

# Update on Human Health Risk Assessment Approach for Organophosphates



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# 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 (ie., 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.
  - Epi studies evaluate OP exposure through measuring urinary biomarkers (DAPS or dialkylphosphate metabolites), which are common to many OPs.

# Expanding Use of PBPK Models

- 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



# OP Risk Summary

- 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





Questions?