Update on OPP Progress on Acute Animal Testing Alternatives
PPDC Meeting Nov. 3, 2016 – Session 7a

OPP developed a Strategic Direction for New Pesticide Testing and Assessment Approaches, consistent with the 2007 NAS report on Toxicity Testing in the 21st Century, which set a new paradigm for toxicity testing. Currently, OPP is focusing on acute toxicity '6 pack' testing alternatives, specifically the following:

- Improving capacity to predict hazard using computational approaches
- Reducing the number of animals used in toxicity tests used to regulate pesticides while simultaneously increasing the information we receive
- Advancing our ability to use information on adverse outcome pathways to inform new toxicity testing strategies

EPA annually receives over 500 acute toxicity 6-pack submissions, and over 50 animals are used for a complete set of 6-pack studies. This waiver guidance could reduce the number of studies conducted by 200-300 each year. In total, working together with stakeholders EPA, in time, can save over 20,000 animals used in laboratory testing annually.

21st Century Milestones in 2016 and 2017

- OPP formed an acute toxicity workgroup made up of members from RD, AD, HED, and BPPD, with input from FEAD, PRD, and EFED.
- A Stakeholder group, made up of industry, government, and NGO's, is meeting regularly to discuss progress, goals, and collaboration opportunities.
- The Director of OPP, Jack E. Housenger, in a letter to stakeholders, outlined OPPs Goals to Reduce Animal Testing. The letter lays out OPP's 3 main objectives; below are OPP's accomplishments towards each objective thus far, and what OPP will be working on in the coming year.

Objective 1: Retrospective analyses of studies currently used in decision making to allow EPA to determine which form the basis of decisions, and which could potentially be waived or eliminated.

OPP:

- Issued a draft Retrospective Analysis & Guidance for Waiving Acute Dermal Toxicity Tests for Pesticide Formulations opened to public comment in March 2016. This was in collaboration with the National Institute of Environmental Health and Sciences – National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NIEHS-NICEATM).
- Anticipates issuing a final Retrospective Analysis & Guidance for Waiving Acute Dermal Toxicity Tests for Pesticide Formulations in the fall of 2016. EPA is now accepting waiver requests for the dermal toxicity studies on pesticide formulations.
- Currently receives about 200-300 dermal formulation toxicity tests annually which most often use 10 animals per test. As a result OPP expects this waiver guidance to save 2,500 or more laboratory animals every year.

Objective 2: Expand the acceptance of alternative methods, such as *in vitro* studies and *in silico*/computational approaches.

OPP:

- Is exploring the expansion of the eye policy currently in place for antimicrobial cleaning products to other pesticide chemicals, and currently analyzing voluntarily submitted paired data in collaboration with NICEATM.
- Participates in the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) skin sensitization workgroup and attended the 2016 International Cooperation on Alternative Test Methods (ICATM) workshop on integrated approaches to testing and assessment for skin sensitization. The workshop will lead to a white paper on alternatives for OECD to accept.
- In FY2017, OPP will be collaborating with NICEATM to analyze voluntarily submitted skin sensitization data with the ultimate goal to draft guidance on acceptance of *in vitro* dermal sensitization studies.
- Is developing EPA Standard Evaluation Procedures (SEPs) for data reviewers to support submissions of alternative studies.
- Anticipates the launch of the GHS Equation pilot for Oral & Inhalation toxicity studies by the end of 2017.

Objective 3: Because of the critical importance of national & international harmonization, EPA is committed reducing barriers within the US among industry and internationally among regulatory bodies.

OPP:

- Issued the Final Process for Establishing & Implementing Alternative Approaches to Traditional *In Vivo* Acute Toxicity Studies, which describes a transparent, stepwise process for evaluating and implementing alternative methods of testing for acute oral, dermal, inhalation toxicity, along with skin and eye irritation and skin sensitization.
- Is currently exploring options for adopting GHS categories for the hazard part of labels.
- Will be starting a voluntary GHS pilot program - side by side submission of the formulation test for oral & inhalation with the GHS additivity equation.
- Is coordinating with Health Canada PMRA on 21st Century science projects and progress.
- In collaboration with NICEATM will develop draft guidance on acceptance of *in vitro* eye irritation studies for all pesticides following NICEATM analysis, in next fall, 2017.
- Is working closely with other federal agencies through the ICCVAM skin sensitization, acute toxicity, and eye workgroups to accelerate progress on adopting alternatives.