

CUMULATIVE RISK ASSESSMENTS IN THE FOOD QUALITY PROTECTION ACT (FQPA)

Mark Whalon from the Department of Entomology and the Center for Integrated Plant Systems, Michigan State University, USA, outlines progress by the Environmental Protection Agency (EPA) towards achieving the FQPA mandate to develop a framework for cumulative risk assessment of pesticides

The Food Quality Protection Act (FQPA) became law August 6, 1996. This legislation requires that the U.S. Environmental Protection Agency (EPA) considers the cumulative effects of pesticides and other substances to human health. Since no methodology to achieve this goal existed in the U.S. pesticide risk assessment framework, the Agency has developed a range of new methods, protocols and tools to achieve the FQPA's mandate.

Within the U.S. EPA, the office of Pesticide Programs has developed a framework for conducting cumulative risk assessment on pesticides. This framework is based on consideration of what the agency in conjunction with the International Life Sciences Institute (ILSI) believed to be common mechanisms of toxicity. That is, a group of pesticide chemistries that exhibit a similar mode of action. Following the establishment of a common mechanism of toxicity groups the Agency has begun conducting aggregate exposure and risk assessment before completing the final FQPA-mandated cumulative risk assessment.

The common mechanism of toxicity grouping process consists of identifying which pesticides exhibit the same mode of action based on scientifically reviewed and reliable data. This process is an attempt to link different pesticides by the same sequence of major biochemical events in target and non-target organisms alike.

EPA sponsored and participated in a work group by the ILSI to develop a common mechanism framework¹. EPA also published a draft *Guidance for Identifying Pesticides that have a Common Mechanism of Toxicity* on August 6, 1998. A revised guidance was published on February 5, 1999 (U.S. Federal Register: 64 FR5795) entitled *Guidance for Identifying Pesticide Chemicals and Other Substances That Have a Common Mechanism of Toxicity*. Finally, the agency consulted with the U.S. Federal Insecticide, Fungicide and Rodenticide Act Scientific Advisory Panel (SAP) in four different sessions between March 1998 and September 1999 to consider the SAP recommended changes.

The aggregate risk assessment portion of the cumulative analysis includes consideration of exposures to a pesticide from food, drinking water and residential/non-occupational sources. Again, ILSI has held workshops and the Agency has sponsored various panel discussions with independent scientists on topics related to aggregate exposure. The Agency has published a number of publications outlining

their framework for aggregate exposure and risk assessment. These publications include: *An Assessment of Methods To Estimate Pesticides In Drinking Water* (1998), *Aggregate Exposure Assessment Workshop Report* (1998), *A Framework For Estimating Pesticide Concentrations In Drinking Water For Aggregate Assessments* (1999) and *Aggregate Exposure Assessment: Model Evaluation and Refinement Workshop* (2001). The EPA has also published several guidance documents related to drinking water exposure assessment including: *Estimating the Drinking Water Component of A Dietary Exposure Assessment* (November 10, 1999), *Standard Operating Procedure for Incorporating Screening-Level Estimates of Drinking Water Exposure in Aggregate Risk Assessments* (October 11, 2000) and *Drinking Water Screening Level Assessments, Part A – Guidance for Use of the Index Reservoir in Drinking Water Exposure Assessments* (October 11, 2000).

EPA has also published guidance on conducting residential exposure assessments including standard operating procedures for residential exposure assessment (January 4, 1999) and a framework for assessing non-occupational/non-dietary exposure to pesticides (January 4, 1999). The Agency also convened various science advisory panels, and public hearings from March 1997 through October 3, 2001. In all, more than twenty such meetings have been held in the last four years.

The U.S. EPA's framework for assessing cumulative risk has involved developing ways to combine various exposures to different substances that have different degrees of toxicity while taking into account various exposure mechanisms and spatial and temporal variables. The Agency has also pursued an open, peer-reviewed process to develop the cumulative risk assessment methods and approaches. This public participation process was pioneered and became routinized during the Tolerance Reassessment Advisory Committee's (TRAC) interaction with the agency in progressing through the individual organophosphate insecticide risk assessments. This public process is composed of six phases and is available over the EPA's web site (www.epa.gov/pesticides/op/status.htm).

The EPA conducted a technical briefing for cumulative risk assessment for the committee to advise on re-registration and transition on August 22, 2001. Many of the materials presented in this open public meeting are available on the above web site. Essentially the Agency has outlined its cumulative methodology and it is now soliciting input opportunities. Cumulative risk assessment steps will likely include:

¹ A Case Study of Organophosphorus Pesticides, *Toxicological Sciences*, 1998, 41,8–20.

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- identifying the common mechanism group
- identifying the potential exposures and roots of exposure
- characterizing and selecting common mechanism end points
- determining the cumulative assessment pesticide groupings
- determining the absolute and relative potencies for all chemistries within a common mechanism group
- developing a point of departure for an index chemical in order to relate (index) all other chemistries in a common mechanism group
- developing detailed exposure scenarios for all routes and durations of exposure using two very sophisticated independently developed modeling systems
- conducting final cumulative risk assessment. The final process will be finalized after interaction across a broad array of stakeholders.

The calendar opposite (Table 1) details critical opportunities for public stakeholder input into the cumulative risk assessment framework. This timeline was published for the USDA-EPA Committee to Advise on Reassessment and Transition (CARAT).

The agency has yet to bring before the FIFRA-SAP a number of continuing issues. These issues include selection and performance of dose-response models, combining cholinesterase data from multiple data sets to derive relative potency and benchmark dose estimates, enumeration of the approach for selection of the index chemicals in cumulative risk assessment and the use of steady state cholinesterase data for estimating both the relative potency and the points of departure for index chemicals in each common mechanism group. The Agency plans to bring these various issues before the FIFRA-SAP on the schedule outlined in Table 1. Further, the Agency plans to post a series of technical briefings on its exposure methodologies in October 2001. It will release its preliminary risk assessments for organophosphates during a technical briefing in December of 2001. Finally, US-EPA will release its revised risk assessment including the cumulative analysis on the August 6, 2002 deadline. For a thorough discussion of this brief summary please see the US-EPA's web site (<http://www.epa.gov/pesticides/cumulative>).

Table 1. Elements of a Public Process for Cumulative Risk Assessment and Expected Timeframes for Revision of Certain Science Policy Papers (2001-2002).

Date	Description
September 2001	Hazard Methodology (Revised RPF Paper) to SAP Science Policy Paper: Release Revised Guidance Documents on the FQPA Safety Factor (Generic)
October 2001	Science Policy Paper: Release Revised Guidance Document on Cumulative Risk Assessment (Generic) Science Policy Paper: Release Proposed Guidance on Relationship of FQPA Safety Factor to Cumulative Risk Assessment (Generic) Technical Briefing on Food, Water and Residential Exposure Methodologies and Approaches in Integration of Multiple Pathways of Exposure
December 2001	Release Preliminary Cumulative Risk Assessment Technical Briefing on Preliminary Risk Assessment
January 2002	60-Day Public Comment Period on Preliminary Risk Assessment Closes
February 2002	Stakeholders Brief Agency on Their Comments
August 2002	FQPA Deadline to Reassess 66% of the Tolerances Complete Revised Cumulative Risk Assessment

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