

US EPA ARCHIVE DOCUMENT

AGENDA

FIFRA SCIENTIFIC ADVISORY PANEL (SAP) OPEN MEETING

February 2 – 5, 2010

FIFRA SAP WEB SITE <http://www.epa.gov/scipoly/sap/>
OPP Docket Telephone: (703) 305-5805
Docket Number: EPA-HQ-OPP- 2009-0851

U.S. Environmental Protection Agency
Conference Center - Lobby Level
One Potomac Yard (South Bldg.)
2777 S. Crystal Drive, Arlington, VA 22202

**Draft Framework and Case Studies on Atrazine, Human Incidents, and the
Agricultural Health Study: Incorporation of Epidemiology and Human Incident
Data into Human Health Risk Assessment**

Please note that all times are approximate (see note at end of Agenda).

Tuesday, February 2, 2010

- 8:30 A.M. Opening of Meeting and Administrative Procedures** – Myrta R. Christian, M.S., Designated Federal Official, Office of Science Coordination and Policy, EPA
- 8:35 A.M. Introduction and Identification of Panel Members** – Steven G. Heeringa, Ph.D., FIFRA Scientific Advisory Panel Chair
- 8:50 A.M. Welcome and Opening Remarks** – Steven Bradbury, Ph.D., Acting Director, Office of Pesticide Programs, EPA
- 9:00 A.M. Welcome and Opening Remarks** – Tina E. Levine, Ph.D., Director, Health Effects Division, Office of Pesticide Programs, EPA
- 9:15 A.M. Overview and Draft Framework for Incorporation of Epidemiology and Human Incident Data into Human Health Risk Assessment**– Anna Lowit, Ph.D., Health Effects Division, Office of Pesticide Programs, EPA
- 9:35 A.M. Retrospective and Ecologic Non-Cancer Epidemiology Studies: Atrazine Studies** – Aaron Niman, Health Effects Division, Office of Pesticide Programs, EPA
- 10:15 A.M. Break**
- 10:30 A.M. Overview of the Agricultural Health Study** – Michael C.R. Alavanja, Dr.P.H. , Senior Investigator, Division of Cancer Epidemiology and Genetics, National Cancer Institute
- 11:10 A.M. The Agricultural Health Study & Office of Pesticide Programs: Comparison of Exposure Assessment Approaches:** Shalu Shelat, Industrial Hygienist, Health Effects Division
- 12:00 P.M. Lunch**

- 1:00 P.M. Human Incident Data-- Retrospective Case Study Using Diazinon:**
Sarah Winfield, Biologist, Health Effects Division
- 1:40 P.M. Summary--** Anna Lowit, Ph.D., Health Effects Division, Office of Pesticide Programs, EPA
- 2:00 P.M. Public Comments**
- 3:00 P.M. Break**
- 3:15 P.M. Public Comments (continued)**
- 5:00 P.M. Adjourn**

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Wednesday, February 3, 2010

- 8:30 A.M. Opening of Meeting and Administrative Procedures** – Myrta R. Christian, M.S, Designated Federal Official, Office of Science Coordination and Policy, EPA
- 8:35 A.M. Introduction and Identification of Panel Members** – Steven G. Heeringa, Ph.D., FIFRA Scientific Advisory Panel Chair
- 8:50 A.M. Follow-up from Previous Day's Discussion** – TBD, Health Effects Division, Office of Pesticide Programs, EPA
- 9:15 A.M. Charge to Panel – Question 1**

Draft Framework for Incorporating Human Epidemiologic & Incident Data in Risk Assessment

OPP's draft framework describes a proposed weight of the evidence (WOE) evaluation that integrates science on exposure, pharmacokinetics, and mode of action derived from experimental animal and human *in vivo* and *in vitro* studies. This proposed WOE uses the "source-to-adverse outcome pathway" and the modified Bradford Hill criteria like that in the Mode of Action (MOA) Framework (Section IV of Draft Framework) as tools for organizing and evaluating these diverse types of data to determine the evidence available on the potential human health consequences of pesticide exposures.

Question 1.1 Section II of the draft framework describes the major types of *epidemiology studies* along with their strengths and limitations, factors to consider when reviewing epidemiology

studies, and ways to use epidemiology data in risk assessment. Please comment on the soundness and completeness of these discussions. If appropriate, please include comments on additional factors for OPP to consider when evaluating the quality and weighing the utility of epidemiology studies in risk assessment/characterization.

Question 1.2 Section III of the draft framework describes the major sources of *human incident data* along with their strengths and limitations. Section III also describes ways to use human incident data in risk assessment. Please comment on the soundness and completeness of these discussions. Please include comments on additional factors to consider when evaluating the quality and weighing the utility of human incident data in risk assessment/characterization.

10:15 A.M. Break

10:30 A.M. Charge to Panel – Question 1 (continued)

Question 1.3 Section IV of the draft framework describes a proposed WOE approach for evaluating human and experimental animal data from *in vitro* and *in vivo* studies. This proposed approach makes use of the “source to adverse outcome pathway” and the modified Bradford Hill criteria (like that in the MOA Framework) as tools for organizing, evaluating, and describing the human health consequence of a particular chemical based on the available data. Please comment on the proposed use of modified Bradford Hill criteria in the context of the source to adverse outcome pathway for integrating a variety of types of data at different levels of biological organization including human incident and epidemiologic data in risk assessment.

Question 1.4 OPP has extensive experience applying the MOA Framework to experimental animal data. However, OPP has not yet completed a WOE approach that also includes epidemiology or human incident data like that proposed in Section IV of the draft framework. Please include in your comments what, if any, additional scientific considerations not discussed in the draft framework OPP should take into account when conducting such WOE analyses.

11:30 A.M. Lunch

12:45 P.M. Charge to Panel – Question 2

Case Study A: Retrospective and Ecologic Non-Cancer Epidemiology Studies

OPP has a dual purpose for developing the Case study A on recent ecologic and retrospective epidemiology studies reporting adverse birth outcomes associated with atrazine exposure. First, the case study illustrates key methodological issues that OPP must consider when integrating ecologic and retrospective epidemiology studies in risk assessment/characterization. Second, this case study reviews several recent studies that will be considered in the re-evaluation of atrazine. Building on the feedback from the SAP at the February, 2010 meeting, these studies will be incorporated in the overall WOE analysis and risk characterization for atrazine. The atrazine WOE is scheduled for review by the FIFRA SAP in September, 2010.

Question 2.1 As discussed in Question 1.1, the draft framework provides general descriptions of the strengths and limitations of ecologic and retrospective epidemiology studies with respect to human health risk assessment. Please describe what you consider to be characteristics of robust,

well-designed ecologic and retrospective epidemiology studies.

Question 2.2 Ecologic and retrospective epidemiology studies are particularly useful in identifying new hypotheses about the human health effects of pesticide exposure and may confirm the human relevance of findings from experimental animal studies. However, these types of studies do not typically include robust characterization of exposure and they do not address confounding factors as well as prospective studies. Although there may be exceptions, generally, ecologic and retrospective epidemiology studies are not sufficiently robust for use in quantitative risk assessment (i.e., for use in deriving a point of departure or in quantitatively informing extrapolation factors, etc). In light of the strengths and limitations of ecologic and retrospective studies, please comment on appropriate ways to use of these types of epidemiology studies in risk assessment/characterization or their utility in problem formulation (e.g. defining additional analyses or research/testing).

Question 2.3 The atrazine case study (Case study A) provides specific examples of ecologic and retrospective epidemiology studies. Please comment on OPP's reviews of the studies discussed in Case study A. In your comments, please provide specific feedback on the OPP's descriptions of each study design, exposure assessment, use of appropriate statistical methods, and ability to address bias and confounding in addition to other factors that may be important in the interpretation of these studies.

2:15 P.M. Break

2:30 P.M. Charge to Panel – Question 2 (continued)

Question 2.4 In light of scientific issues discussed in Questions 2.1-2.3, OPP requests input from the SAP on factors to consider when integrating these studies in the atrazine WOE analysis currently under development.

3:00 P.M. Charge to Panel – Question 3

Case Study C: Human Incident Data-- Retrospective Case Study Using Diazinon

EPA is undertaking an effort to more systematically and transparently review and use human incident data in risk assessment/characterization or in problem formulation than has been done previously. As part of this effort, a case study using human incident data on diazinon is included.

Question 3.1 Case study C describes various analyses and evaluations that can be conducted when evaluating human incident data. Please comment on ability to use incident data for the following types of analyses: trend of incidents over time, frequency of reported symptoms, common product clusters, frequency of repeated exposure scenarios, and assessment of children vs. adult symptom profiles), in the diazinon case study and suggest alternative and/or additional analyses, if appropriate.

Question 3.2 OPP plans to conduct analyses of human incident data like that described in Case study C for other pesticides undergoing registration review. In light of scientific issues

discussed in Questions 3.1, OPP requests input from the Panel on factors to consider when evaluating the reliability of human incident data and determining the relative weight that should be placed on such data in risk assessment/characterization or in problem formulation.

4:30 P.M. Adjourn

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Thursday, February 4, 2010

- 8:30 A.M. Opening of Meeting and Administrative Procedures** – Myrta R. Christian, M.S, Designated Federal Official, Office of Science Coordination and Policy, EPA
- 8:35 A.M. Introduction and Identification of Panel Members** – Steven G. Heeringa, Ph.D., FIFRA Scientific Advisory Panel Chair
- 8:50 A.M. Follow-up from Previous Day's Discussion Opening of Meeting and Administrative Procedures** – TBD, Health Effects Division, Office of Pesticide Programs, EPA
- 9:15 A.M. Charge to Panel – Question 4**

Case Study B: The Agricultural Health Study Comparison of Exposure Assessment Approaches

The Agricultural Health Study (AHS) is a large long-term prospective epidemiological study that is collecting data on the health and work practices of licensed pesticide applicators in Iowa and North Carolina. The AHS is focusing particularly on the exposure of applicators to 50 chemicals, including many of the most widely used pesticides. The study also collects information on other possible agricultural exposures, and many lifestyle factors. Investigators with the AHS have published over 100 publications on a variety of topics including characteristics of the cohort and cancer and non-cancer health outcomes that have been observed in the cohort (<http://aghealth.nci.nih.gov/>).

Question 4.1: The Agency believes prospective epidemiology studies with robust exposure assessment, like the AHS, have the greatest potential for use in risk assessment especially for enhancing problem formulation and risk characterization. Please comment on appropriate ways to use of these types of epidemiology studies in risk assessment.

Question 4.2: The Agency uses a predictive, scenario-based approach to calculate risks associated with the registered use patterns of pesticides. Estimates of risk based on varying levels of protective equipment, application methods, and use conditions are presented. The results of these assessments are used to specify label conditions that are required to support the new registration or continued registration of pesticides. In contrast, the goal of epidemiologic exposure assessment within the AHS is to develop a relative exposure ranking of individuals who are actual pesticide users within a cohort. It is not feasible to directly measure actual exposure in observational analyses such as the AHS. The AHS exposure information is ascertained from questionnaires completed by individual cohort members. Because the AHS and the Agency have different purposes for evaluating pesticide applicator exposure, there are inherent differences in the occupational handler exposure methodologies between the AHS and Agency. How to reconcile these differences in order to make optimal use of the AHS is developing regulatory policy is under investigation by a collaborative effort between EPA's OPP and investigators involved with the AHS. Case study B details a three step analysis plan for accomplishing this goal. Please comment on the proposed plan for comparing the exposure assessment approaches between the Agency and the AHS. Please include in your comments the scientific value of this comparison along with additional and/or alternative analyses which could be conducted.

10:30 A.M. Break

10:45 A.M. Charge to Panel – Question 4 (continued)

Question 4.3: The Agency has a long-term goal to understand the extent to which findings from the AHS are generalizable to other populations, such as pesticide applicators in states other than North Carolina and Iowa or those who may be exposed to pesticides through other pathways and under different use conditions. Please provide suggestions for analyses which could be conducted to make best use of the results of AHS in a broader regulatory context.

12:00 P.M. Lunch

1:00 P.M. Charge to Panel – Discussion continued (as needed)

2:30 P.M. Break

2:45 P.M. Charge to Panel – Discussion continued (as needed)

4:30 P.M. Adjourn

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Friday, February 5, 2010

- 8:30 A.M. Opening of Meeting and Administrative Procedures** – Myrta R. Christian, M.S, Designated Federal Official, Office of Science Coordination and Policy, EPA
- 8:35 A.M. Introduction and Identification of Panel Members** – Steven G. Heeringa, Ph.D., FIFRA Scientific Advisory Panel Chair
- 8:50 A.M. Follow-up from Previous Day's Discussion Opening of Meeting and Administrative Procedures** – TBD, Health Effects Division, Office of Pesticide Programs, EPA
- 9:15 A.M. Charge to Panel – Discussion continued (as needed)**
- 11:30 A.M. Adjourn**

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