National Pesticide Program

A Strategic Vision for a 21st Century Testing & Assessment Paradigm

Dr. Steven Bradbury, Director
Office of Pesticide Programs
US Environmental Protection Agency

EPA
United States
Environmental Protection
Agency

National Pesticide Program

- MISSION
  - Best Possible Regulatory Decisions to Protect Public Health and the Environment
  - Rely on All Available and Relevant Scientifically Sound Information

EPA
United States
Environmental Protection
Agency

National Pesticide Program

- At a Glance
  - Over 5,000 regulatory decisions annually
  - Approximately 1,100 active ingredients & 19,000 products
  - Reevaluation of existing pesticides on a regular schedule to ensure safety standards continue to be met

EPA
United States
Environmental Protection
Agency

National Pesticide Program At a Glance

- Safety evaluations required for both human health & ecological risks
  - ‘Conventional‘, biochemical, antimicrobial active ingredients
  - Food-use & non-food use inert ingredients
- Data required for registration
  - Vary across types of pesticide chemicals
    - Extensive for food use, conventional active ingredients to minimal for non-food use inert ingredients

EPA
United States
Environmental Protection
Agency

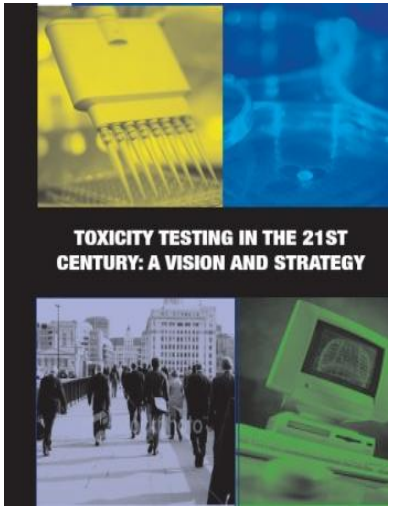
National Pesticide Program Challenges

- Large Number of Chemicals to Review with Many Possible Adverse Outcomes
- Finite Resources and Time
- Public Expectations for Scientific Soundness, Transparency, and Timeliness
- Science Increasingly Complex & Changing
  - New Risk Assessment & Management Challenges Always Arise

EPA
United States
Environmental Protection
Agency

2007 NRC - Toxicity Testing in the 21st Century: A Vision & Strategy

- Sponsored by EPA
- Committee recognized improvements in:
  - Technologies to evaluate perturbations in biological pathways (what a chemical does)
  - Data storing, analysis & management



EPA
United States
Environmental Protection
Agency

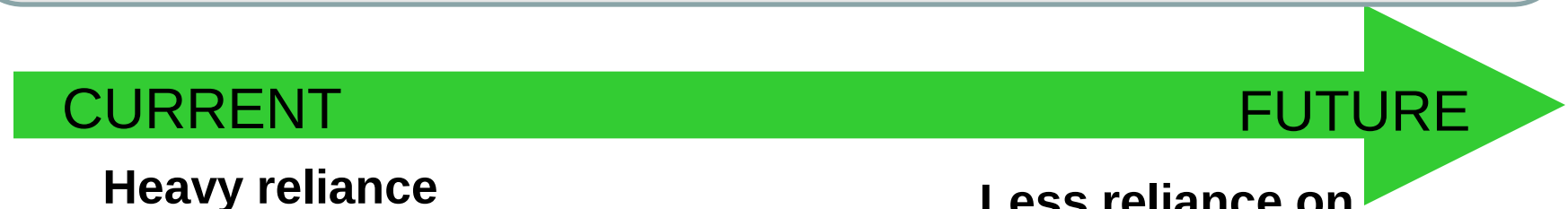
2007 NRC - Toxicity Testing in the 21st Century: A Vision & Strategy

- Use cell-based (high through put) assays to understand how chemicals perturb normal cellular functions (i.e., toxicity pathway)
  - Establish relationships of perturbations with "adverse outcomes"
- Develop in vitro to in vivo extrapolation methods
- Integrate results to predict hazard/risk

Broader coverage of chemicals & endpoints
Reduce cost & time of testing
Use fewer animals

OPP Vision for a New Toxicology Testing & Assessment Paradigm

Program Priority
Work toward transitioning new 21st century technologies, to enhance the efficiency & effectiveness of chemical risk management



Heavy reliance on animal studies

Generate information for all possible outcomes

Based on traditional toxicity tests

Less reliance on animal studies

Tailor data generation

Based on understanding of toxicity pathways

EPA United States Environmental Protection Agency

Integrated Approaches to Testing & Assessment (IATA)

- **INTEGRATE** existing information
  - Use information from new technologies with combined estimates of exposure in a manner that leads to better predictions of risk for regulatory endpoints
- **FORMULATE** plausible & testable hypotheses
- **TARGET** in vivo testing on chemicals & endpoints of concern

United States Environmental Protection Agency

Integrated Approaches to Testing & Assessment (IATA)

- Originated from OECD
  - Dec 2007 workshop hosted by EPA
- Consistent with
  - 2007 NRC Report
  - EPA's (SPC-FTTW) Strategic Plan for Evaluating the Toxicity of Chemicals

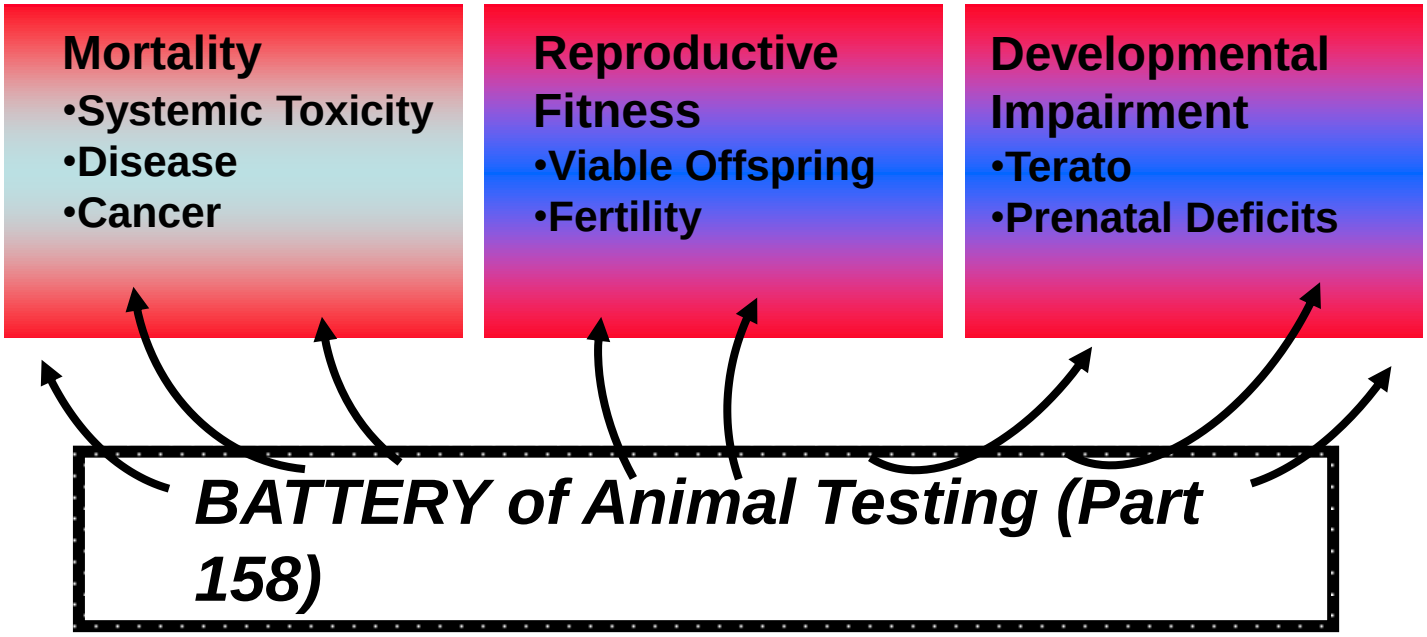
EPA United States Environmental Protection Agency

Integrated Approaches to Testing & Assessment" (IATA)

- Not new
  - Long history with chemicals lack data
    - Industrial Chemical Program, pesticide inert ingredients
- Incorporates various tools and types of information
- Evolves with science

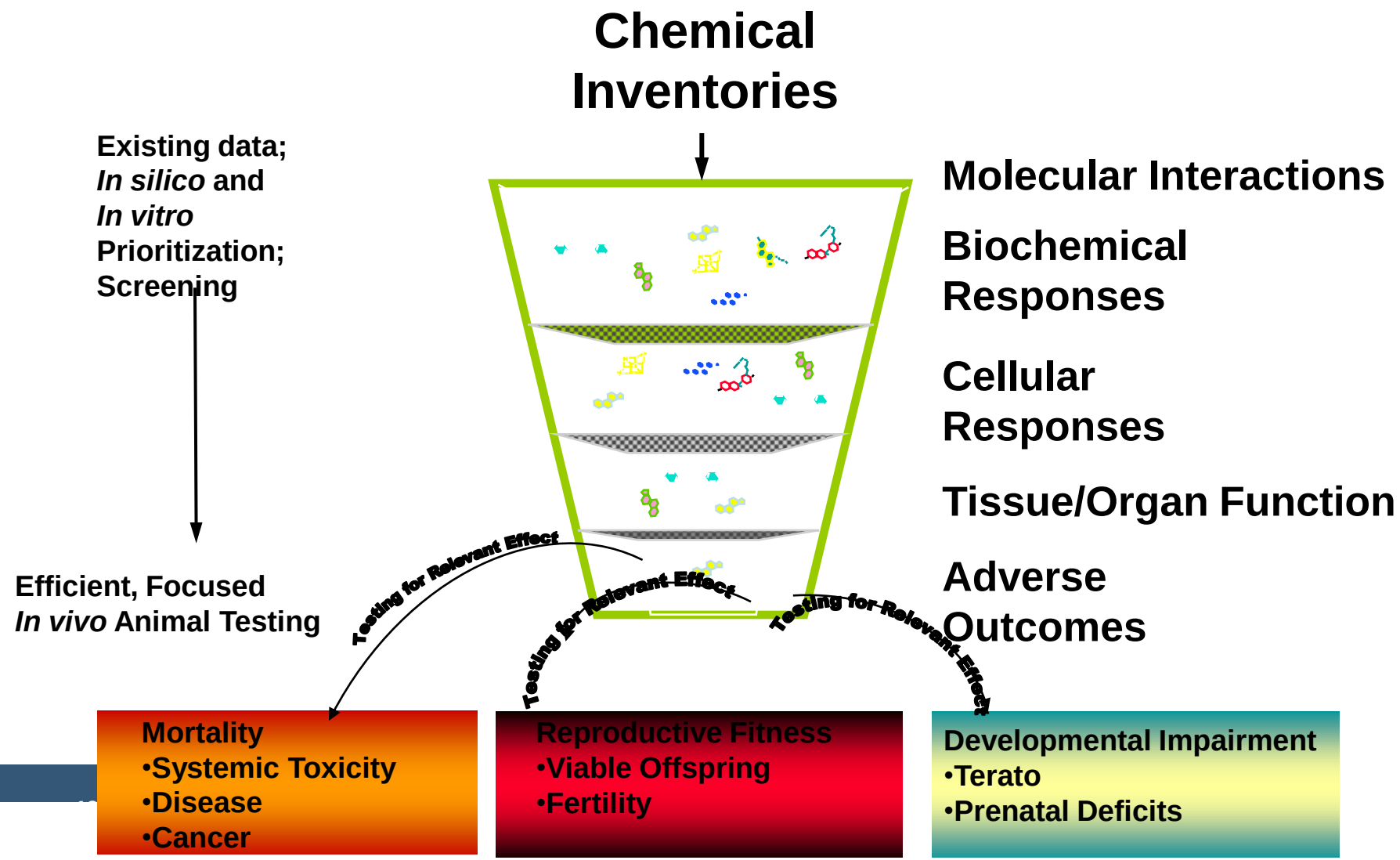
Current Testing Paradigm

Risk Managers Focus on Potential Adverse Outcomes

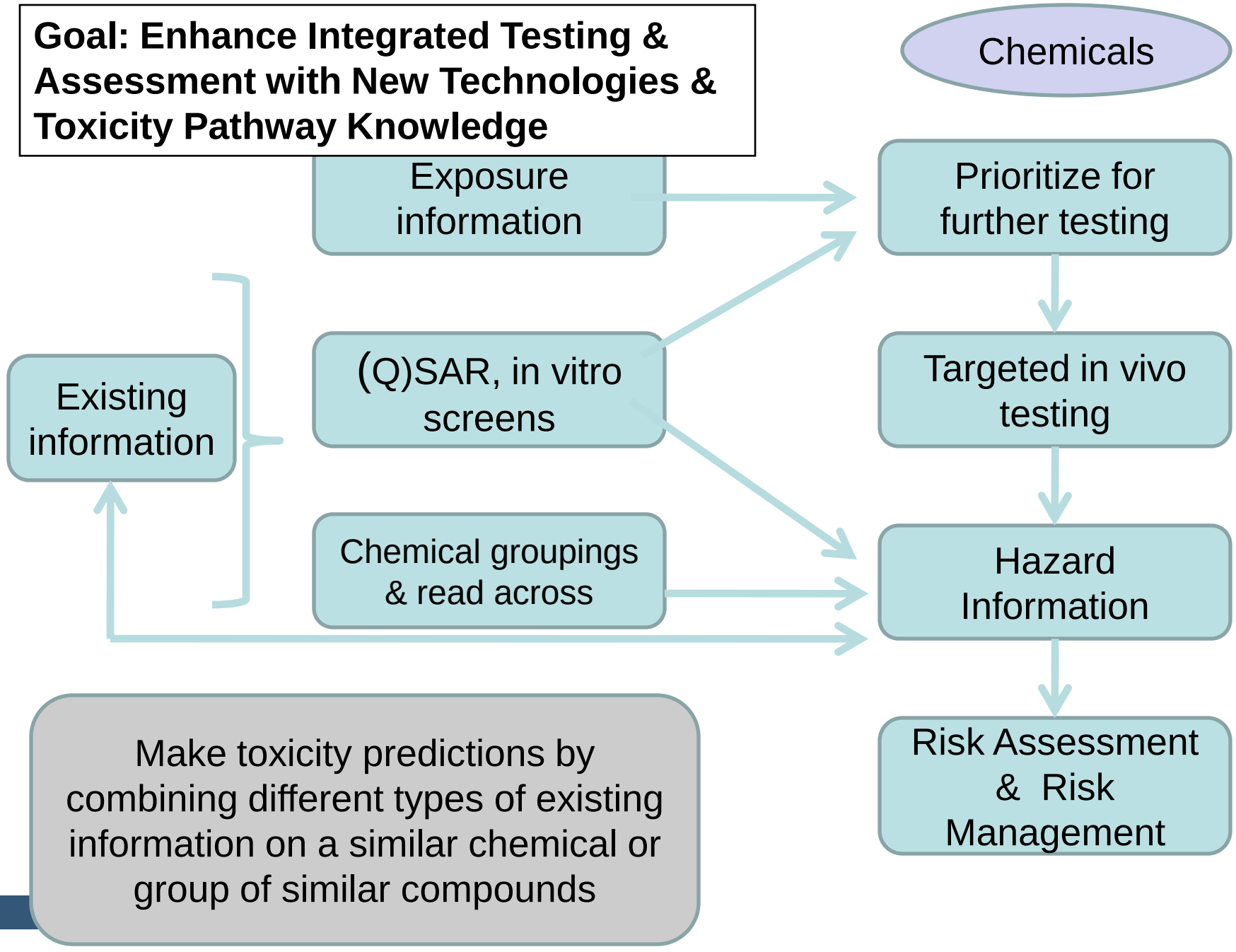


Generates animal data for all possible outcomes to determine which possible effects are relevant

New Integrated Paradigm



Goal: Enhance Integrated Testing & Assessment with New Technologies & Toxicity Pathway Knowledge



Make toxicity predictions by combining different types of existing information on a similar chemical or group of similar compounds

Near Term Goal: 1-3 years

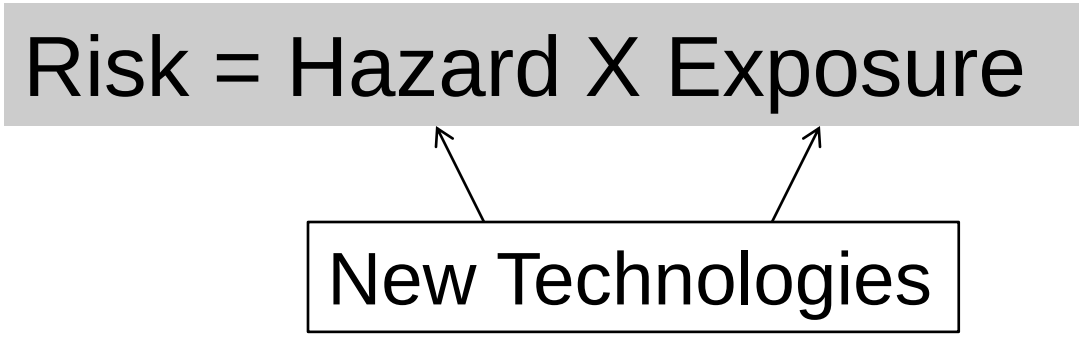
Transition New Predictive Methods

- Strengthen priority setting/screening for data-poor compounds by using new predictive methods to fill data gaps and to guide targeted in vivo testing
- Maximize the value obtained from each in vivo study
- Transition away from chemical-by-chemical approaches by leveraging knowledge on groups of chemicals with shared properties

EPA
United States
Environmental Protection
Agency

Transition New Predictive Methods

- Integrate into existing risk assessment paradigm



- Use new methods in real time and real world situations
- Evaluate & refine through an iterative process

Paradigm Shift: Increasing Effectiveness & Efficiency

All Chemicals

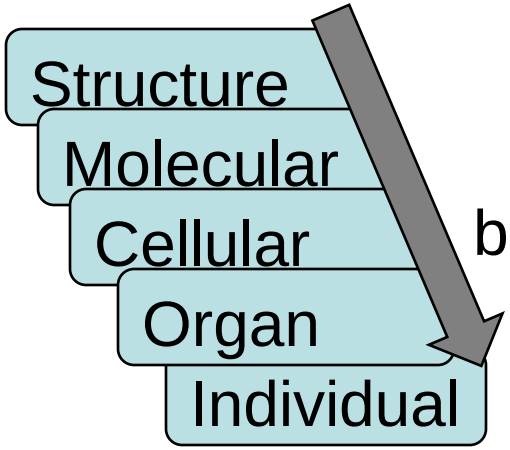
Routinely use in silico & in vitro models to predict adverse consequences for critical toxicities

Long Term Goal

Less reliance on animal studies

Tailor data generation

Based on understanding of toxicity pathways



Understand linkage of biological events to adverse outcome

EPA
United States
Environmental Protection
Agency

Partnerships & Collaborations

- Internal Partners
  - EPA regulatory and research programs
- External Partners
  - State, Federal & International Agencies
  - Stakeholders

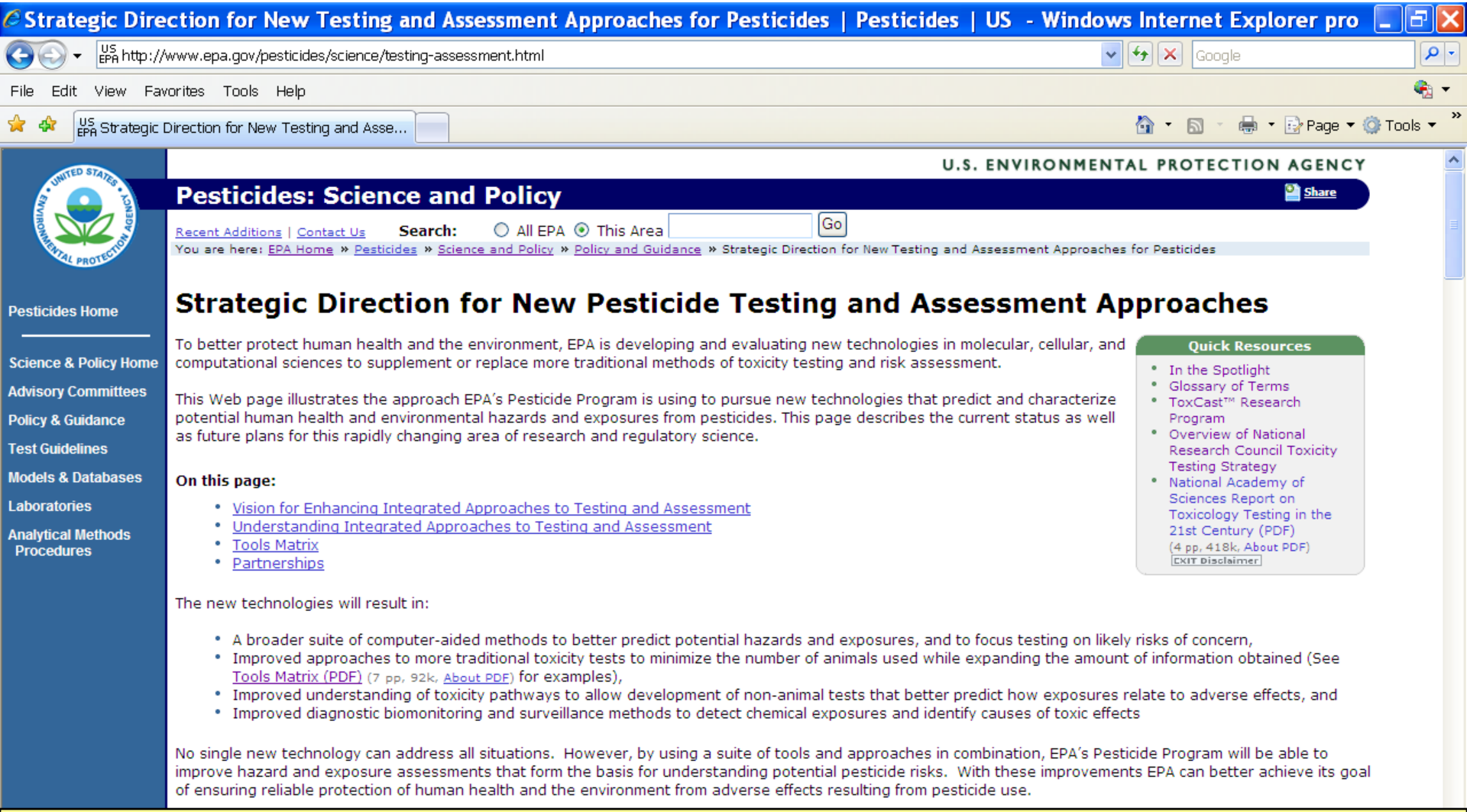
International Partnerships

- Global Acceptance
- Information Sharing
- Common Application Tool Boxes
- Mutually Accepted Test Guidelines
- Harmonize Frameworks & Guidance

Organization for Economic Cooperation & Development
North American Free Trade Agreement
International Program for Chemical Safety
European Food Safety Authority, etc.

Stakeholder Engagement

- What are these tools & how will they be applied?
- What is the expected timeline for transition to new tools?
- Why are changes needed?
- What are the expected improvements in health and environmental protection?
- How will we recognize success & failure?



http://www.epa.gov/pesticides/science/testing-assessment.html

United States Environmental Protection Agency

Achievable with strong scientific & stakeholder support through a transparent process

"Integrative Approaches to Testing & Assessment" using 21st Century Technologies