ICCVAM Public Forum: Update from EPA's Office of Pesticide Programs

Anna B. Lowit, Ph.D.
Co-Chair, ICCVAM
Senior Science Advisor
US EPA, Office of Pesticide Programs
lowit.anna@epa.gov
703-308-4135 (w), 703-258-4209 (c)

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Background: Pesticides

- Office of Pesticide Programs is a licensing program regulating pesticide products in the U.S.
  - One of the major roles is to review effects of pesticides on human and ecological health

- EPA's Office of Pesticide Programs has developed a Strategic Direction for New Pesticide Testing and Assessment Approaches
  - http://www.epa.gov/pesticides/science/testing-assessment.html.
  - A broader suite of computer-aided methods to better predict potential hazards and exposures, and to focus testing on likely risks of concern;
  - Improved approaches to more traditional toxicity tests to minimize the number of animals used while expanding the amount of information obtained;
  - Improved understanding of toxicity pathways to allow development of non-animal tests that better predict how exposures relate to adverse effects.

Guiding Principles for Data Needs for Pesticides

- Guiding Principles for Data Requirements
  - Purpose: provide consistency in the identification of data needs, promote and optimize full use of existing knowledge, and focus on the critical data needed for risk assessment.
  - http://www.epa.gov/pesticides/regulating/data-require-guide-principle.pdf
- "…ensure there is sufficient information to reliably support registration decisions that are protective of public health and the environment while avoiding the generation and evaluation of data that does not materially influence the scientific certainty of a regulatory decision…."
- "…avoid unnecessary use of time and resources, data generation costs, and animal testing."

Acute Toxicity "6 Pack"

- Letter to Stakeholders on EPA Office of Pesticide Programs Goal to Reduce Animal Testing from Jack E. Housenger, Director Office of Pesticide Programs.
  - https://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2016-0093-0003

Guideline	Study Type	Food Use	Non-Food Use
870.1100	Acute oral toxicity – Rat	R	R
870.1200	Acute dermal toxicity – Rat /Rabbit	R	R
870.1300	Acute inhalation toxicity – Rat	R	R
870.2400	Primary eye irritation – Rabbit	R	R
870.2500	Primary dermal irritation – Rabbit	R	R
870.2600	Dermal sensitization – Guinea Pig	R	R

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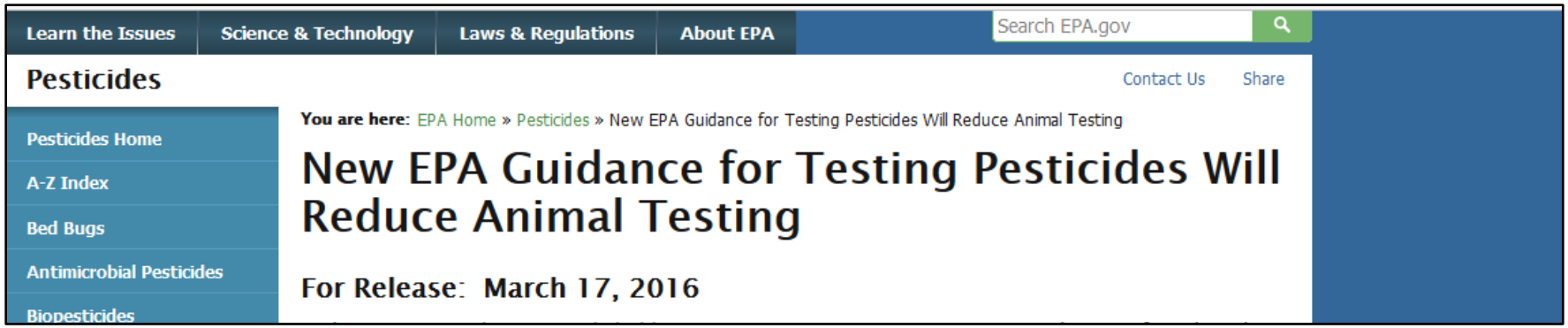
  - Working in partnership with other governmental entities, industry and non-governmental organizations (NGOs) and need continued robust participation and support to achieve our mutual goal.
  - Activities fall under three main objectives
    - Critically evaluating which studies form the basis of OPP decisions;
    - Expanding acceptance of alternative methods and;
    - Reducing barriers such as challenges of data sharing among companies and international harmonization to adopting alternative methods in the U.S. and internationally.

Acute Toxicity "6 Pack"

- Acute Dermal Pesticide Formulation Toxicity Testing
  - Collaboration between EPA & NICEATM
  - Analyze the relative contribution of data from acute oral and dermal toxicity tests to pesticide hazard classification and labelling
  - Collected acute lethality dermal and oral toxicity data from rat studies with pesticide formulations



Draft for Public Comment

March 11, 2016

Retrospective Analysis & Guidance for Waiving Acute Dermal Toxicity Tests for Pesticide Formulations

4.0 Waiver Guidance.

The agency believes this retrospective analysis fully supports a conclusion that waivers can be granted of acute dermal toxicity studies for formulations. The agency will be soliciting public comment on this draft policy. Registrants may begin submitting waiver requests through existing processes to respective OPP division.

https://www.epa.gov/pesticides/new-epa-guidance-testing-pesticides-will-reduce-animal-testing

Reducing Barriers to Adopting Alternative Methods

- *PROCESS FOR ESTABLISHING & IMPLEMENTING ALTERNATIVE APPROACHES TO TRADITIONAL IN VIVO ACUTE TOXICITY STUDIES*
  - https://www.epa.gov/sites/production/files/2016-03/documents/final_alternative_test_method_guidance_2-4-16.pdf
- This document 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 (often referred to as the “six pack studies”).

Reducing Barriers to Adopting Alternative Methods

- Starting a voluntary pilot program where registrants may send the *in vivo* acute lethality study for oral and inhalation formulation/product testing as currently required and simultaneously submit the calculations using the GHS dose additive mixtures equation.
  - Hope to rapidly collect a dataset evaluating the ability of the GHS mixtures equation to predict the acute toxicity categories from oral and inhalation routes in formulation/product testing.
  - Pending the outcome of that analysis, may be able to substantially reduce the use of animals.

Reducing Barriers to Adopting Alternative Methods

- Exploring options for adopting GHS categories for the hazard portion of the pesticide label.
  - Currently, OECD is developing guidelines for alternative assays (i.e., in vitro) using the GHS categories but not US EPA toxicity categories.
  - Creating such a crosswalk from GHS to USEPA categories can be accomplished for some *in vitro* assays but has shown to be a significant challenge for others.
  - Possible that may have to go through rulemaking proceedings to change how the hazard labeling is conducted.
  - Issues are complex---plan to begin engaging stakeholders on these issues in the coming weeks and months.

Alternative Assays: Eye Irritation

- Currently have a policy in place to accept eye irritation assays for antimicrobial cleaning products
- Interested in extending use of alternative assays for other classes of pesticides
- Voluntary data collection effort for conventional pesticides
  - >200 pairs of *in vitro-in vivo* data provided by industry
  - NICEATM will be analyzing

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Questions?