

US EPA ARCHIVE DOCUMENT



National Pesticide Program

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

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National Pesticide Program

- MISSION

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

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



National Pesticide Program

At a Glance

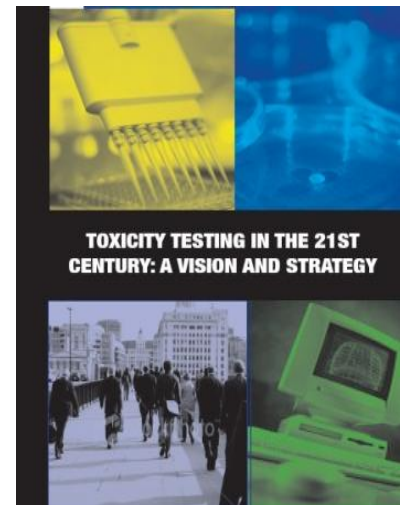
- Safety evaluations required for both human health & ecological risks
 - ‘Conventional’, biochemical, antimicrobial active ingredients
 - Food-use & non-food use inert ingredients
- Data required for registration
 - Vary across types of pesticide chemicals
 - Extensive for food use, conventional active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

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

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



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

CURRENT

**Heavy reliance
on animal studies**

**Generate information
for all possible outcomes**

**Based on traditional toxicity
tests**

FUTURE

**Less reliance on
animal studies**

Tailor data generation

**Based on
understanding
of toxicity pathways**

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

Integrated Approaches to Testing & Assessment (IATA)

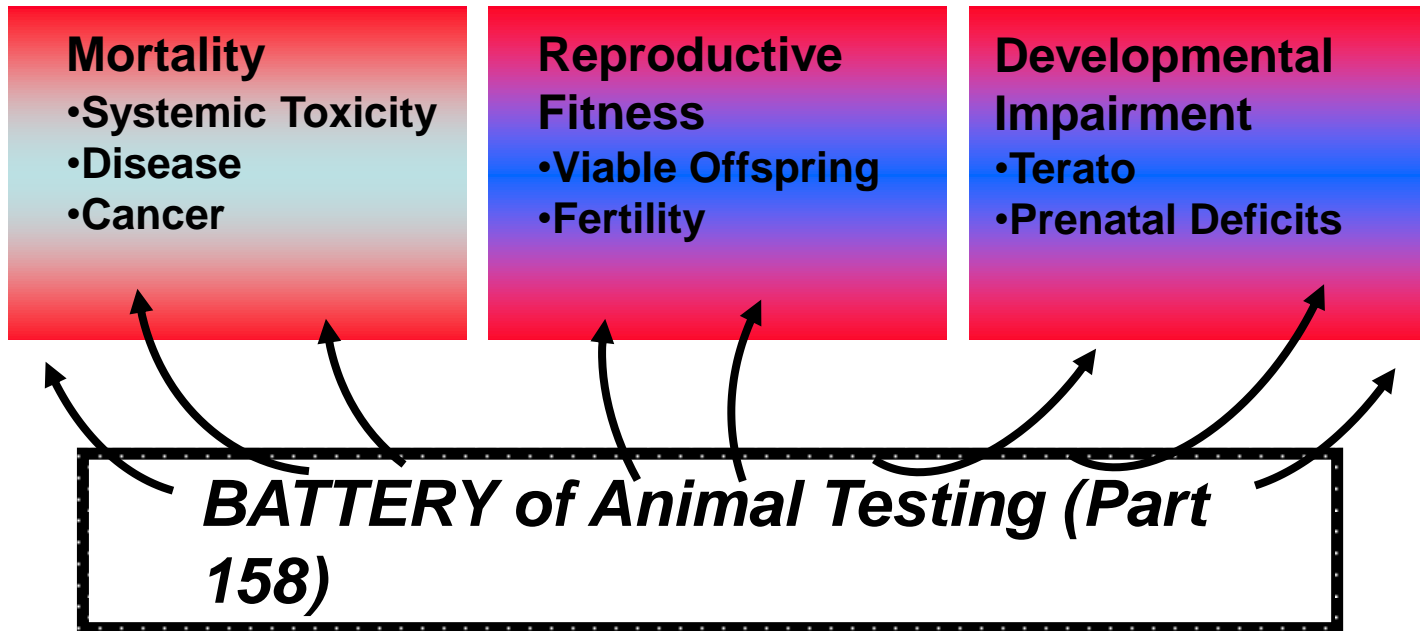
- Originated from OECD
 - Dec 2007 workshop hosted by EPA
- Consistent with
 - 2007 NRC Report
 - EPA's (SPC-FTTW) Strategic Plan for Evaluating the Toxicity of Chemicals

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



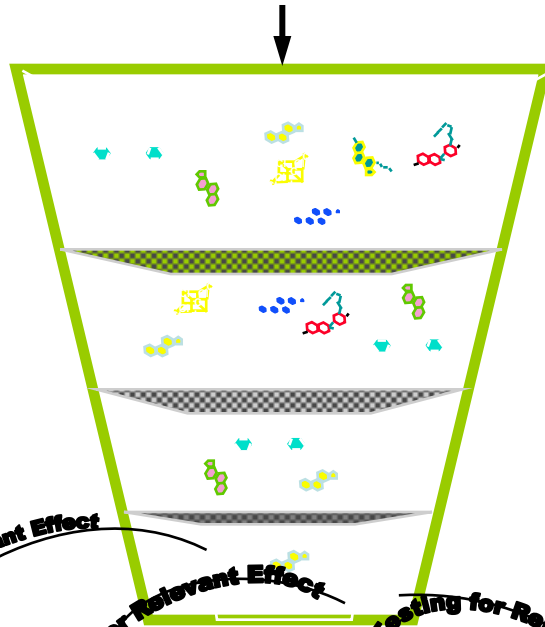
Generates animal data for all possible outcomes to determine which possible effects are relevant

New Integrated Paradigm

Chemical Inventories

Existing data;
In silico and
In vitro
Prioritization;
Screening

Molecular Interactions
Biochemical Responses
Cellular Responses
Tissue/Organ Function
Adverse Outcomes



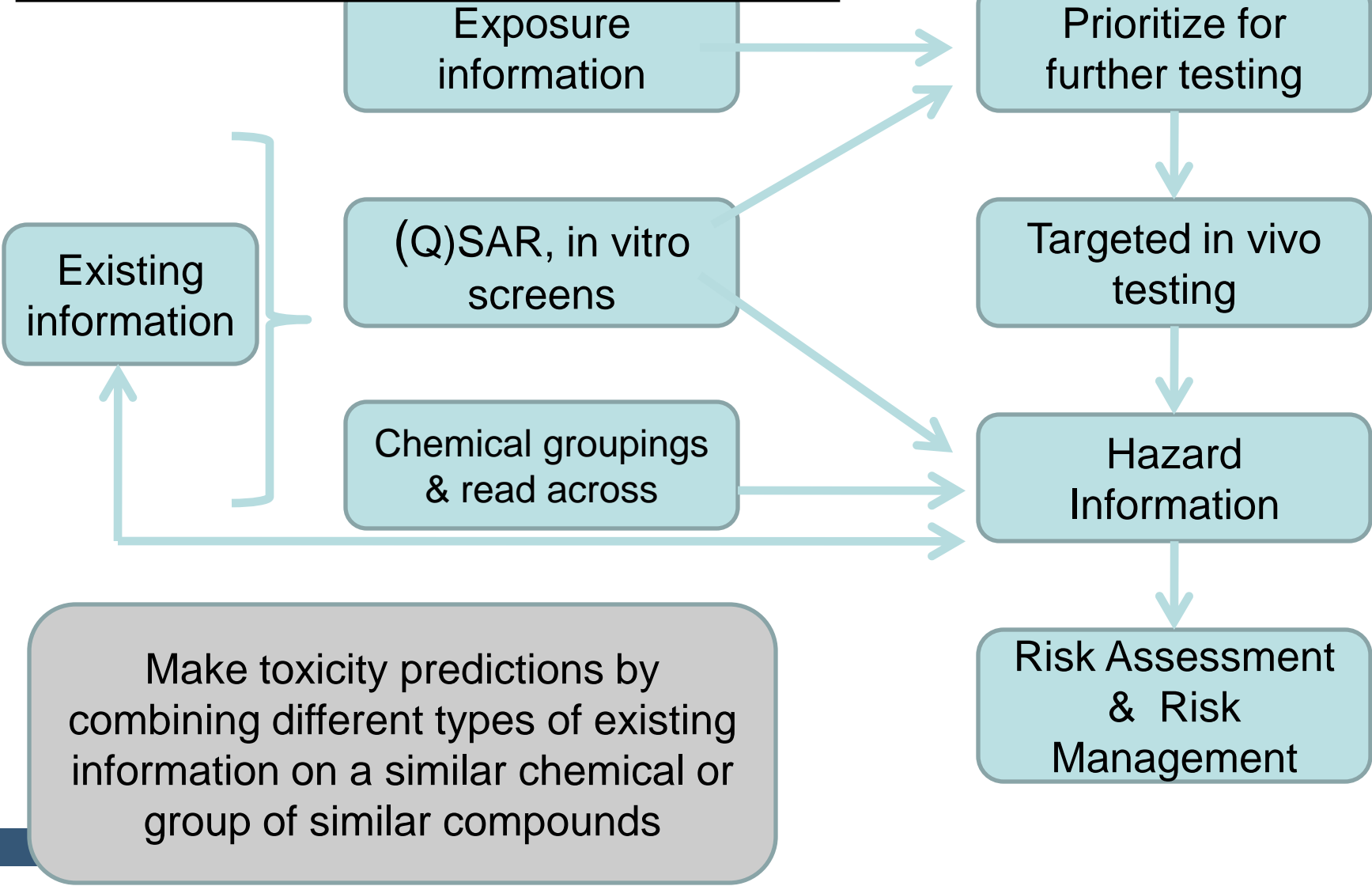
Efficient, Focused
In vivo Animal Testing

Mortality
• Systemic Toxicity
• Disease
• Cancer

Reproductive Fitness
• Viable Offspring
• Fertility

Developmental Impairment
• Terato
• Prenatal Deficits

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



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

Transition New Predictive Methods

- Integrate into existing risk assessment paradigm

Risk = Hazard X Exposure



New Technologies

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

Paradigm Shift: Increasing Effectiveness & Efficiency

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

All Chemicals

Long Term Goal

Less reliance on animal studies

Tailor data generation

Based on understanding of toxicity pathways

Structure

Molecular

Cellular

Organ

Individual

Understand linkage of biological events to adverse outcome

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?



Pesticides: Science and Policy



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Strategic Direction for New Pesticide Testing and Assessment Approaches

To better protect human health and the environment, EPA is developing and evaluating new technologies in molecular, cellular, and computational sciences to supplement or replace more traditional methods of toxicity testing and risk assessment.

This Web page illustrates the approach EPA's Pesticide Program is using to pursue new technologies that predict and characterize potential human health and environmental hazards and exposures from pesticides. This page describes the current status as well as future plans for this rapidly changing area of research and regulatory science.

On this page:

- [Vision for Enhancing Integrated Approaches to Testing and Assessment](#)
- [Understanding Integrated Approaches to Testing and Assessment](#)
- [Tools Matrix](#)
- [Partnerships](#)

The new technologies will result in:

- A broader suite of computer-aided methods to better predict potential hazards and exposures, and to focus testing on likely risks of concern,
- Improved approaches to more traditional toxicity tests to minimize the number of animals used while expanding the amount of information obtained (See [Tools Matrix \(PDF\)](#) (7 pp, 92k, [About PDF](#)) for examples),
- Improved understanding of toxicity pathways to allow development of non-animal tests that better predict how exposures relate to adverse effects, and
- Improved diagnostic biomonitoring and surveillance methods to detect chemical exposures and identify causes of toxic effects

No single new technology can address all situations. However, by using a suite of tools and approaches in combination, EPA's Pesticide Program will be able to improve hazard and exposure assessments that form the basis for understanding potential pesticide risks. With these improvements EPA can better achieve its goal of ensuring reliable protection of human health and the environment from adverse effects resulting from pesticide use.

Quick Resources

- [In the Spotlight](#)
- [Glossary of Terms](#)
- [ToxCast™ Research Program](#)
- [Overview of National Research Council Toxicity Testing Strategy](#)
- [National Academy of Sciences Report on Toxicology Testing in the 21st Century \(PDF\)](#)
(4 pp, 418k, [About PDF](#))
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- Pesticides Home
- Science & Policy Home
- Advisory Committees
- Policy & Guidance
- Test Guidelines
- Models & Databases
- Laboratories
- Analytical Methods Procedures

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

Achievable with strong scientific & stakeholder support through a transparent process

“Integrative Approaches to Testing & Assessment” using 21st Century Technologies