Update on Human Health Risk Assessment Approach for Organophosphates

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October 21, 2015
OP Risk Assessment Update Outline

- Hazard Strategy
- OP Safety Factors
- Exposure Summary
- Risk Summary
- PBPK Update
- FY16/17 Plan
OP Hazard Strategy

- Evaluated ChE data for parent and oxon
- Updated/generated BMDs for RBC & Brain ChE across oral, dermal & inhalation routes
- Most sensitive compartment used for single chemical assessment
- Life-stage comparison from gestation & postnatal CCA studies
- Endpoints selected
  - Acute (including females specific if needed)
  - Chronic replaced with steady-state due to equilibrium for enzyme inhibition (i.e., no further inhibition after 2-3 weeks)
OP Safety Factors

- OP 10X position paper published for 60-day comment September 2, 2015
  - Paper based on data from laboratory animals and mechanistic studies along with human epidemiological data
  - Systematic Review of scientific literature for laboratory animal studies & epidemiology studies
- 10X FQPA factor for each OP evaluated based on uncertainty in the human dose-response relationship for neurodevelopmental effects.
  - Uncertainty regarding neurodevelopmental outcomes as seen in the body of available epidemiological studies.
  - Epidemiological studies evaluate OP exposure through measuring urinary biomarkers (DAPS or dialkylphosphate metabolites), which are common to many OPs.
In Science and Decisions: Advancing Risk Assessment, the NAS recommends that the agency "...continue and expand use of the best, most current science to support and revise default assumptions."

Recent advances in in vitro to in vivo extrapolation and computational modeling provide new opportunities to develop models for developing efficient and robust data-derived inter- and intra-species extrapolation factors.

Inter- and intra-species uncertainty factors could increase or decrease from default 10x.

OPP is developing a tiered framework tiered approach for developing efficient PBPK models using new technologies.

http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/developing-tiered-framework-extrapolation-modeling
OP Exposure Summary

- **Dietary:**
  - Used DEEM
  - Provides overall (365 day) exposure estimates
  - Drinking water incorporated directly

- **Occupational and Residential Assessments**
  - Utilized standard assessment methods and SOPs
  - Spray Drift Assessment
  - Addressed volatilization screening assessment
Preliminary Draft Risk Assessments generally identified risks for various exposure pathways.

- Dimethoate
- Dicrotophos
- Profenofos
- Ethoprop
- Terbufos
- Tribufos
- Chlorpyrifos-methyl
FY16/17 OP Plan

- Addressing comments received from OP 10X position paper along with the 7 draft risk assessments.
- OP PRAs that are scheduled for public comment during FY16
  - TCVP, Acephate, Malathion, Coumaphos, Chlorethoxyfos, Bensulide, Phosmet, Phostebupirin, Diazinon
- OP PRAs scheduled for FY17
  - DDVP, Naled, Trichlorfon