OPP Progress on Acute Animal Testing Alternatives
PPDC Meeting November 1, 2017 – Session 5

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 250-300 acute toxicity 6-pack submissions, and over 50 animals are used for a complete set of 6-pack studies. In total, working together with stakeholders on EPA, in time, can save over 10,000 animals used in laboratory testing annually.

In a 2016 letter to stakeholders, the previous Director of OPP, Jack E. Housenger, outlined OPPs Goals to Reduce Animal Testing (https://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2016-0093-0003). 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 has finalized the Retrospective Analysis & Guidance for Waiving Acute Dermal Toxicity Tests for Pesticide Formulations. This document was developed 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).
- 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.
- OPP is beginning to explore the potential for expanding this waiver guidance to acute dermal toxicity studies for active ingredients.

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

- In December, 2016, OPP started a voluntary pilot program to evaluate the usefulness and acceptability of a mathematical tool (the GHS Mixtures Equation), which is used in the

Globally Harmonized System of Classification and Labeling of Chemicals (GHS) as an alternative to animal oral and inhalation toxicity studies for pesticide formulations (https://www.epa.gov/pesticide-registration/mixtures-equation-pilot-program-reduce-animal-testing). OPP is still accepting submissions under this pilot and expects to develop an evaluation in 2018.

- OPP continues to explore the expansion of the eye policy currently in place for antimicrobial cleaning products to other pesticide chemicals. >300 Pairs of *in vivo- in vitro* studies have been provided by multiple registrants for evaluation by OPP and NICEATM.
- OPP, in collaboration with OPPT, NICEATM, the European Union Reference Laboratory for alternatives to animal testing (EURL-ECVAM), and Health Canada submitted a project proposal to the OECD for developing non-animal based approaches for skin sensitization.
- Multiple government and stakeholder laboratories are working to further develop and optimize alternative approaches for skin sensitization, skin irritation and eye irritation. OPP expects significant progress in 2018 towards non-animal approaches for skin sensitization, skin irritation and eye irritation.

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

- A stakeholder group, made up of industry, government, and NGO's, is meeting regularly to discuss progress, goals, and collaboration opportunities.
- OPP is coordinating with Health Canada PMRA on 21st Century science projects and progress and has started discussions with Brazil ANVISA.
- OPP is working closely with other federal agencies through the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) skin sensitization, acute toxicity, and skin and eye technical workgroups to accelerate progress on adopting alternatives.