BILLING CODE 6560-50-P

**ENVIRONMENTAL PROTECTION AGENCY**

**[EPA-HQ-OPP-2017-0180; FRL-9962-78]**

# FIFRA Scientific Advisory Panel; Notice of Public Meeting; Request for Ad Hoc Expert Nominations

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Notice.

**SUMMARY:** There will be a 4-day meeting of the Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (FIFRA SAP) to consider and review physiologically based pharmacokinetic modeling to address pharmacokinetic differences between and within species.

**DATES:** The meeting will be held on October 24, 2017 to October 27, 2017, from approximately 9 a.m. to 5 p.m.

*Comments*. Written comments should be submitted on or before September 11, 2017. FIFRA SAP may not be able to fully consider written comments submitted after September 11, 2017. Requests to make oral comments should be submitted on or before September 25, 2017 by contacting the Designated Federal Official (DFO) listed under **FOR FURTHER INFORMATION CONTACT.** For additional instructions, see Unit I.C. of the **SUPPLEMENTARY INFORMATION**.

*Nominations*. Nominations of candidates to serve as ad hoc members of FIFRA SAP for this meeting should be provided on or before [*INSERT DATE* 45 DAYS *FROM DATE OF PUBLICATION IN THE* **FEDERAL REGISTER**].

*Webcast.* This meeting may be webcast. Please refer to the FIFRA SAP website

at *https://www.epa.gov/sap* for information on how to access the webcast. Please note that the webcast is a supplementary public process provided only for convenience. If difficulties arise resulting in webcasting outages, the meeting will continue as planned.

*Special accommodations*. For information on access or services for individuals with disabilities, and to request accommodation of a disability, please contact the DFO listed under **FOR FURTHER INFORMATION CONTACT** at least 10 days prior to the meeting to allow EPA time to process your request.

**ADDRESSES:** *Meeting*: The meeting will be held at the Environmental Protection Agency, Conference Center, Lobby Level, One Potomac Yard (South Bldg.), 2777 S. Crystal Dr., Arlington, VA 22202.

*Comments*. Submit your comments, identified by docket identification (ID) number EPA-HQ-OPP-2017-0180, by one of the following methods:

• *Federal eRulemaking Portal*: *http://www.regulations.gov*. Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute.

• *Mail*: OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.

• *Hand Delivery*: To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.html*.

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets*.

*Nominations, requests to present oral comments, and requests for special accommodations*. Submit nominations to serve as ad hoc members of FIFRA SAP, requests for special accommodations, or requests to present oral comments to the DFO listed under **FOR FURTHER INFORMATION CONTACT**.

**FOR FURTHER INFORMATION, CONTACT:** Dr. Marquea D. King, DFO, Office of Science Coordination and Policy (7201M), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; telephone number: (202) 564-3626; email address: *king.marquea@epa.gov*.

**SUPPLEMENTARY INFORMATION:**

**I. General Information**

*A. Does this Action Apply to Me?*

This action is directed to the public in general. This action may be of interest to persons who are or may be required to conduct testing of chemical substances under the Federal Food, Drug, and Cosmetic Act (FFDCA) and FIFRA. Since other entities may also be interested, the Agency has not attempted to describe all the specific entities that may be affected by this action.

*B. What Should I Consider as I Prepare My Comments for EPA?*

1. *Submitting CBI*. Do not submit CBI information to EPA through regulations.gov or email. If your comments contain any information that you consider to be CBI or otherwise protected, please contact the DFO listed under **FOR FURTHER INFORMATION CONTACT** to obtain special instructions before submitting your comments.

2. *Tips for preparing your comments*. When preparing and submitting your

comments, see the commenting tips at *http://www.epa.gov/dockets/comments.html*.

*C. How May I Participate in this Meeting?*

You may participate in this meeting by following the instructions in this unit. To ensure proper receipt by EPA, it is imperative that you identify docket ID number EPA-HQ-OPP-2017-0180 in the subject line on the first page of your request.

1. *Written comments*. Written comments should be submitted, using the instructions in **ADDRESSES** and Unit I.B., on or before September 11, 2017, to provide FIFRA SAP the time necessary to consider and review the written comments. FIFRA SAP may not be able to fully consider written comments submitted after September 11, 2017.

2. *Oral comments*. The Agency encourages each individual or group wishing to make brief oral comments to FIFRA SAP to submit their request to the DFO listed under **FOR FURTHER INFORMATION CONTACT** on or before September 25, 2017, in order to be included on the meeting agenda. Requests to present oral comments will be accepted until September 25, 2017 and, to the extent that time permits, the Chair of FIFRA SAP may permit the presentation of oral comments at the meeting by interested persons who have not previously requested time. Oral comments before FIFRA SAP are limited to approximately 5 minutes unless arrangements have been made prior to September 25, 2017. The request should identify the name of the individual making the presentation, the organization (if any) the individual will represent, and any requirements for audiovisual equipment. In addition, each speaker should bring 15 copies of his or her oral remarks and presentation slides (if required) for distribution to FIFRA SAP at the meeting by the DFO.

3. *Seating at the meeting*. Seating at the meeting will be open and on a first-come basis.

4. *Request for nominations to serve as ad hoc expert members of FIFRA SAP for this meeting*. As part of a broader process for developing a pool of candidates, both U.S. citizens and permanent residents who can demonstrate that they are actively seeking U.S. citizenship will be considered. For each meeting, FIFRA SAP staff routinely solicits the stakeholder community for nominations of prospective candidates for service as ad hoc members of FIFRA SAP. Any interested person or organization may nominate qualified individuals to be considered as prospective candidates for a specific meeting. Individuals nominated for this meeting should have expertise in one or more of the following areas: Physiologically-based pharmacokinetic (PBPK) modeling, pharmacokinetics, pharmacodynamic (PD) modeling, *in vitro* to *in vivo* extrapolation, human health risk assessment, neurotoxicity, organophosphate pesticides, pyrethroids pesticides, *N*-methyl carbamate pesticides, fungicides, acetylcholinesterase inhibition, and exposure assessment. Nominees should be scientists who have sufficient professional qualifications, including training and experience, to be capable of providing expert comments on the scientific issues for this meeting. Nominees should be identified by name, occupation, position, address, email address, and telephone number. Nominations should be provided to the DFO listed under **FOR FURTHER INFORMATION CONTACT** on or before [*INSERT DATE* 45 DAYS *FROM DATE OF PUBLICATION IN THE* **FEDERAL REGISTER**]. The Agency will consider all nominations of prospective candidates for this meeting that are received on or before that date. However, final selection of ad hoc members for this meeting is a discretionary function of the

Agency.

The selection of scientists to serve on FIFRA SAP is based on the function of the Panel and the expertise needed to address the Agency's charge to the Panel. No interested scientists shall be ineligible to serve by reason of their membership on any other advisory committee to a Federal department or agency or their employment by a Federal department or agency, except EPA. Other factors considered during the selection process include availability of the potential Panel member to fully participate in the Panel's review, absence of any conflicts of interest or appearance of lack of impartiality, independence with respect to the matters under review, and lack of bias. Although financial conflicts of interest, the appearance of lack of impartiality, lack of independence, and bias may result in disqualification, the absence of such concerns does not assure that a candidate will be selected to serve on FIFRA SAP. Numerous qualified candidates are identified for each Panel. Therefore, selection decisions involve carefully weighing a number of factors including the candidates' areas of expertise and professional qualifications and achieving an overall balance of different scientific perspectives on the Panel. In order to have the collective breadth of experience needed to address the Agency's peer review charge for this meeting, the Agency anticipates selecting approximately 13 ad hoc scientists.

FIFRA SAP members are subject to the provisions of 5 CFR Part 2634 -- Executive Branch Financial Disclosure, Qualified Trusts, and Certificates of Divestiture, as supplemented by EPA in 5 CFR part 6401. In anticipation of this requirement, prospective candidates for service on FIFRA SAP will be asked to submit confidential financial information which shall fully disclose, among other financial interests, the

candidate's employment, stocks, and bonds, and where applicable, sources of research support. EPA will evaluate the candidate's financial disclosure form to assess whether there are financial conflicts of interest, appearance of a lack of impartiality, or any prior involvement with the development of the documents under consideration (including previous scientific peer review) before the candidate is considered further for service on FIFRA SAP. Those who are selected from the pool of prospective candidates will be asked to attend the public meetings and to participate in the discussion of key issues and assumptions at these meetings. In addition, they will be asked to review and to help finalize the meeting minutes and the final meeting report. The list of FIFRA SAP members participating at this meeting will be posted on the FIFRA SAP website at *https://www.epa.gov/sap* or may be obtained from the OPP Docket at *http://www.regulations.gov*.

## II. Background

### *A. Purpose of FIFRA SAP*

FIFRA SAP serves as the primary scientific peer review mechanism of EPA's Office of Chemical Safety and Pollution Prevention (OCSPP) and is structured to provide scientific advice, information and recommendations to the EPA Administrator on pesticides and pesticide-related issues as to the impact of regulatory actions on health and the environment. FIFRA SAP is a Federal advisory committee established in 1975 under FIFRA that operates in accordance with requirements of the Federal Advisory Committee Act (5 U.S.C. Appendix). FIFRA SAP is composed of a permanent panel consisting of seven members who are appointed by the EPA Administrator from nominees provided by the National Institutes of Health and the National Science Foundation. The FIFRA SAP

is assisted in their reviews by ad hoc participation from the Science Review Board (SRB). As a scientific peer review mechanism, FIFRA SAP provides comments, evaluations, and recommendations to improve the effectiveness and quality of analyses made by Agency scientists.

*B. Public Meeting*

The 2009 National Research Council's report "Science and Decisions" recommends that the EPA use the best, most current science to support or revise the default assumptions in risk assessment. In addition, the 2013 Institute of Medicine's report on "Environmental Decisions in the Face of Uncertainty" further recommends that replacing default uncertainty factors with data-derived extrapolation factors (DDEFs) that delineate the differences between species would reduce uncertainty in risk assessment. Such inter- and intra-species extrapolation factors can be derived using a PBPK modeling approach to organize mechanistic data on properties that determine the absorption, distribution, metabolism, and excretion (ADME) of chemicals that enter the body. In the 2006 document on "Approaches for the Application of Physiologically Based Pharmacokinetic (PBPK) Models and Supporting Data in Risk Assessment", the Agency recognizes that PBPK model analysis is a scientifically sound approach that allows for estimating the internal dose of a chemical or its metabolite at a target site, and can act as a means to evaluate and describe the uncertainty in a risk assessment.

PBPK models incorporate the relevant physiology, chemistry, biochemistry that determines the ADME processes, and thus, they are useful for predicting internal dosimetry related to a certain chemical within and outside the testing conditions (e.g., species, dose ranges). PBPK models have been used to assist high-to-low dose, route-to-

route, aggregation of exposure from multiple routes, and inter-species extrapolations that are necessary for estimating human health risks based on the results of animal toxicity studies. The physiological structure of PBPK models also allows for examining the effects of changing physiology, such as aging, early life-stage, or pregnancy. The temporal change in the dose metric simulated by a PBPK model can also be linked to a PD model to predict quantitative changes in biological effects, such as acetylcholinesterase (AChE) inhibition.

Several registrants, including the Council for the Advancement of Pyrethroid Human Health Risk Assessment (CAPHRA), Tessenderlo Kerley Inc. (TKI), FMC/Cheminova, and Syngenta, are developing PBPK (or PBPK-PD) models for the chemicals: Acibenzolar, carbaryl, deltamethrin, dimethoate, malathion, and permethrin. All six models will include life-stage physiological changes from birth to adulthood, so that dose metrics can be predicted at any age. These life-stage models, however, will not include gestation and lactational phases, therefore; it is not expected that these models will have the capability to predict dose metrics in pregnant women or fetuses or breastfeeding exposures. These models are intended as a means to estimating inter- and intra-species data derived extrapolation factors and/or human points of departure (PoD) for various exposure scenarios (e.g., routes of exposure). For dimethoate, malathion, and carbaryl, the PBPK models will be coupled with PD models to predict AChE inhibition in red blood cells (RBCs) and other tissues (e.g., brain).

The purpose of the October 2017 SAP will be to review five PBPK or PBPK-PD models (carbaryl, deltamethrin, dimethoate, malathion, and permethrin) for the purposes of model structures, mathematical representations, parameter estimations, computer

implementations, variability and uncertainty analysis, and model predictive capabilities, as well as the appropriateness of their applications in human health risk assessments. The details for each model, including their inputs, parameters and associated distributions, and the model code, written in software program acslX or R, will be provided for five (not including acibenzolar) chemicals as part of the background materials for the meeting. The agency will solicit comments from the SAP members on the evaluation of these PBPK (or PBPK-PD) models regarding their capability to predict appropriate internal dose metrics in humans. In addition, the SAP members will be asked to evaluate the appropriateness of using these models for intended risk assessment purposes, such as deriving chemical-specific DDEFs to replace default uncertainty factors, or estimating human PoDs for various exposure scenarios (e.g., dietary, drinking water, and worker exposures). Finally, the SAP members will be asked to comment on the potential for using these models as a basis for extrapolation to other chemicals within the same chemical class.

For the sixth PBPK model (acibenzolar), developed in Simcyp, details including inputs, parameters and associated distributions, will be provided as background materials. The SAP members, however, will not be asked to review the Simcyp model code. Instead, the agency will solicit comments from the SAP members as a consultation on this model as primarily a proof-of-concept study, highlighting newer *in vitro* and *in silico* based approaches. This model is not anticipated to be used in a risk assessment by the Agency.

*C. FIFRA SAP Documents and Meeting Minutes*

EPA's background paper, charge/questions to FIFRA SAP, and related supporting

materials will be available on or before August 11, 2017. In addition, a list of candidates under consideration as prospective ad hoc panelists for this meeting will be available for public comment by mid to late August (see link for listing of nominees to appear in mid to late August at *https://www.epa.gov/sap*). Comments should be provided to the DFO listed under **FOR FURTHER INFORMATION CONTACT** on or before the deadline listed on the website given above. Your comments will be placed in the public docket by the DFO. You may obtain electronic copies of most meeting documents, including FIFRA SAP composition (i.e., members and ad hoc members for this meeting) and the meeting agenda, at *http://www.regulations.gov* and the FIFRA SAP website at *https://www.epa.gov/sap*.

FIFRA SAP will prepare meeting minutes summarizing its recommendations to the Agency approximately 90 days after the meeting. The meeting minutes and final report will be posted on the FIFRA SAP website or may be obtained from the OPP Docket at *http://www.regulations.gov*.

**Authority:** 7 U.S.C. 136 *et. seq*.; 21 U.S.C. 301 *et seq*.

Dated: May 25, 2017,

Stanley Barone Jr.,

*Director,* Office of Science Coordination and Policy.
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