

Meeting the Needs of a Paradigm Shift: A Regulatory Perspective

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- Pesticides are poisons
- Require extensive data set
- Alternatives focus on reduction in number of animals per test, and more humane endpoints to reduce pain & suffering
- Alternatives provide very small part of the data needed to evaluate a new pesticide
- To move to alternative testing more new tests need to be developed and validated
- EPA is moving toward embracing the Toxicity Testing in the 21st Century Paradigm

Acute	- Corrositex
Lethality	- Up & Down
methods	- Fixed Dose
	- Acute Toxic Class
Eye	- Pilot -antimicrobial
Irritation	cleaning products
	- BCOP and ICE
Skin / Dermal	Reaching consensus on OECD <i>in vitro</i> dermal irritation guidelines
	ICCVAM LLNA dermal sensitization refinement
	Working with Canada & California on alternative techniques for dermal absorption



OPPTS Strategic Direction

Transition toward new integrative & predictive 21st century techniques, to increase efficiency and effectiveness of testing & assessment

Animal Testing: Reduce, Refine, Replace

- 2005 OPPTS-ORD White Paper
- 2007 NAS Report on Testing in the 21st Century
- 2009 Agency's Strategic Plan for Evaluating the Toxicity of Chemicals

Use of computational tools is not new to evaluate & assign priorities for follow-up actions (e.g., industrial chemical program)



Managing Chemical Risks

Challenge: Assessing Data-Limited Chemicals

- •Near Term (5 years) Goal
 - -Integrated Approaches to Testing & Assessment
 - "Enhanced Tool Box" Create means to efficiently & credibly predict toxic potency & exposure levels and to focus information needs
 - -Situations
 - E.g., HPV/MPVs, pesticide inerts, certain antimicrobials, metabolites & degradates of pesticide actives



Managing Chemical Risks

Challenge: Reducing Uncertainty

- Long Term (5-15 years)
 - Develop means to move, in a credible & transparent manner to hypothesis & mechanismdriven, risk-based approaches that focus on effects most relevant to risk assessment & risk management
 - "omics" technology in identifying toxicity pathways
 - PDPK modeling
 - Improved human exposure modeling





Partnerships

Agencies & International Organizations

- Collaborate on development & application of predictive computational models
- Promote development of common databases
- Harmonize frameworks/guidance
- Build common application tool boxes

-e.g., OECD QSAR Tool Box





Stakeholder Engagement

Pesticide Program Dialogue
 Committee (PPDC)



- Workgroup on 21st Century Toxicology/New Integrated Testing Strategies Workgroup
- Purpose is to advise on communication & transition
 - Improve understanding of the perspectives of all stakeholders regarding a new testing paradigm
 - Ensure that we receive public input as we develop key science
 & regulatory products
 - Develop common public understanding about the use of new tools



Stakeholder Engagement

Overarching Questions:

- Why are changes in the current paradigm needed?
- How will the new paradigm change risk assessments or risk-based decisions?
- What is the expected timeline for transition to use of new tools?
- What are the expected impacts on health and environmental protection?
- How will we recognize failures in the new paradigm?





Enhanced Integrated Testing & Assessment Incorporating the 3 R's

• Where we need to be in the near term

 Accelerated/enhanced priority setting/screening & focused animal testing

Where we would like to be in the long term

 Greater reliance on hypothesis & mechanism-based assessments

What needs to happen

- Advance collaborative research agenda to develop scientific basis
- -Partnerships, stakeholder input, peer review, consensus building, staff training, development of new polices, etc.