

US EPA ARCHIVE DOCUMENT

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?