AGENDA

Federal Insecticide, Fungicide, and Rodenticide Act
Scientific Advisory Panel Meeting
January 31-February 2, 2012

Scientific Issues Associated with Common Effects Methodology developed by the Office of Pesticide Programs and the Office of Water

Docket number: EPA-HQ-OPP-2011-0898 **OPP Docket Tel: 703-305-5805**

Please note that all times are approximate
(See note at the end of the Agenda)

Tuesday, January 31, 2012

9:00 A.M. **Opening of Meeting and Administrative Procedures** – Sharlene Matten, Ph.D. Designated Federal Official, Office of Science Coordination and Policy, EPA

9:05 A.M. **Introduction and Identification of Panel Members** – Janice Chambers, Ph.D., DABT, FIFRA Scientific Advisory Panel, Session Chair

9:15 A.M. **Opening Remarks** – Donald Brady, Ph.D., Director, Environmental Fate and Effects Division, Office of Pesticide Programs, EPA and Elizabeth Behl, M.S., Director, Health and Ecological Criteria Division, Office of Science and Technology, Office of Water, EPA

9:30 A.M. **Introduction, Background, Status, and OPP and OW Data Requirements and Effects Characterizations** – Kristina Garber, M.S., Environmental Fate and Effects Division, Office of Pesticide Programs, EPA and Joe Beaman, M.S., Health and Ecological Criteria Division, Office of Science and Technology, Office of Water, EPA

10:15 A.M. **Break**

10:30 A.M. **Potential Use of Predictive Toxicology Tools in Characterizing Effects of Chemical Stressors to Aquatic Animals –** Christine Russom, Mid-Continent Ecology Division, Office of Research and Development, EPA

11:15 A.M. **Analysis of Sensitivity Distributions for Estimation of Acute Hazard Concentrations to Aquatic Animals –** Matthew Etterson, Ph.D., Mid-Continent Ecology Division, Office of Research and Development, EPA

12:15 P.M. **Lunch**

1:15 P.M. **Extrapolation Factors for Derivation of Acute Aquatic Life HC5s: Emphasis on Acetylcholinesterase Inhibitors –** Russell Erickson, Ph.D., Mid-Continent Ecology Division, Office of Research and Development, EPA

2:15 P.M. **Analysis of Chronic Toxicity Data and Acute Chronic Ratios (ACRs) in Support of Deriving Chronic HC5s: Acetylcholinesterase Inhibitors –** Russell Erickson, Ph.D., Mid-Continent Ecology Division, Office of Research and Development, EPA

3:00 P.M. **Break**

3:15 P.M. **Estimating Aquatic Plant Community Hazard Concentrations for Pesticide Effects –** Glen Thursby, Ph.D., Atlantic Ecology Division, Office of Research and Development, EPA

5:00 P.M. **Adjournment**

Wednesday, February 1, 2012

9:00 A.M. **Opening of Meeting and Administrative Procedures** – Sharlene Matten, Ph.D., Designated Federal Official, Office of Science Coordination and Policy, EPA

9:05 A.M. **Introduction and Identification of Panel Members** – Janice Chambers, Ph.D., DABT, FIFRA Scientific Advisory Panel, Session Chair

9:10 A.M. **Follow-up from Previous Day's Meeting** – Kristina Garber, M.S., Office of Pesticide Programs, EPA

9:20 A.M. **Public Comments**

10:30 A.M. **Break**

10:45 A.M. **Charge Question 1: QSARs for Predicting Acute Toxicity for Aquatic Animals**

Effect characterizations in both United States Environmental Protection Agency's (USEPA) Office of Water (OW) and Office of Pesticide Programs (OPP) rely on toxicity estimates for various taxa. The USEPA investigated the use of some readily available Quantitative Structure Activity Relationship (QSAR) tools **(**described in **Appendix A)** to predict acute toxicity values to represent sensitive taxa which could potentially fill gaps in available empirical toxicity data. Three publicly available QSAR models were examined, including: Ecological Structure Activity Relationships (ECOSAR), Toxicity Estimation Software Tool (TEST), and the Organization for Economic Cooperation and Development (OECD) QSAR Toolbox. These tools are increasingly used by USEPA risk assessors to determine the potential toxicity of various chemicals, including pesticide degradates. The white paper's analyses of ECOSAR, TEST and the OECD Toolbox suggest that, at this time, 1) the chemical domains for most models within these QSAR tools do not include sufficient data for pesticide active ingredients and therefore these models are not currently robust estimators of the toxicity for modes of action (MOAs) that are unique to pesticides (*e.g.,* acetylcholinesterase (AChE) inhibitors), 2) current models are generally populated with data for species for which toxicity data are typically submitted under FIFRA, and generally, could not be used to fulfill other taxonomic data requirements defined in the 1985 guidelines, and 3) more

toxicologically relevant molecular descriptors and structural alerts need to be identified for use in building models for MOAs associated with pesticide active ingredients.

a) *Appendix A of the white paper includes a review of the utility of ECOSAR, TEST and the OECD toolbox for quantifying sensitive acute toxicity values for aquatic animals exposed to pesticides. Please comment on the strengths and weaknesses of the methods, results and conclusions associated with this review.*

b) *The analysis discussed in Appendix A of the white paper used empirical toxicity data for AChE inhibitors to evaluate the predictions of specific QSAR tools. Please discuss the applicability of the conclusions based on AChE inhibitors to other pesticide MOAs. Although not part of the current analysis, please comment on the ability of SAR tools to quantitatively predict the toxicity of chemicals with non-specific MOAs for sensitive animals (e.g., pesticide degradates and some herbicide with a narcosis MOA), that may be within the domain of applicability of these tools.*

c) *Please comment on potential modifications to the existing versions of ECOSAR, TEST and the OECD toolbox that could improve their quantitative capability relative to estimating acute toxicity values for aquatic animals exposed to specific pesticides. For example, expansion of QSAR models within existing tools to better include pesticide active ingredients within their domain of applicability, expansion of the model training sets to cover taxa associated with data gaps, development of models based on MOA, inclusion of parameters other than the logarithm of the octanol-water partition coefficient (i.e., log P) to describe toxicity.*

12:00 P.M. Lunch

1:00 P.M. Charge Question 2: Web-ICE for Predicting Acute Toxicity for Aquatic Animals

The white paper investigated the use of Web-based Interspecies Correlation Estimation models (Web-ICE) to predict acute toxicity values and potentially fill data gaps (described in **Appendix B)**. The review of the current version of Web-ICE suggests that, when using the minimum acute toxicity data for aquatic animals that are typically submitted to fulfill requirements under FIFRA (*i.e.*, data for *Daphnia magna*, rainbow trout and bluegill sunfish), Web-ICE appears to generate the most precise predictions of toxicity for closely related fish species (*e.g.*, within the same family). If toxicity data are available for either rainbow trout or bluegill sunfish, Web-ICE may be useful for predicting the toxicity of a chemical to some species of fish. The current review of this tool indicates that Web-ICE does not have sufficient data to fulfill the minimum data requirements across all taxa defined in the 1985 Guidelines when there are only acute surrogate data available for rainbow trout, bluegill and *D. magna;* however, this may change with future updates.

a) *Appendix B of the white paper includes a review of the utility of Web-ICE for quantifying sensitive acute toxicity values for aquatic animals exposed to pesticides. Please comment on the strengths and weaknesses of the methods, results and conclusions associated with this review.*

b) *Please comment on potential modifications to the existing version of Web ICE that could improve its ability to predict the acute toxicity values of pesticides to different species of aquatic animals. For example, expansion of the tool to consider MOA, addition of data for infrequently tested species that may fulfill the data requirements defined in the 1985 guidelines.*

2:00 P.M. Charge Question 3: Use of SSDs to estimate HC5 using varying amounts of data

As described in **Appendix C**, USEPA investigated the use of species sensitivity distributions (SSDs) with varying amounts of empirical data to estimate the fifth percentiles of sensitivity distributions of toxicity data (termed the "HC5"). Analyses performed by USEPA for this effort suggest that SSDs have limited utility when test data points are limited, specifically where biological diversity is not sufficient to represent the distribution of taxa sensitivity. The analyses further suggest that SSDs applied to datasets that satisfy existing taxonomic requirements with extrapolation constants (as defined in **Appendix C**) would likely result in lower and yet reasonable approximations of the HC5.

a) Appendix C of the white paper includes a description of the analyses of SSDs. Please comment on the strengths and weaknesses of the methods, results and conclusions associated with this analysis.

In **Appendix C**, several potential avenues for future work on SSDs were described, including i) extension of methods for ordered data to all continuous distributions ii) development of stepwise methods, including decision points, for data analysis to incorporate information on the relationship of MOA and taxa sensitivity, and iii) the use of random effects methods for handling cases in which more than one test result is available for a given taxon.

b) Please comment upon additional analyses relative to SSDs that could be considered by USEPA that may result in improved confidence in estimates of HC5 values using various amounts of data that are typically available for registered pesticides.

3:00 P.M. Break

3:15 P.M. Charge Question 4: Extrapolation Factors for Estimating Acute HC5s with a Specified Level of Confidence

The USEPA OW's aquatic life criteria (ALC) involve calculation of the "Final Acute Value" (FAV) as the fifth percentile of acute toxicity values for genera of aquatic animals, and impose certain minimum data requirements (MDRs) for such calculations. To provide some assessment of effects when insufficient data are available for calculating an FAV, USEPA's Great Lakes Water Quality Guidance (GLWQG) specified extrapolation factors (EFs) by which the acute toxicity value for the most sensitive tested aquatic animal genus could be divided to provide a conservative estimate for what the FAV should be if sufficient data was available (U.S.EPA 1995). In this case, conservative estimates of the FAV are generated by accounting for uncertainty in possible EF values, which generally results in an underestimate of the FAV that may be generated using a data set that would be considered complete according to the 1985 Guidelines. The EFs incorporated into the GLWQG were based on analyses by Host et al. (1995) of toxicity test datasets used in freshwater ALC that existed at that time; these analyses involved repeatedly subsampling (resampling) of these datasets to assess the relationship of the lowest toxicity values in datasets of a specified size and composition to FAVs based on larger datasets.

The analyses described in **Appendix D** of this white paper builds upon the analysis conducted by Host et al. (1995) by (a) utilizing more recent aquatic toxicity data and data for chemicals that do not have an ALC, (b) developing EFs for different MOAs to reduce uncertainty, (c) paying specific attention to EFs for OPP minimum data requirements for acute toxicity testing of aquatic animals, and (d) generating EFs using statistical distributions descriptive of acute toxicity values for different taxonomic groups and based on multiple chemicals, rather than resampling toxicity data for individual chemicals. These analyses

established the feasibility of establishing EFs for certain MOAs, demonstrated how a distributional rather than a resampling approach can more effectively exploit data to develop MOA-specific EFs, and documented the relationship between OPP and OW benchmarks. In addition, the current efforts considered how EF applicability and meaning might be affected, relative to the GLWQG, by different strategies for assigning reference HC5 and for summarizing EF distributions.

a) *Please comment on the extent to which consideration of MOA decreases uncertainty associated with HC5 values that are estimated using EFs.*

b) *Please comment on the strengths and limitations of both the resampling and distributional methodologies for developing MOA-specific EFs, and provide suggestions on their further development and application to other MOAs. Please provide suggestions for deriving EFs for chemicals with MOAs that have limited amounts of empirical toxicity data.*

c) *Please comment on the strengths and limitations of the different approaches in the Host et al. (1995) and the current work for assigning reference HC5s and summarizing EF distributions.*

4:30 P.M. Charge Question 5: Use of ACRs to estimate chronic toxicity endpoints or HC5 values for acutely sensitive species

Chronic toxicity data are generally available for fewer species than are tested to determine acute toxicity. Acute-chronic ratios (ACRs) are a common tool used to estimate chronic effect thresholds for taxa lacking chronic toxicity data. Both OPP and OW currently use ACRs developed for specific chemicals to estimate chronic effect levels. ACR distributions have been developed for broad groups of chemicals without consideration of MOA or taxa (*e.g.*, mixed pesticides by TenBrook et al. 2010; all chemicals by Host et al. 1995). **Appendix E** of the white paper considers the application of ACRs developed for chemicals within the same MOA to estimate chronic effects for chemicals with the same MOA and lacking any chemical-specific ACRs. Analysis of ACR data specifically for AChE inhibitors identified patterns in the ACR distributions. Most notably, ACRs for invertebrates were smaller than those for fish. Although fish had larger ACRs, this did not translate to higher chronic sensitivity of fish to AChE inhibitors, because of their very low acute sensitivity. In fact, analyses showed that concentrations protective of acute toxicity to invertebrates would simultaneously protect fish from chronic effects. By extension, for AChE inhibitors, applying an invertebrate-based ACR to the acute HC5 (*i.e.*, fifth percentile of a sensitivity distribution) should provide a chronic HC5 protective of both fish and invertebrates. When comparing ACRs developed for broad groups of chemicals and taxa to ACRs for aquatic invertebrates exposed to AChE inhibitors, they were approximately 2 fold different.

a) *Please comment on the strengths and weaknesses of using chemical-specific ACRs to estimate chronic effect thresholds for other species and taxa.*

b) *Please comment on the strengths and weakness of applying "default" ACRs derived from other chemicals to extrapolate from an acute HC5 to a chronic HC5, including the relative merits of values derived for MOA-specific (e.g., for AChE inhibitors) or more generalized (e.g., Host et al. 1995) distributions.*

c) *Are there other methods for estimating a chronic HC5 that the panel believes would be technically superior to ACR-based approaches? For example, TCE models (described in USEPA 2010a), distributional approaches (e.g., de Zwart 2002, Douboudin et al. 2004; described in USEPA 2010b).*

5:30 P.M. Adjournment

Thursday, February 2, 2012

9:00 A.M. **Opening of Meeting and Administrative Procedures** – Sharlene Matten, Ph.D., Designated Federal Official, Office of Science Coordination and Policy, EPA

9:05 A.M. **Introduction and Identification of Panel Members** – Janice Chambers, Ph.D., DABT, FIFRA Scientific Advisory Panel, Session Chair

9:10 A.M. **Follow-up From Previous Day's Meeting** – Kristina Garber, M.S., Office of Pesticide Programs, EPA

9:20 A.M. **Panel Discussion of Charge Question 5 cont'd**

10:30 A.M. **Break**

10:45 A.M. **Charge Question 6: Estimating the HC5 for Aquatic Plants**

As with animals, there has been uncertainty regarding the extent to which available data reflect the range of sensitivities that may be present for aquatic plants. This effort focuses on the potential uses of EFs and SSDs to estimate the HC5 relevant to aquatic plants. As described in **Appendix F**, the primary analyses investigated the use of the standard aquatic plant species submitted to fulfill FIFRA data requirements in estimating the HC5. These species, which are referred to in the white paper as "the FIFRA-5" include: *Pseudokirchneriella subcapitata* (a freshwater green alga), *Anabaena flos-aquae* (a freshwater cyanobacterium), *Navicula pelliculosa* (a freshwater diatom), *Skeletonema costatum* (a saltwater diatom) and *Lemna gibba* (the aquatic vascular plant, duckweed). The analysis described in **Appendix F** suggested that estimating the HC5 using the FIFRA-5 will result in a reasonable approximation of the HC5 of an aquatic plant community.

a) *Appendix F of the white paper includes an analysis of the use of EFs and SSDs combined with the FIFRA-5 to estimate the HC5 for aquatic plants. Please comment on the strengths and weaknesses of the methods, results and conclusions associated with this analysis.*

b) Please comment on other aquatic plant species or test endpoints that may be considered in order to generate more certain estimates of the HC5 for aquatic plants.

c) Please comment on the strengths and limitations of normalizing plant toxicity endpoints to a standard metric (i.e., EC50 for growth rate).

d) Please comment on the extent to which consideration of MOA may decrease uncertainty associated with HC5 values for aquatic plants.

12:30 P.M. **Lunch**

1:30 P.M. **Continued Panel Discussion (as necessary)**

3:00 P.M. **Adjournment**

Please be advised that agenda times are approximate; when the discussion for one topic is completed, discussions for the next topic will begin. For further information, please contact the Designated Federal Official for this meeting, Dr. Sharlene Matten, telephone: (202)-564-0130, fax: (202) 564-8382, or email: matten.sharlene@epa.gov.