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## National Pesticide Program

### A New Toxicology Testing Paradigm: Meeting Common Needs



## 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

### OPP AT A GLANCE

- Gateway to pesticide market, where sales over \$11 B/yr
- Over 5,000 regulatory decisions annually
- Approximately 1,100 active ingredients and 19,000 products
- Reevaluation of existing pesticides on a regular schedule to ensure safety standards continue to be met

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## National Pesticide Program

### OPP AT A GLANCE

- Safety Evaluation Done for all Pesticide Chemicals
  - Agricultural chemicals
  - Antimicrobials and Consumer products
  - Inert ingredients
- Data Availability/Quality Varies Extensively
- New Risk Assessment/Management Challenges Always Arise

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## **National Pesticide Program CHALLENGES**

- Science Increasingly Complex and Changing
- Large Number of Chemicals to Review with Many Possible Adverse Outcomes
- Finite Resources and Time
- Sufficient, Credible Information to Make a Decision, not an Overwhelming Amount of Information
- Public Expectations for Scientific Soundness, Transparency, and Timeliness

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## **National Pesticide Program**

### **Vision for a New Toxicology Testing and Assessment Paradigm**

- Integrative
- Hypothesis-Driven
- Efficient

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## Why a Shift in Paradigm?

- Improve ability to carry out EPA mission of protecting public health and the environment
- Increase efficiency by focusing the regulated community, government, and interested parties on a pesticide's most likely hazards of concern
  - Determine what specific effects data for each chemical and exposure situation are essential to assess and manage risks appropriately
  - Use screening and priority setting to eliminate the need for requiring a battery of tests focused on all possible adverse outcomes

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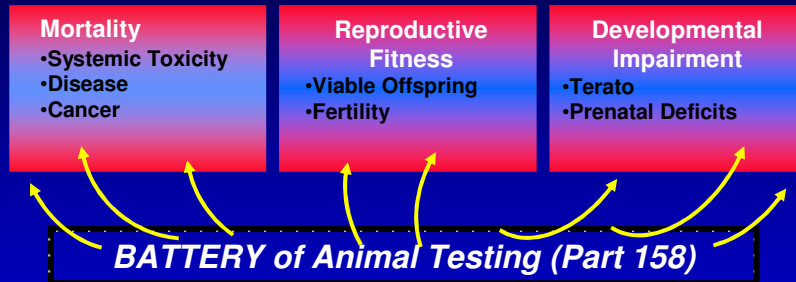
## Why a Shift in Paradigm?

- Lower the costs for the government and taxpayers because the Agency could avoid reviewing unnecessary tests
- Eliminate complex and expensive *in vivo* testing for the pesticide-producing industry
- Reduce the use of animals in testing

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## Current Paradigm

- Risk Managers Focus on Potential Adverse Outcomes



- Current Toxicology Testing Paradigm Generates In Vivo Animal Data for all Possible Outcomes to Determine which of all Possible Effects are Relevant

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## Implementing Change

- Development and implementation of a new, integrated approach to the testing and assessment of pesticides will be a challenge and will take place over the next 10 years
- Scientific tools and knowledge must be advanced and public understanding and confidence must be developed
- National Academy of Science study

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## **EPA – Pesticide Program Plan for Paradigm Change**

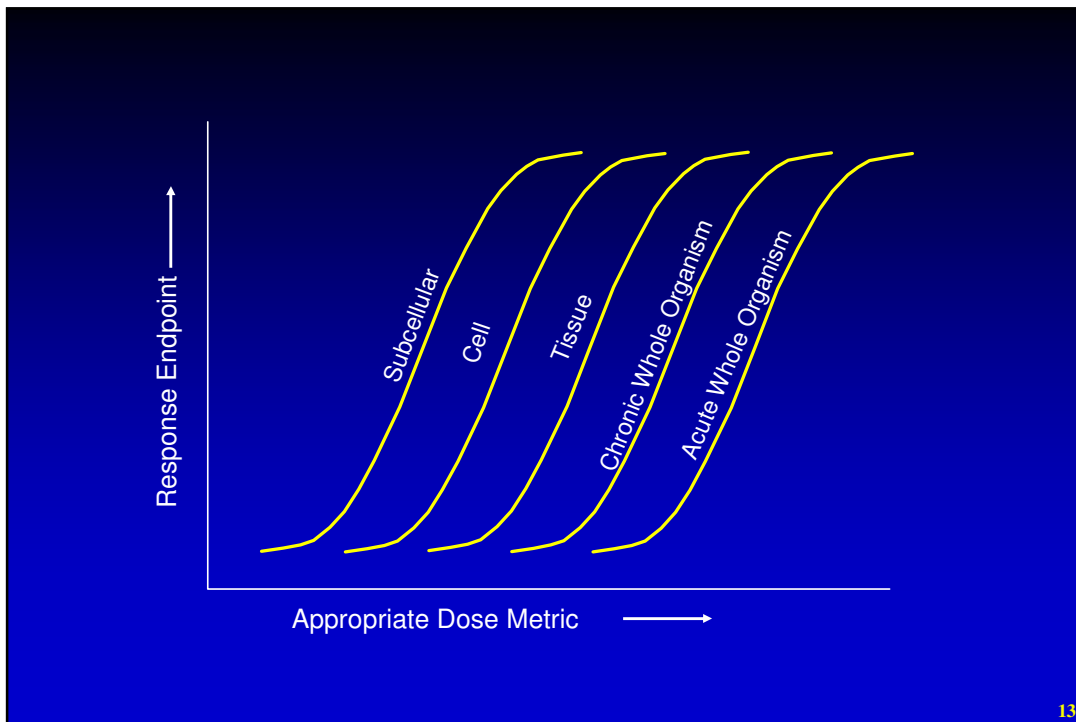
- Analyze and Update Current Data Requirements
  - Proposed Changes to Regulations on Testing Requirement
  - Retrospective Analyses of Pesticide Data for Key Endpoints
- Support Development and Use of Enhanced and New Testing Approaches and other Analytic Techniques
  - ILSI/HESI Proposed Tiered Approach
  - Inert Ingredient SAR Analysis
- Advance Research Agenda
  - Greater Reliance on Emerging Tools of Computational Toxicology

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## **Retrospective Analyses of Pesticide Database**

- Ongoing Reviews
  - Dog Toxicity Studies
  - Rodent Cancer Studies
  - Rat Multi-generation Reproductive Studies
  - Rat Neurodevelopmental Toxicity Studies
- Incorporate Lessons Learned into Regulatory Practice

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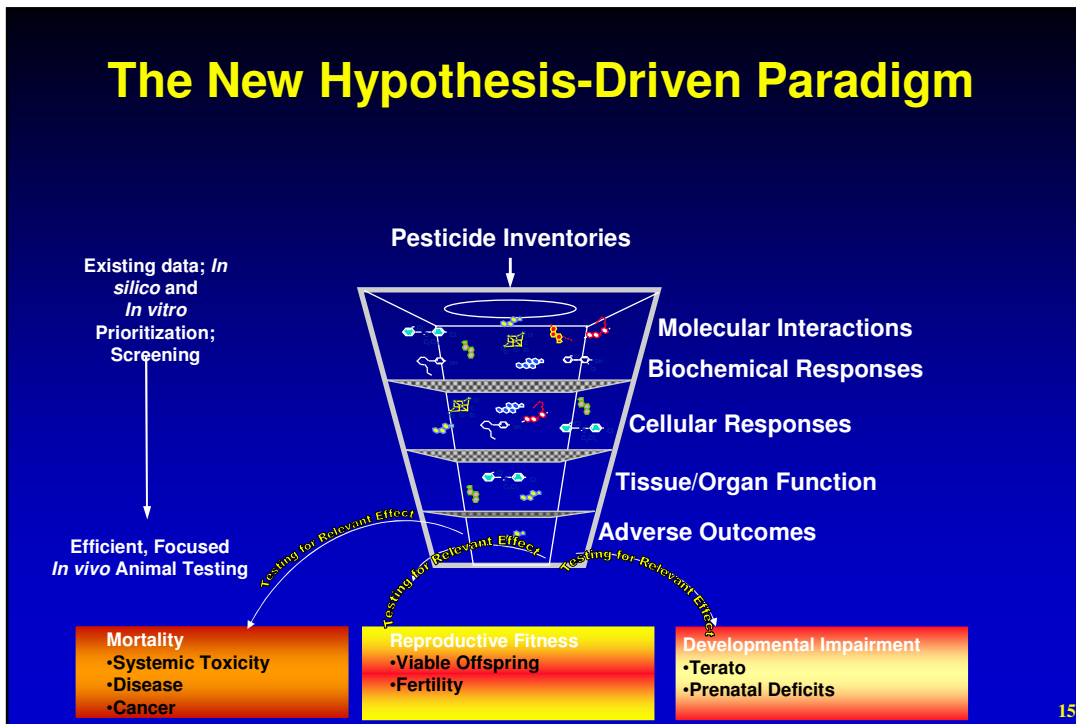
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## Enhanced and New Testing Approaches

- **Short Term Goal**
  - Make existing animal testing paradigm more efficient, reliable & responsive to our risk assessment & management needs
    - FQPA Issues (lifestage susceptibilities, mechanisms of toxicity, etc)
- **ILSI-HESI Proposed Tiered Approach**
  - Important Springboard
    - Reduces animal usage by optimizing study designs & takes risk assessment needs & exposure characteristics into account
  - More Foundation & Consensus Building Needed
    - Retrospective & prospective analyses

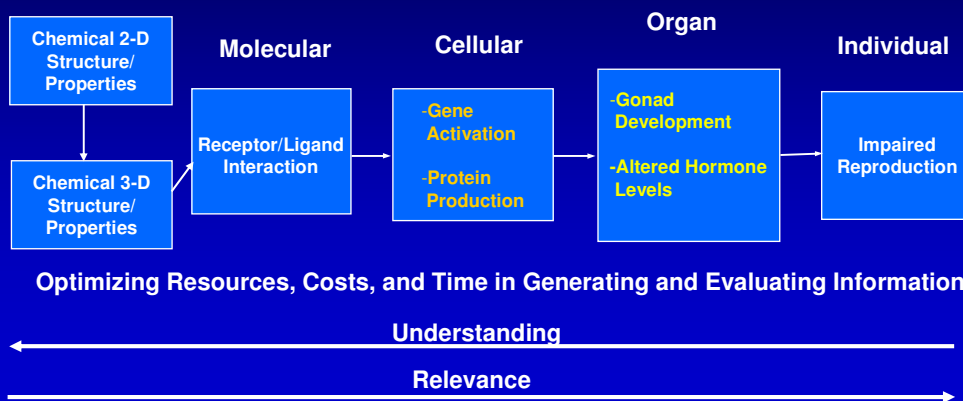
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# The New Hypothesis-Driven Paradigm



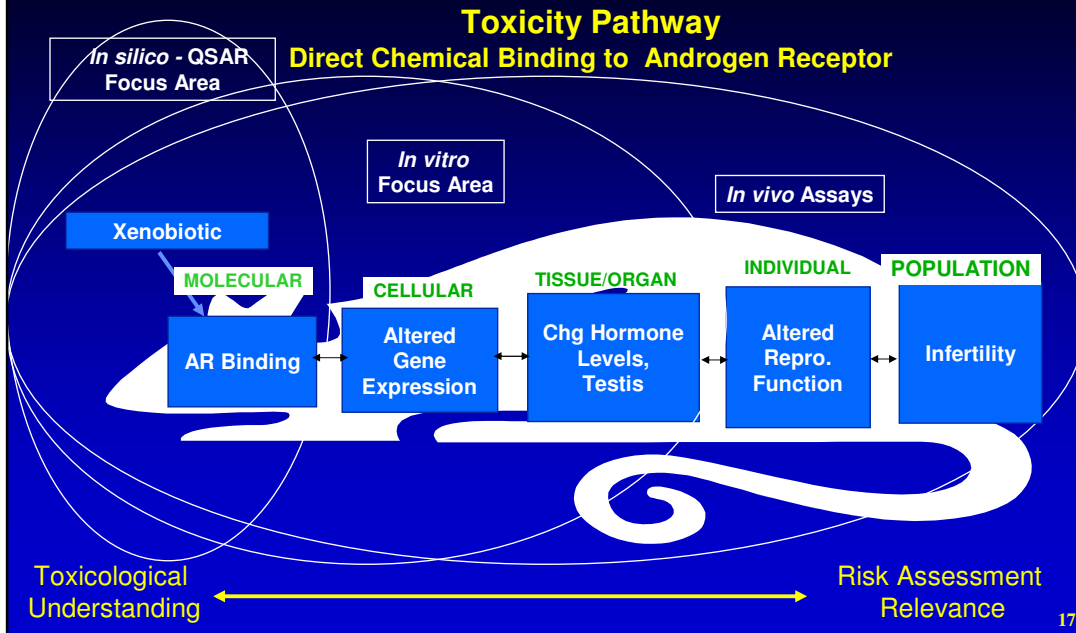
# Example: Receptor-Mediated Pathways

## Linkage Across Levels of Biological Organization



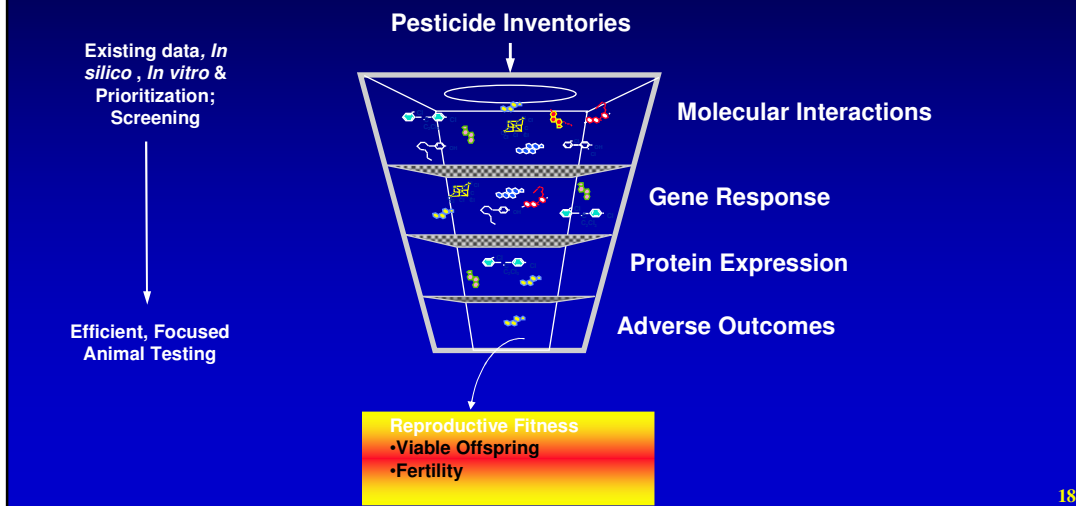


## A New Toxicology Testing Paradigm: Meeting Common Needs



## The New Hypothesis-Driven Paradigm

Example: Receptor-Mediated Pathway



## Next Steps

- Work with the regulated community and other stakeholders
- Support the development and use of enhanced and new testing approaches and other analytic techniques
- Incorporate lessons learned into regulatory practice on a case-by-case basis.
- Ultimately, explore and make appropriate changes to regulations and test guidelines

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## Coordination and Alignment

- Coordinate EPA's regulatory and research programs (OPPTS/ORD – computational toxicology program)
- Partner with other Federal Agencies (e.g., FDA, NIEHS)
- Partner with regulatory and research agencies in other countries (e.g., Canada, Australia, EU Member States) through existing international fora (e.g., NAFTA, OECD, WHO)
- Work with scientific community and other stakeholders (ILSI/HESI, Federal Advisory Committees, NAS)

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