

**U.S. Environmental Protection Agency
Science Advisory Board**

Final Minutes of Public Meeting March 1, 2006

Committee: EPI Suite Review Panel.

Date and Time: March 1, 2006 from 1 - 3 Eastern Time advertised in the Federal Register Notice, February 1, 2006. Volume 71, Number 21. Page 5317-5318

Location: By telephone only, run from room 3610E, 1025 F Street Northwest, Washington D.C.

Purpose: The purpose of this teleconference is to prepare the Panel and the Agency for the March 7-9, 2006 face-to-face meeting by responding to panelists' preliminary questions and identifying areas where additional information is needed. (These materials are posted at the SAB's website, www.epa.gov/sab and will be found in the FACA file for this meeting)

Materials Available: The following materials were distributed before the meeting:

1. agenda
2. preliminary charge
3. roster and biosketches
4. website to access EPI Suite
5. responses to the charge questions from individual panelists

Attendees: Because this was a conference call, there are no sign-in sheets.

The following individuals from the Workgroup were present for most or all of the call:

The chair, **Dr. Michael J. McFarland**, Associate Professor, Department of Civil and Environmental Engineering, Utah State University, Logan, UT, and members:

Dr. Robert L. Chinery, Research Scientist, Environmental Protection Bureau, New York State Department of Law, Albany, NY

Dr. Christina E. Cowan-Ellsberry, Professional Staff, Risk Science, Policy and Regulatory Sciences Department, The Procter & Gamble Company, Cincinnati, OH

Dr. Miriam L. Diamond, Professor, Department of Geography, University of Toronto, Toronto, Ontario, CANADA

Dr. William J. Doucette, Professor, Department of Civil and Environmental Engineering in the Utah Water Research Laboratory and, Center for Environmental Toxicology, Utah State University, Logan, UT

Dr. David A. Dzombak, Professor, Department of Civil and Environmental Engineering, Carnegie-Mellon University, Pittsburgh, PA

Dr. Anton J. Hopfinger, Research Professor, Deans Office Administration, University of New Mexico, NM.

Dr. Michael W. Murray, Staff Scientist, Great Lakes Field Office, National Wildlife Federation, Ann Arbor, MI

Dr. Thomas F. Parkerton, Advanced Sci Assoc, Toxicology & Environmental Sciences, ExxonMobil Biomedical Sciences, Annandale, NJ

Dr. Kevin H. Reinert, Principal Toxicologist, AMEC Earth and Environmental, Plymouth Meeting, PA

Dr. Daniel T. Salvito, Manager - Environmental Program, Research Institute for Fragrance Materials, Woodcliff Lake, NJ

Dr. Hans Sanderson, Director, Environmental Safety, International and Regulatory Affairs, Soap and Detergent Association, Washington, DC

Dr. Louis J. Thibodeaux, Jesse Coates Professor, Gordon A. & Mary Cain Department of Chemical Engineering, College of Engineering, Louisiana State University, Baton Rouge, LA

Dr. Deborah H. Bennett was not able to participate; Drs. Dzombak and Salvito were not able to stay until the end of the call.

The following individuals from the SAB Staff Office were present for part or all of the call: Anthony Maciorowski, Associate Director for Science and Kathleen White, DFO. Cathy Fehrenbacher, Bob Boethling, and Lawrence Libelo from EPA's OPPT were present.

The following individuals from the public were present: John Carbone of the Rohm and Haas Company, Jean Rhodes of Promerus LLC, Gerry Wood (a consultant), Cynthia Klein-Banai of the University of Illinois at Chicago, David J. Kent of Keller and Heckman LLP, Diana Graham of Keller and Heckman LLP, Noel C. Scrivner of DuPont Engineering, Jayashree Srinivasan of Accelrys. The total number of people who participated in the call was approximately 35.

Summary

The meeting went largely according to the agenda.

At the end of the meeting, Dr. McFarland summarized major points for the Agency.

The following is a chronological summary of the meeting.

1. Welcome, Roll Call, and Opening Remarks

The DFO saw no need to repeat the introduction given on the February 22 call and asked that anyone with questions about the process contact her off line. At 1:05 the chair welcomed the Panel, the Agency and the public and reviewed the agenda for today's call.

2. Briefings by OPPT

At the February 22 teleconference, panelists prepared and circulated initial individual responses to the charge questions. OPPT's Cathy Fehrenbacher reviewed the questions and the responses provided and then provided additional information to the Panel.

(A) There were a number of questions about other EPA models and the endpoints addressed in them. OPPT responded with a brief description of other agency models that estimated properties. OPPT went to the EPA Council on Environmental Regulatory Models' website which describes the most widely used Agency models and data bases. ORD is developing ASTER. At the SPARC website she found information on the endpoints included in the SPARC model.

(B) There were a series of requests for clarification of how OPPT uses the EPI Suite tool and whether or not the Panel was to consider only how OPPT uses the model or how various offices within EPA use the model. OPPT's preference is that the Panel focus on their office. Therefore, they gathered information from the new chemicals program and information for the exposure tools website along with historical programmatic information to write a brief document. OPPT included some facts and figures. OPPT typically evaluates 2000 new chemicals a year. However, they only receive new chemical measured data in about 5% of notifications. OPPT has only a short period to prepare its assessment, often working on 10-20 assessments on any given day and is lucky to have a few hours to give each. Most of the new chemicals are submitted as Confidential Business Information which means EPA has to use PC based models (not ones, like SPARC, that are internet based).

Diamond asked about the implications of the evaluation – can the applicant go into high volume production. The decision on a new chemical applies to the importer or manufacturer. The proposed volume could be very small or very large. EPI Suite is used in an environmental fate assessment which is part of a screening level risk assessment. EPA makes determinations based on those assessments for each new chemical.

Thibodeaux asked Diamond's question in a different way. EPI Suite is a screening level tool. Is EPI Suite the only evaluation that is done prior to approval of a new chemical? Fehrenbacher responded that it is not. There is another process for each new chemical that begins with an assessment of its chemistry. This is followed by a report on human health and ecological toxicity and environmental fate and transport. Some of EPI Suite's outputs may be used to inform the human health and ecotox assessments.

Doucette asked if there was a flow-chart of where the outputs of EPI Suite have been used. Fehrenbacher said there was a flowchart of the PMN process, but not of how the output of EPI Suite is actually used. She thinks that EPI Suites outputs are used to inform, rather than as input to other processes.

Chinery confirmed that these are all screening level assessments (health, eco, etc.) not the full blown risk assessments some people may be imagining. Fehrenbacher agreed. She reminded the Panel all this happens within 1-2 weeks. Screening level tools are used. The new chemicals have yet to be commercialized so there is no monitoring data, there is likely to be no measurement of basic physical-chemical properties.

Diamond feels it is instructive to know what output is being used where in the assessment of new chemicals. She knows now where KOW is going and asked about fate. Boethling said that the information is provided to inform the other assessments, but it is not quantitative.

Reinert expressed it this way - the outputs from fugacity or other parts of EPI Suite are used to inform other modules of the re view process, as Boethling and Fehrenbacher have said. For example, if EPI Suite shows the chemical does not partition to air, the human health assessment would focus on other exposure paths. Another panelist confirmed that no decision would be made on the results of EPI Suite alone.

Parkerton is struggling with understanding “is the model fit for the purpose” Fehrenbacher recognizes it is a difficult question. That’s why they pulled together information that focused on the use of EPI Suite as a screening tool.

Diamond is finding the discussion helpful. It is good to understand what screening level means, especially in the light of the comments from the Chamber of Commerce. Fehrenbacher explained that they would not use EPI Suite to make risk management decisions under other programs where the decisions would have significant environmental or economic impact.

Salvito asked whether the questions was the degree of conservativeness or accuracy? Does it tend to produce false positives or false negatives. Another panelist said any reputable company should look at the output of EPI Suite and, if the results are screwy, do some studies. Sometimes, based on the overall screening assessment, the Agency does require further testing.

TSCA does not require companies to generate new data for new chemicals. However, if EPA is concerned about the new chemical and wants to restrict it, EPA can issue a “5E consent order or Significant New Use Rule”. If EPA has high concerns, they could ban pending testing or say that they can manufacture only after testing, or require that testing be triggered by a certain production volume. Fehrenbacher doesn’t know how often they ask for testing, but they generally regulate only 5-10% of the new chemicals and most of those probably have a testing requirement.

(C) There were several questions about the Agency's Information Quality Guidelines, so OPPT summarized the guidelines which emphasize qualities such as objectivity, utility, and as well as the Agency's finding that EPI Suite does meet the guidelines. They also summarized the process they used to develop and refine the EPI Suite model. Boethling provided two things. One is the one Fehrenbacher just addressed which addresses how and when OPPT decides to make new enhancements to EPI Suite. He also addressed whether or not EPI Suite's estimations were class specific, which, for the most part, they aren't.

(D) The Agency cut and paste from the on-line HELP Guides into a word file, converted into PDF and sent. Because of the conversions some of the graphics and tables do not look as good in the PDF files as they do on line. Cowan-Ellsberry asked for some help.

(E) The Agency also sent references for EPI Suites modules.

3. Additional Questions

(A) Reinert thought the flow chart was a good idea.

He would like to know if there is a periodic review of the literature for new data to see how the current data base could be enhanced. Boethling says this occurs irregularly as budget and time permit.

He would like to know, when there is conflicting data, how EPA chooses which ones to pick.

Was something written up about how SPARC results compare with EPI Suite? Boethling says there is no formalized process, just spot checking. Sanderson says yes by SPARC. Fehrenbacher said that, at one time ORD researchers in Athens were comparing SPARC and EPI Suite; they'll check. Sanderson said he would send the paper he has.

How were the default selections made? Boethling said there is no simple answer and there is much of it in the HELP files.

(B) Doucette also has a question about the values in the database. He understands that the values in the database have been peer reviewed. He wondered if there was a specific set of criteria the peer reviewers used to select which default value will pop up. Similarly, is there any peer evaluation of potentially new models that could replace existing modules for the same property, such as Henry's Law Constant? Boethling said he tried to address this in what he wrote and the DFO sent. There is no formal process; it is an *ad hoc* process. McFarland said the panel could recommend a systematic, transparent process.

(C) Dzombak said that one of the responses discusses the use of EPI Suite for existing chemicals. He asked what circumstances, other than HPV, would a chemical come into EPI Suite. Fehrenbacher said EPI Suite would be used for any chemical in the absence of data. There are a number of voluntary programs where external people bring existing chemicals to

EPA for evaluation, including (green chemistry? DfE? Children?) Thibodeaux followed up - if there was nothing in physprop, has structure and a measured value of KOW, but wants water solubility. He could use WATER-NT or other approaches within EPI Suite to estimate solubility. Boethling agreed that it could be done and which you picked would depend on the

Also, if a chemical pops up in the media, it might be quickly used to answer an internal question.

Hopfinger asked what happened to chemicals like polymers and organometallics that can't be assessed in EPI Suite. Boethling responded that you could run EPI Suite for any chemical you can write a formula for, including metals and polymers. That doesn't mean you should because EPI Suite is not suited to them. Hopfinger asked about surfactants that might have a critical micelle concentration which affects fish but EPI Suite doesn't address. Fehrenbacher said these are well known limitations of EPI Suite. They wouldn't use it in those circumstances and hopes other don't.

Dzombak asked how many new chemicals are submitted a year that aren't suited to EPI Suite and how does OPPT address them. Boethling said the proportion is substantial; he wouldn't be surprised if it was 50%, OPPT uses submitted information, information gathered from the literature, and professional judgement. Diamond asked how they would know whether the chemicals are suited or not. Fehrenbacher thinks the staff is familiar enough to apply EPI Suite where it is needed.

Diamond asked for some clarification, referencing Boethling's slide 8 from last week which gave examples of EPI Suite modules, but is not comprehensive as ECOSAR is missing. Diamond found a bunch of other models in EPI Suite – Cowan-Ellsberry suggested that they might have been at the EPA website, not within EPI Suite; Diamond confirmed that was the case.

Dzombak remarked that the charge questions are at a high level and that, therefore, the review is not of the detail of the sub-models. The Panel should focus on the issues applicable to all or most of the sub-models.

4. Preliminary Feedback

At 2 p.m. McFarland asked the panelists to provide some initial independent individual reaction to the charge questions to give the Agency some feedback. Doucette, McFarland, and the DFO had a brief discussion of whether – since not all panelists had written – this would compromise the generation of independent advice. The DFO thought, given the circumstances, the perfect should not become the enemy of the good.

Hopfinger addressed Question 1Ai on additional properties, quickly summarizing the inputs he had received as of this time. No one suggested dropping any properties. There were two ways of looking at what properties might be added. Aquatic toxicity gets a lot of emphasis currently, in comparison to soil and atmospheric with so the question arises of what might be added. The

other approach is to look at the properties involved: (1) direct physical-chemical properties, (2) more biological properties, such as skin penetration, and (3) more pharmacological properties such as eye irritation. Diamond asked about marine toxicity.

Thibodeaux addressed 1Aii, making two points. First, he thought environmental transfer coefficients were important. He was involved with a model homogenization process a few years ago where they started with the same parameters but came up with very different answers until they considered the transfer coefficients. Second, he referenced OPPT's slide 31 from last week's conference call where he thought some of the values were arbitrary and an ES&T article. He asked whether more attention should be paid to where the chemical finds itself in the environment – something that better defines the reactivity of the reagent. Based on her look at BIOWIN, Diamond agreed.

Another panelist mentioned work that could be used to expand and improve the training set for BCF. This may be low hanging fruit. Reinert said this response could depend heavily on the response to 1Ai. Perhaps once the additional properties are identified in 1Ai, a more systematic

Dzombak addressed 1Aiii. In his view, the big issue in upgrading EPI Suite is the chemicals that are not relevant to the tools in EPI Suite that focus on low-molecular weight, non-polar compounds. Also in relation to 1Bi, the accuracy of the model for its uses. How accurate is accurate enough is an important question. Usually they are thought of “an order of magnitude or more” – is that good enough?

Cowan-Ellsberry and Hopfinger think there should be some domain analysis. There was another comment about uncertainty analysis and approaches to reducing uncertainty when other sources of uncertainty might overwhelm those in EPI Suite

Reinert addressed 1Bi on accuracy of the modules. EPI Suite is a screening tool with about an order of magnitude of accuracy. It is only as accurate as the input data and the calculation procedures. There are potential issues around verification of data, default selection, the use of estimates v experimental data. About 60% of the HELP files had something to say about accuracy and he hasn't gotten through them yet.

Diamond addressed 1Bii which deals with validation. She spoke of what can be validated, what can't; how validation can be done, and what we mean when we say we are confident in a model.

Salvito addressed 1Biii on whether some models were better validated than others. He reflected on false positives and false negatives in the context of a screening model. Sanderson said, for a screening model, the Europeans will accept a lot of inaccuracy, as long as the model is very conservative.

Parkerton addressed 1Biv, comparing EPI Suite's results with those from the individual model and it does look like they are working together. However, there are some issues regarding SMILES strings and CAS Numbers. In some cases, it makes little difference, but – in

BIOWIN – one approach can be much more conservative than the other. The user might not understand, however. Another issue is that it is unclear to him what the inputs are to the three fate models. It's not necessarily that the modules aren't working correctly, just that it isn't transparent.

Sanderson addressed 1Biv which is concerned with the extent to which the modules work together to generate estimates correctly. Experienced users do not appear to be having problems. EPI Suite is generally accepted and up to date enough for a screening level tool. You have to balance being correct, user friendly, and transparent.

Doucette addressed 1Cii on whether there were other estimation methods which should be considered in upgrading EPI Suite. Rather than adding other estimation methods for the same properties that already exist in EPI Suite (rather than for new properties) is to point to references and locations for other models rather than including them. Some models represent some classes of compounds better than others. Others addressed it as more of a wish list, including values at different temperatures, PKAs, anaerobic biodegradation, etc. SPARC can calculate a lot of the same p-chem properties as EPI Suite, but from a different perspective. One of SPARC's limitations is that it has to be done on the web.

Murray addressed 2A, the convenience to the software. He only had minor comments on the functionality which he did not feel were worth time on the conference call as they are not substantial issues. Cowan-Ellsberry said a lot of the modules have more options than are obvious than when you run it from the EPI Suite interface that people should be more aware of. Also, lots of websites let you sign up to get new versions when they come out. She didn't realize until last week's conference call that there was a new version out. Doucette thought he'd gotten a notification that the new version was available.

Cowan-Ellsberry addressed 2B which deals with the user's guide. She has been going through the guides and making comments. There are a lot of capabilities there that aren't widely recognized. Bennett had commented that we might need more step-by-step.

Bennett, who has the lead for 2C, which deals with the design and use of EPI Suite's user guide, was not able to be on today's call. A panelist said it would be nice to be able to see the experimental data for the compound and that there were ways to improve the outputting of the results. Cowan-Ellsberry said their could be better link to the references/

Hopfinger addressed 2D which addresses various ways to describe the structure for EPI Suite. He is keen on adding a structure drawing program as a way of outputting because it is widely used in many relevant disciplines. Also, it will help later with three dimensionality and isomers. Nonetheless, he sees no reason that EPA would have to write it when they could just integrate an existing package. Doucette has chemdraw give him the SMILES string to paste into EPI Suite.

Murray addressed 2E which deals with additional factors that could enhance convenience and overall utility. He had comments about isomers, the batchwise process. He had a few comments on how measured values are selected.

Salvito addressed 2F which deals with whether property estimates expressed in units that are easily understood by a broad cross section of potential users, not just scientists and engineers with advanced technical training. On reflection, he thought there might be improvements possible.

Parkerton addressed 2G which deals with the adequacy of information on accuracy/validation conveyed to the user by the program documentation and/or the program itself. If you take a compound for which there are no related compounds in the model, the output should have a notation that there are no notations of this type in the training set.

OPPT had to leave at this point. The DFO suggested, as the panel was almost finished, it continue; she will send her notes to OPPT..

Chinery addressed 3Ai and II which deals with the adequacy of science and necessary improvements for currently identified uses. EPI Suite is probably acceptable for use as a screening tool, for inputs to lower level risk assessments, and for making decisions about testing. More information on uncertainty would be useful in the user's manual. The manuals should include a more extensive discussion of the limitations.

Cowan-Ellsberry addressed 3B on additional uses. She had a question about the scope – is it additional uses within OPPT or any additional use. Various people had different ideas about the scope; the DFO believed this was the only area where they could go as broad as they wanted.

EPI Suite has been used for PBT screening, for the globally harmonized system. Hopfinger had a different twist that there might be users out there who would find it valuable who didn't even know it exists. A panelist made a comment about intake function to provide a more systematic way to rank human exposure. This is the efficiency with which the chemical would get to the population. Bennett and McKone have written on this. Reinert thought EPI Suite would be useful for design of animal tests, for the development of waivers if the relationship is strong enough. Nanomaterials is an issue to be addressed. It could be a very powerful way to guide data collection and research within the Agency.

5. Public Comment

At 3:10 the chair mentioned the written public comment from the Chamber of Commerce, then asked if there were anyone who wanted to provide oral public comment. There was a question about whether additional comments could be accepted. They can. There were no other public comments.

6. Discussion of Next Steps

Given the short time before the next meeting, the chair felt that the individual independent comments received should be sent to the whole panel. This will allow the coordinators to brief the whole Panel on the preliminary response to the charge. Sanderson suggested that the coordinator make an integrated response and provide the contributors with all the responses so that they can object if their writings were mis-represented. Reinert asked whether it was necessary to resend all the individual comments as the DFO is collecting them? There seemed to be agreement on this approach.

Individual comments are due Friday and integrated comments due on Monday. If support reviewers know they won't have time or energy to respond, they should tell the DFO so the lead coordinator won't be waiting.

In support of the March 7-9 meeting, the DFO will prepare a Table of Contents of what would have been in the binders if the Panel had used them and place it with reference copies on a memory stick.

Respectfully Submitted:

/S/

Ms. Kathleen White
Designated Federal Official

Certified as True:

/S/

Dr. Michael McFarland, Chair
EPI Suite Review Panel

These will be found in the FACA file and/or at the SAB's website:

1. Federal Register Notice
2. Agenda for the meeting
3. Workgroup roster
4. Comments prepared by individual workgroup members in advance
of the meeting
5. Email approving minutes