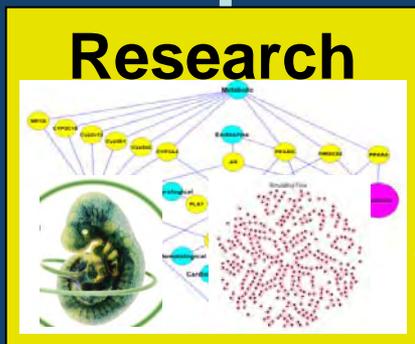
- Screening & prioritization
- Thousands of chemicals
- Unknown hazard but potential exposures
- High-throughput & QSAR-driven
- Molecular & cellular mechanisms
- Minimize false negatives

Tier 2 Assessments

- Narrow scope decision-making
- Hundreds of chemicals
- Limited hazard &/or exposures
- Add med. throughput/high content assays
- Add tissue/organism level integration
- Science-based defaults & upper confidence limits

Tier 3 Assessments

- Major regulatory decision-making
- Dozens of chemicals
- Known hazards & nationwide exposures
- Add all other relevant assays
- Add in vivo bioassay, clinical & epidemiology
- Best estimates of risk, probabilities, uncertainties



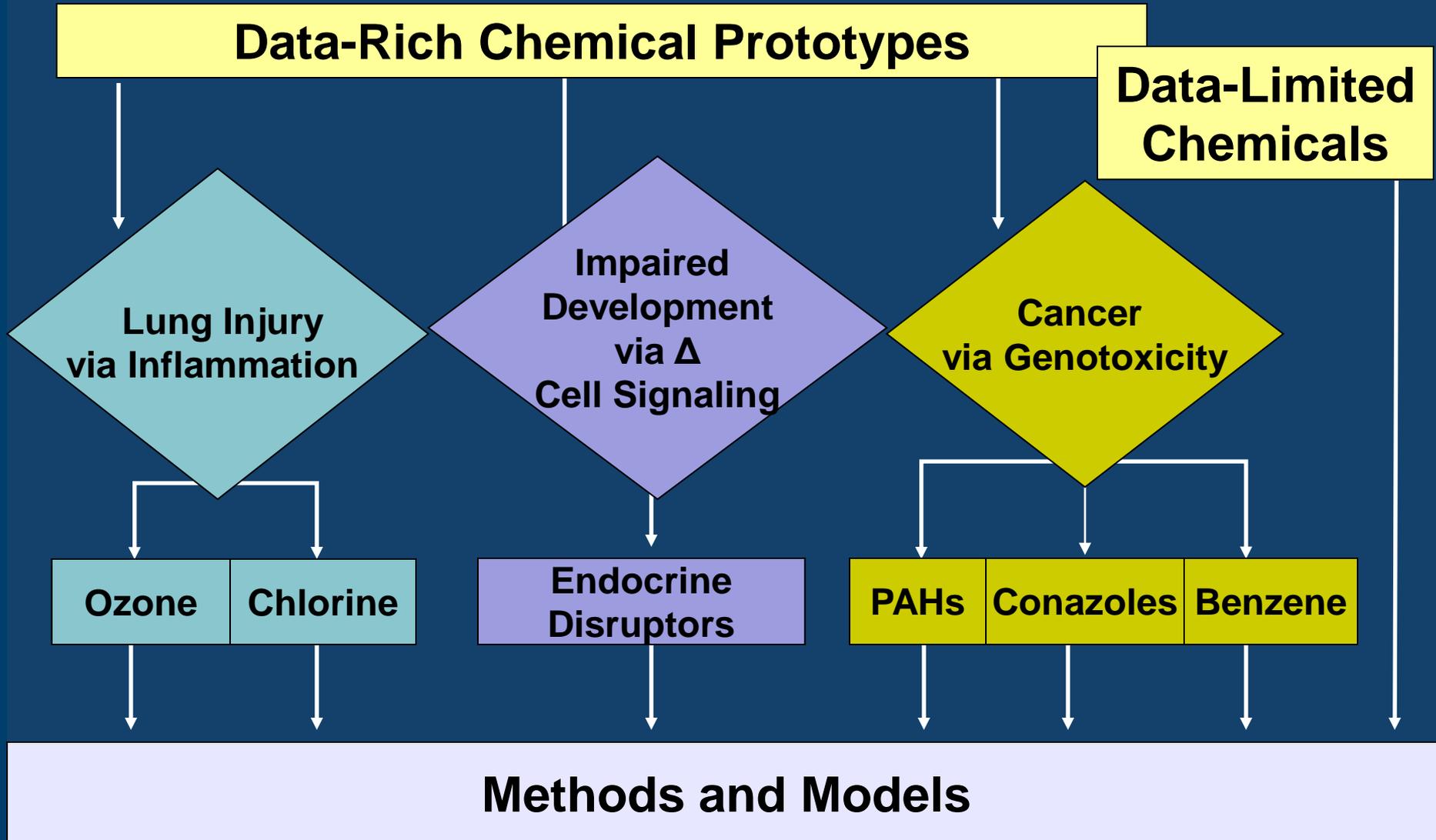
➔ Input to Decision-making

➔ Testing, Research, Assessment Loop

Questions to be Tackled

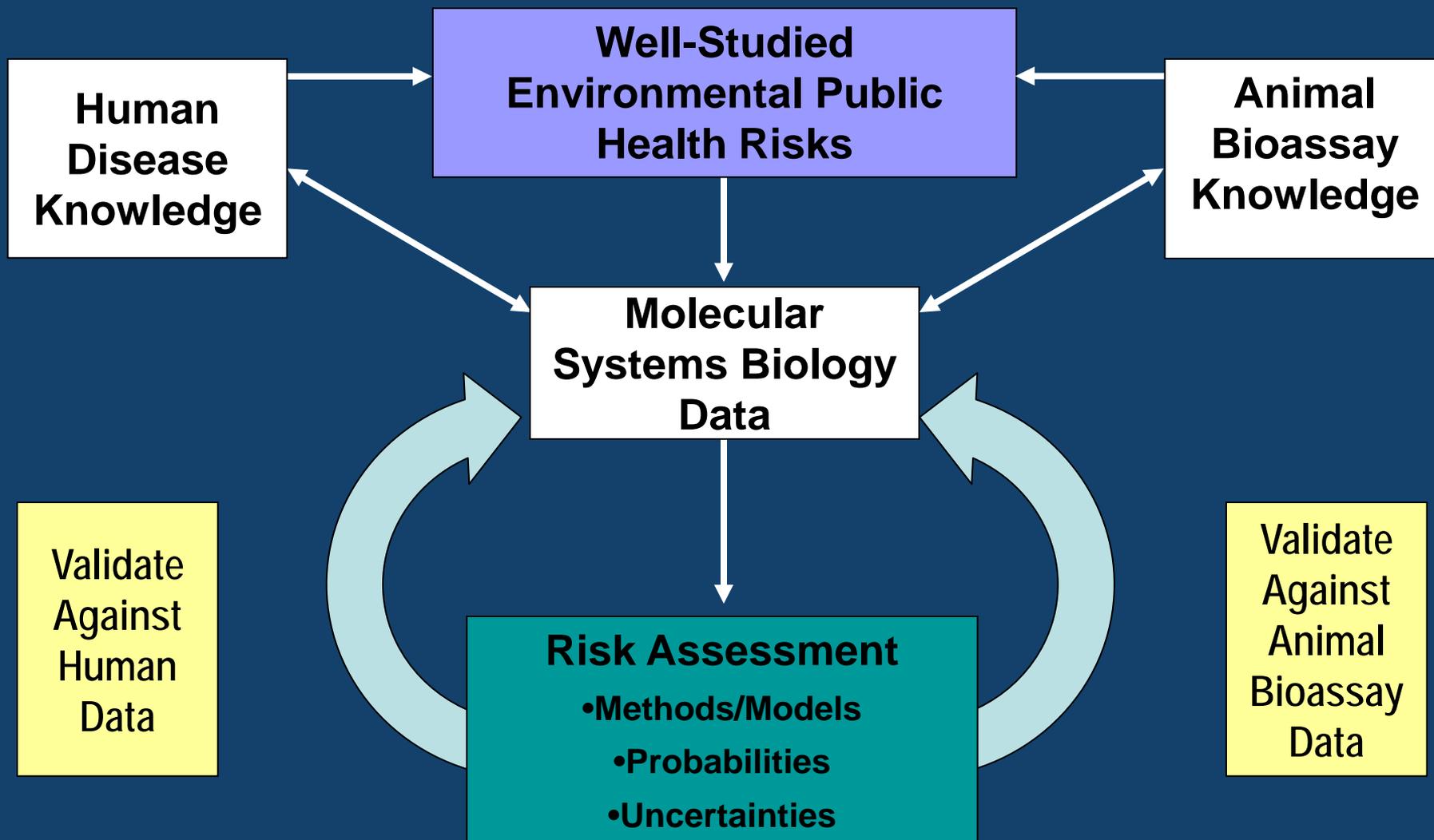
- Identify specific disease signatures?
- Estimate relative potencies based on molecular events?
- Improve our understanding of currently problematic issues:
 - responses at environmental concentrations,
 - inter- and intra-species variability, and
 - mixtures exposures and other stressors?
- Better characterize human risks?

Overview of Projects



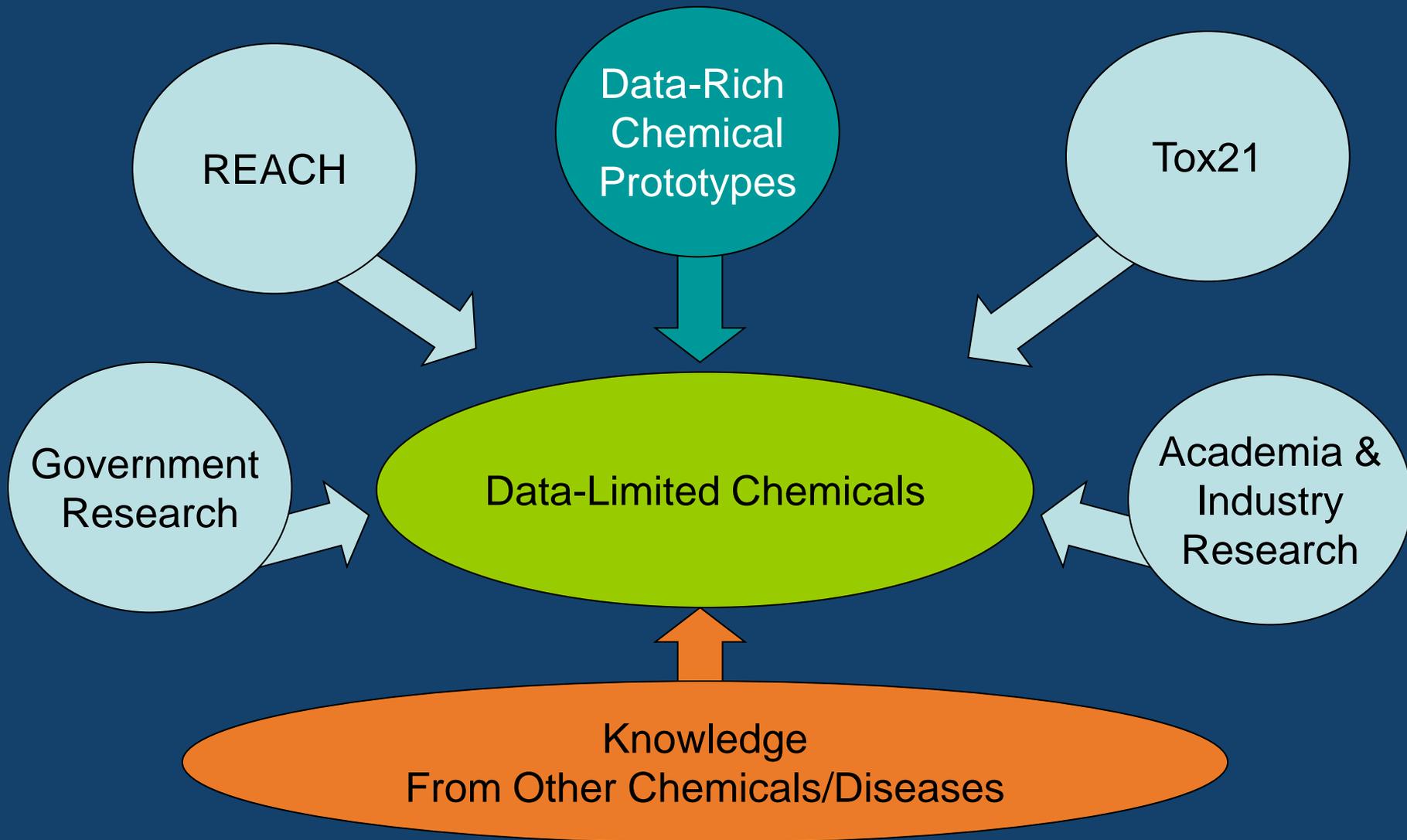
General Approach – Data-Rich Chemicals

Reverse Engineer Prototypes



General Approach – Data-Limited Chemicals

Forward Engineer Prototypes





NexGen

The Prototypes Workshop

November 1-3, 2010
Research Triangle Park, NC

Data-Rich Prototypes

The goals for the first two days were to:

- Refine early-stage prototype concepts
- Diversity of opinions vs. consensus
- Summarize options for expanded future work and research needs.

Data-Limited Chemicals

The goals of the third day of the workshop were to:

- Identify and discuss a wider variety of new data, methods, and knowledge.
- Consider how information from new approaches may augment, extend, or replace traditional data in health assessment.
- Summarize options for expanded future work and research needs.

November Workshop Themes

Some themes heard:

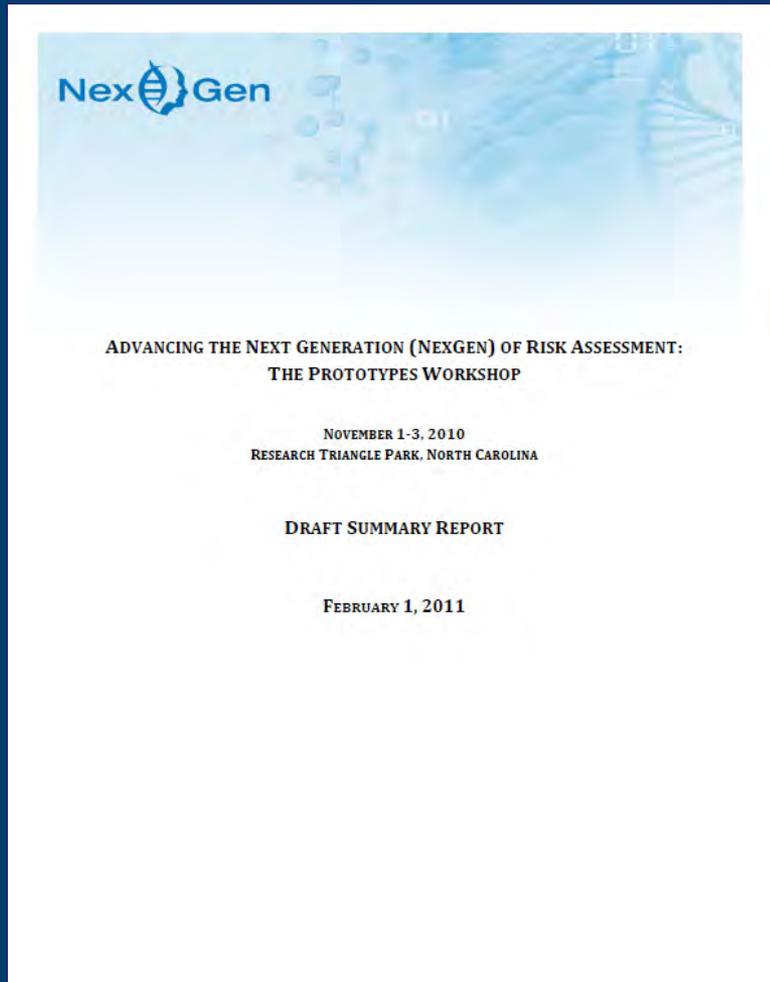
- ✓ Develop specific plans for what molecular and systems biology approaches could be utilized in the near term.
- ✓ Start using approaches as they currently exist and recognize that these approaches are iterative and will continue to develop in stages.
- ✓ More broadly elucidate networks or related pathways that serve as signatures.
- ✓ Mine the literature and molecular biology databases, and evaluate the weight of evidence for various pathways.

November Workshop Themes

Themes heard (continued):

- ✓ Use data-rich chemicals to extrapolate mechanisms and responses for data-limited chemicals when feasible.
- ✓ Develop approaches that incorporate population variability and susceptibility at environmentally relevant exposures.
- ✓ Obtain data on a series of standardized complex mixtures and develop approaches for analysis.
- ✓ Integrate and compare data sets (e.g., epidemiology, in vitro) in a systems biology approach to develop integrated models of human risk.

November Workshop Report



- Draft summary report:
<http://epa.nexgen.icfi.com>
- For updates on NexGen:
 - <http://epa.gov/risk/nexgen>
 - User-friendly articles & videos;
 - Selected technical papers
 - Links to other web sites



NexGen

Public Dialogue Conference

February 15 & 16, 2011
Washington, DC

Purpose of Conference

We want to provide you an opportunity to learn about the NexGen program in its early phases and to ask questions.

We want to hear your ideas about the challenges we face, your thoughts on the path forward.



Conference Participants

- Who is attending?
 - Public interest groups, societies, and other NGOs
 - Industry
 - Federal agencies
 - State agencies
 - Academics
 - Media/press
 - Interested public
- Complete list of participants in your workshop folder.

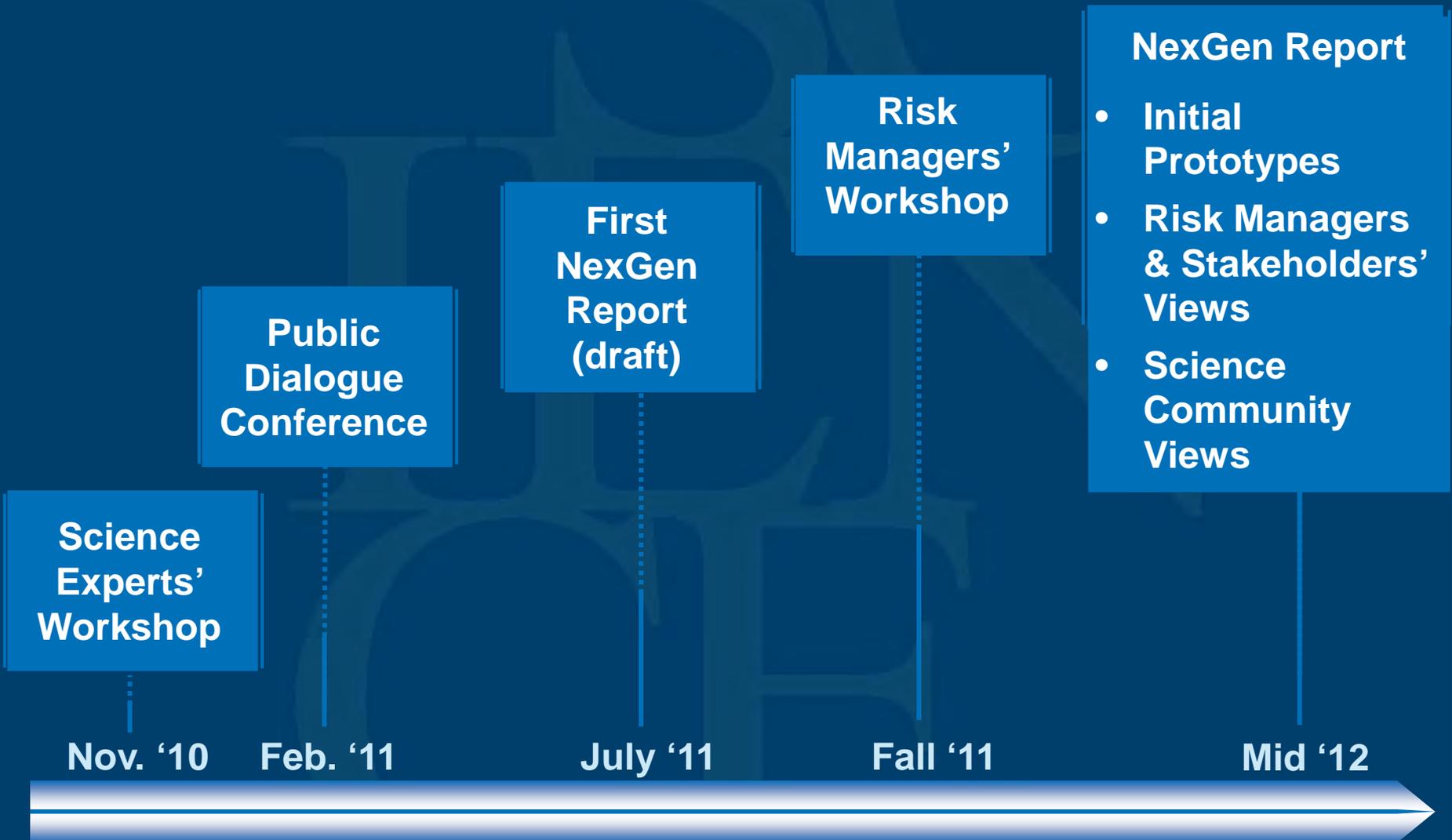
Conference Format

- Plenary Sessions
 - This overview
 - Proposed draft Framework
 - Two **example** data-rich prototypes:
 - Ozone
 - Benzene
 - Approaches for chemicals with limited data
- Breakout Group Sessions - 4 sets of questions



What is next?

NexGen Health Assessment Timeline



Please visit EPA's NexGen Web site for more
information:

www.epa.gov/risk/nexgen

