

ATTACHMENT 1

Issues for February, 2005 FIFRA Scientific Advisory Panel Meeting

Similar to the scientific peer process followed for the Cumulative Risk Assessment (CRA) for the Organophosphorus Pesticides (OPs), OPP plans to consult with the FIFRA Science Advisory Panel (SAP) to seek expert review, advice, and recommendations at each major step in development of the CRA for the N-methyl carbamates. The following text describes the general framework being considered by EPA as it develops its CRA for the N-methyl carbamate pesticides focusing on the SAP meeting scheduled for mid-February. This framework is meant to provide the SAP members along with the public with an overview of the various aspects of the assessment.

February 15-18, 2005:

FIFRA SAP Meeting:

N-methyl carbamate pesticide cumulative risk assessment: Pilot Cumulative Analysis

At the February 2005 SAP meeting, EPA plans to discuss key issues related to hazard assessment, PBPK/PD modeling of carbaryl, drinking water exposure assessment, and the integration of hazard and exposure.

Hazard assessment:

EPA acknowledges that there are toxicological characteristics unique to the N-methyl carbamates which need to be considered in a cumulative risk assessment for this group. Specifically, the mechanism of action for this group of pesticides is carbamylation of the AChE active site leading to rapid recovery of inhibition. OPP is collaborating with laboratory scientists and statisticians from EPA's National Health and Environmental Effects Research Laboratory (NHEERL) to evaluate biological and empirical aspects of recovery. EPA expects to solicit comment on specific issues related to dose-response modeling of AChE data, empirical estimation of time to recovery, and the impact of the laboratory method used to measure AChE inhibition on estimates of relative potency.

PBPK/PD Modeling for Carbaryl:

OPP is collaborating with scientists from EPA's National Exposure Research Laboratory (NERL) to develop a PBPK/PD model for carbaryl within the Exposure Related Dose Estimating Model (ERDEM) Platform (Blancato et al., 2002; Okino et al. 2004). The carbaryl model will form the

basic structure of a generalized model for the N-methyl carbamates. A Quantitative Structure Activity Relationship (QSAR) database of physicochemical descriptors and provisional PK and PD parameter values has been assembled for selected N-methyl carbamates. The completeness and representativeness of the QSAR database will influence the application of the PBPK/PD model for use in the cumulative risk assessment of the N-methyl carbamates. EPA will solicit comment on specific aspects of the appropriate use of ERDEM for this Risk Assessment.

Drinking water exposure assessment:

Unlike the OP CRA where the only anticipated exposure to OP pesticides in drinking water was expected to be from surface water sources, OPP must consider both surface- and ground-water sources of drinking water for the N-methyl carbamates. OPP will solicit comment from the SAP on the use of one or more existing ground-water models to provide a pilot ground-water exposure assessment for the carbamates. OPP also expects to request feedback from the panel on approaches for refining regional drinking water exposures in the event that such exposure from surface and/or ground-water sources contributes substantially to the cumulative exposure in one or more regions.

Integration of hazard and exposure assessment:

EPA will present a pilot cumulative analysis of food, water, and residential exposure. This analysis will be presented using three different exposure models: LifeLine, CARES, and Calendex. This presentation will also include a discussion of the unique challenges related to rapid recovery of AChE inhibition posed by this group of pesticides and different approaches for considering these characteristics in the quantitative estimates of cumulative risk. EPA expects to request the panel to provide comment on potential approaches for integrating hazard and exposure for this group and specifically characterizing recovery in risk estimates.