**PPDC 21st Century Toxicology/ New Integrated Testing Strategies Workgroup**
**Where Vision Meets Action: Practical Application of 21st Century Methods**
**July 9, 2013 Stakeholder Workshop Summary**

Overview: On July 9, 2013, the Office of Pesticide Programs (OPP) hosted a one-day, non-technical public workshop in Arlington, Virginia to provide an opportunity to dialogue with stakeholders on how OPP envisions applying new science to change the way we evaluate the risks of pesticides, and to examine the challenges and benefits of making this transition.

**Workshop Objectives:**

1. Explore the regulatory application of alternative 21st Century methods to transition away from traditional chemical testing approaches,
2. Examine the challenges of making this transition, and
3. Discuss building confidence in these alternative methods in the support of pesticide registrations. This workshop builds on the 2010 workshop on the Office of Pesticide Program's strategic vision and application of 21st Century science to improve and transform pesticide risk management by enhancing our ability to use integrated approaches to testing and assessment (IATA).

**Perspectives on Practical Application of 21st Century Methods:**

The meeting opened with speakers from the Agency who provided an overview of current efforts to apply new science to the evaluation of the risks of pesticides. Click on the link for presentations.

**Welcome and Introduction – Steven Bradbury, PhD, Director, Office of Pesticide Programs (OPP), Office of Chemical Safety and Pollution Prevention (OCSPP)** discussed progress in OPP towards reaching 21st Century Toxicology goals. The OPP IATA/Strategic Direction can be found here: http://www.epa.gov/opp00001/science/testing-assessment.html#understand

**Plenary Speaker, Overview of Research Program – Tina Bahadori, National Program Director, Chemical Safety for Sustainability Program, Office of Research and Development (ORD),** discussed the research being conducted in the Chemical Safety for Sustainability Program. More information on the CSS Program can be found here: http://www2.epa.gov/aboutepa/about-chemical-safety-sustainability-research-program
Presentation link: http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/plenary.pdf

Following this, an explanation of the Adverse Outcome Pathway (AOP) Framework was given, which is fundamental to applying 21st Century integrated approaches to testing and assessment. Presentations of case studies by representatives from the Agency, government, and animal advocacy/environmental activist organizations on developments currently being applied, or are anticipated to be used in OPP, followed.

**Session One: Understanding the Adverse Outcome Pathway (AOP) Framework – Kevin Crofton, ORD,** provided an introduction to the AOP framework and tools**.** Presentation link: http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session1.pdf

**Session Two: Case studies of New Science Advances in AOP Pathway Development and Regulatory Application – Scott Glaberman, OPP,** explained the current use of AOP's and the challenges involved in the regulatory context**.** Presentation link: http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session2-adverse.pdf

**Case Study 1: Evolving the Endocrine Disruptor Program (EDSP) – Pat Schmieder, ORD,** described the current understanding of the Estrogen Receptor Expert System. Presentation link: http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session2-casestudy1.pdf

**Mary Manibusan, Director of EDSP, OCSP** described the evolving Endocrine Disrupter Screening Program. More information on the EDSP can be found here: http://www.epa.gov/endo/index.htm
Presentation link:
http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session2-edsp.pdf

**Case Study 2: OECD Dermal Sensitization AOP** - **Kristie Sullivan, Physicians Committee for Responsible Medicine (PCRM)** described OECD's AOP Program**.** More information can be found here: **http://www.oecd.org/env/ehs/testing/**
Presentation link:
http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session2-skin.pdf

**Joanna Matheson, Consumer Product Safety Commission (CPSC)** provided a regulatory perspective on the OECD dermal sensitization AOP. Presentation link:
http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session2-oecd.pdf

**Case Study 3: Using AOP's to Quantitatively Predict Chemical Impacts on Fish Reproduction – Ed Perkins, USACE and Amy Perkins, OPP,** described using AOP's to help model complex systems relating to fish impacted by installation activities. Presentation link:
http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session2-aop.pdf

**Case Study 4: Endocrine Disruptors, Thyroid AOP – Kevin Crofton, ORD and Tim McMahon, OPP,** described an example of how AOP's can be used, with triclosan as an example. Presentation link: http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session2-inte-approach.pdf

Perspectives on the benefits and challenges of making this transition were then presented by representatives from government, industry and animal advocacy/environmental activist organizations.

**Session Three: Benefits and Challenges to Implementation of Alternative 21st Century Methods**

**Nasser Assaf, Valent BioSciences**: Discussed the work of the Council for the Advancement of Pyrethroid Human Risk Assessment (CAPHRA).
Presentation link: http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session3-agerelated.pdf

**Sean Gehen, Dow**: Gave an industry perspective on new the alternative 21st century methods.
Presentation link: http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session3-crop.pdf

**Catherine Willett, Humane Society**: Provided an animal advocacy perspective on the benefits and applicability of a shift to alternative 21st century methods. Presentation link: http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session3.pdf

**Jennifer Sass, NRDC**: Provided a perspective on the benefits and challenges of implementing alternative 21st century methods. Presentation link: http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session3-sass.pdf

**Suzanne Fitzpatrick, FDA**: Provided a perspective on advancing regulatory science through several 21st century innovations. Presentation link: http://epa.gov/pesticides/ppdc/testing/2013/july/workshop/session3-advancing.pdf

**Session Four: Panel discussion "Building Confidence in the Regulatory Application of Alternative 21st Century Methods for Evaluating Pesticides"** - Erik Janus, Monsanto (Moderator)

**Panelists:** Jennifer McLain, OPP; Suzanne Fitzpatrick, FDA; Kristie Sullivan, PCRM; Jennifer Sass, NRDC; Nasser Assaf, Valent BioSciences; Rick Becker, American Chemistry Council

**Key Topics from Panel Perspectives and Stakeholder Discussions throughout Workshop**

Benefits of 21st Century methods

- Reducing animal testing was a benefit agreed upon by all
- More efficient assessment of greater number of chemicals, endpoints, species, etc. New tools will provide a more informed risk assessment (tox endpoints, uncertainty)

Methods validation, regulatory acceptance and global harmonization of new test guidelines are critical steps to advance the science and achieve the benefits

- Open and transparent, independent peer review is important
- All stakeholders need to be engaged
- Performance-based approaches to methods validation are needed to complement existing peer review processes such as the FIFRA SAP

How can EPA and its partners continue to drive this work?

- Statutes give EPA flexibility to use the best science possible. EPA wants to implement practical applications of the science – today; engaging stakeholders will enable this transition to be successful.
- More collaboration (interagency, public-private, international) is critical to moving science forward; EPA must engage all stakeholders.
- Stakeholders want EPA to establish "metrics for success" for the transition to 21st C methods
- EPA must ensure process-related actions, such as expending resources for data management and developing data use guidance and standardized submission formats for alternative methods.
- Advancements can be achieved through individual companies working with EPA on novel studies.
    - Develop new testing strategies grounded in biology to define data needs
    - Use current knowledge to be smarter about the need for studies
- Collaboration and information sharing with scientific community and the use of multidisciplinary teams also reduce uncertainty and incorporate new information.

How to merge traditional toxicology assessment techniques with newer approaches? When is AOP ready to be used in regulatory decision-making?

- Traditional model is still the foundation that informs newer approaches. Currently, AOP is a component of overall risk assessment process, not the primary tool.
- A determination of when an AOP is ready to be used depends on how it will be used
- Qualitative applications can be used before quantitative applications are realized; weight of evidence used to minimize uncertainty
- Demonstrating clear, quantitative linkages will be essential to use of AOPs in risk assessment
- The OECD AOP project will facilitate information sharing and advance AOP development. It is important for government, NGOs, and industry to support the project.
- Models aren't perfect. Important to use other information and data in addition to mechanistic data
- Developing multiple methods for a single purpose are not necessarily redundant since they help improve approaches