

**Summary Minutes of the  
U.S. Environmental Protection Agency (EPA)  
Science Advisory Board (SAB) Ecological Processes and Effects Committee  
Augmented for the Advisory on EPA's Aquatic Life Criteria**

**Meeting, June 30 – July 1, 2008**

Committee Members: See Committee Roster – Appendix A

Date and Time: Monday, June 30, 8:30 a.m. - 5:15 p.m.; Tuesday, July 1, 8:00 a.m. - 12:30 p.m. Eastern Daylight Time

Location: EPA Science Advisory Board Conference Center, 1025 F Street, N.W., Washington, D.C.

Purpose: The purpose of this meeting was to provide advice on derivation of aquatic life criteria for contaminants of emerging concern (CECs)

Attendees: Committee Chair: Dr. Judith Meyer

Committee Members: Dr. Fred Benfield  
Dr. Richelle Allen-King  
Dr. G. Allen Burton  
Dr. Peter Chapman  
Dr. Kenneth Dickson  
Dr. Karen Kidd  
Dr. Wayne Landis  
Dr. Ellen Mihaich  
Dr. Charles Rabeni  
Dr. Amanda Rodewald  
Dr. James Sanders  
Dr. Daniel Schlenk  
Dr. Heiko Schoenfuss  
Dr. Geoffrey Scott  
Mr. Timothy Thompson  
Dr. Glenn Van Der Kraak

EPA SAB Staff: Thomas Armitage, Designated Federal Officer  
Anthony Maciorowski, SAB Office  
Thomas Miller, SAB Office

EPA Staff: Joseph Beaman EPA/Office of Water (OW)  
Heidi Bell EPA/OW



Dr. Anthony Maciorowski, Deputy Director of the EPA SAB Office, welcomed the Committee members and thanked them for providing advice to EPA on aquatic life criteria for contaminants of emerging concern (CECs)

### **Introduction of Members, Purpose of Meeting, and Review of the Agenda**

Dr. Judith Meyer, Chair of the SAB Ecological Processes and Effects Committee provided introductory remarks. She stated that the Committee would be reviewing an EPA White Paper that contained recommendations to address technical issues facing the Agency in deriving aquatic life water quality criteria for contaminants of emerging concern. She noted that the White Paper focused in particular on endocrine disrupting chemicals, and that several experts in the area of endocrine disrupting chemicals were participating on the Committee with members of EPEC to provide advice to EPA at the meeting.

Dr. Meyer then reviewed the meeting agenda. She stated that: 1) During the morning EPA would provide background briefings and respond to the Committee's questions; 2) later in the morning and in the afternoon the Committee would discuss responses to each of the questions and develop consensus responses (she noted that members of the Committee had already developed preliminary responses to the charge questions); 3) members had been asked to lead the discussion of one of the charge questions and to incorporate the points discussed into the written response for their assigned question; and 4) time had been reserved on the second day of the meeting to develop and review the written responses to the questions. She stated that she would like to develop drafts of the charge question responses before adjourning. She then asked Committee members and public participants to identify themselves. Following introductions Dr. Meyer asked EPA to present opening remarks and background information to the Committee.

### **Remarks from EPA**

*Remarks from Ms. Suzanne Rudzinski (EPA Office of Water)*

Ms. Suzanne Rudzinski, Deputy Director of the Office of Science and Technology in EPA's Office of Water thanked the Committee for advising the Agency on the important issue of water quality criteria for contaminants of emerging concern. She stated that EPA was considering how the Agency's water quality criteria guidelines could be adapted to derive aquatic life water quality criteria for emerging contaminants of concern such as endocrine disrupting chemicals. She noted that was important to receive input on this issue from the Science Advisory Board and that she looked forward to receiving the Committee's report.

*Remarks from Dr. Edward Ohanian (EPA Office of Water)*

Dr. Edward Ohanian, Director of the Human Health and Ecological Criteria Division in EPA's Office of Water described some of the challenges facing EPA in developing

aquatic life criteria for contaminants of emerging concern. Slides of Dr. Ohanian's presentation are provided in Appendix D. Dr. Ohanian described EPA's authority to develop aquatic life criteria under Section 304 of the Clean Water Act. He stated that criteria were currently derived using procedures set forth in the 1985 EPA document, *Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic organisms and Their Uses* (the Guidelines). He noted that contaminants of emerging concern (CECs) such as some pharmaceuticals and personal care products that disrupt the endocrine system, posed technical challenges in developing aquatic life criteria. He stated that these contaminants were often detected in the environment at very low concentrations and in some cases could cause sublethal effects. These contaminants may also cause effects only to certain taxa of aquatic organisms during particular exposure windows or life stages. Dr. Ohanian stated that EPA had developed the White Paper to provide recommendations for interpreting the 1985 Guidelines in order to derive aquatic life criteria for CECs. He noted that the White Paper showed how aquatic life criteria could be derived for CECs in a way that was explicitly consistent with the 1985 Guidelines. Dr. Ohanian also described the relationship between the White Paper and other ongoing work to revise the Guidelines. He stated that proposed Guidelines revisions were presented to the SAB in 1985, but current efforts regarding CECs were not addressed in those proposed revisions. He stated that work to develop the White Paper would complement other Guidelines revisions under consideration.

#### *Questions from the Committee*

Members asked EPA managers and staff a number of questions. A member asked how restrictive EPA was in its definition of CEC and whether selenium would be considered to be a CEC. EPA staff responded that a draft water quality criterion had been developed for selenium and that this chemical is a contaminant of emerging concern. A member asked how other contaminants that had been known to cause problems would be treated. EPA staff responded that this would depend on the mode of action and whether the contaminants caused human or ecological effects.

A member asked how EPA intended to address dietary exposure to contaminants and food chain effects. EPA staff responded that the dietary pathway would be considered in other guidance to be developed.

A member asked whether ecological risk assessment was part of water quality criteria development. EPA staff responded that there was a distinct relationship between the water quality criteria derivation process and ecological risk assessment. EPA staff noted that the process of water quality criteria derivation involved looking at toxicological characteristics of chemicals and mode of action within the framework of ecological risk assessment. The member stated that evaluating mode of action should be part of problem formulation in the risk assessment framework.

EPA staff described other ongoing efforts to address issues such as dietary exposure. Staff stated that in the White Paper EPA had not made recommendations concerning the development of a tissue residue-based approach to deriving water quality criteria. Staff

stated that EPA was interested in hearing the Committee's views on important issues that may not have been addressed in the White Paper. A member asked whether EPA's intent in developing the White Paper was to ultimately derive criteria that would provide guidance for enforceable water quality standards. EPA staff stated that this was the ultimate intent.

*Remarks from Mr. Joseph Beaman (EPA Office of Water)*

Mr. Joseph Beaman of EPA's Office of Water presented an overview of the focus of the Agency's White Paper on aquatic life criteria for contaminants of emerging concern. Slides of Mr. Beaman's presentation are provided in Appendix E. Mr. Beaman stated that the White Paper discussed some of the major technical issues that challenge the development of aquatic life water quality criteria for contaminants of emerging concern. He also stated that the White Paper presented specific technical recommendations reflecting the best available science that addressed those technical issues. He noted that some technical issues not included in the White Paper were currently being addressed under separate criteria derivation or Guidelines revision efforts.

*Remarks from Dr. Russell Erickson (EPA Office of Research and Development)*

Dr. Russell Erickson of EPA's Office of Research and Development presented the technical issues and recommendations in the Agency's White Paper on aquatic life criteria for contaminants of emerging concern. Dr. Erickson's presentation slides are provided in Appendix E. He stated that the White Paper focused in particular on endocrine disrupting chemicals and that recommendations in the paper were presented in the context of an endocrine disrupting chemical (ethynylestradiol or EE2). However, he noted that many of the points discussed in the paper were broadly applicable to other classes of contaminants. Dr. Erickson summarized the recommendations pertaining to the following technical issues: 1) relevance of acute toxicity effect concentrations in setting aquatic life criteria for CECs; 2) defining minimum data requirements regarding taxonomic coverage; 3) use of non-resident species in criteria development; 4) defining appropriate chronic toxicity data; 5) selection of effect endpoints upon which to base criteria; and 6) involvement of an expert panel.

*Questions from the Committee*

The Chair stated that the White Paper appeared to deal mainly with endocrine disrupting chemicals. She asked why EPA had focused almost exclusively upon this class of contaminants. EPA staff responded that the Agency thought that endocrine disrupting chemicals were an important class of contaminants and therefore chose to explore how the Guidelines could be adapted to address them. In addition, EPA found that there was sufficient knowledge about some of these chemicals to take action. However, the Agency also wanted to provide recommendations that pertained to other classes of contaminants.

The Chair asked EPA how well the Agency could account for the effects of mixtures of contaminants in deriving criteria. EPA staff responded that the Agency had conducted some research to look at the toxicity of mixtures but more work was needed in this area.

A member remarked that it would be a good idea to identify important principles that should be addressed in revising the Guidelines. He stated that it would be useful to update the conceptual model for the Guidelines. He noted that the conceptual model for the original Guidelines was appropriate, but that science had evolved. He stated that a process was needed to apply current knowledge to the Guidelines. EPA staff responded that some thought was being given to how recommended Guideline adaptations might be expressed in the context of a problem formulation ecological risk assessment paradigm.

A member asked whether EPA had considered how to address the emerging issue of antibiotic resistant pathogens. He noted that in this case developing a dose-response curve might not be the best approach. EPA staff responded that this issue required additional consideration. The member suggested that if the criteria derivation framework were adaptable, an expert panel could consider how such issues should be addressed. There were no further comments so the Chair stated that after a break the Committee would hear public comments.

### **Public Comments**

Following the break, public comments were offered by the following persons representing the U.S. Food and Drug Administration (FDA): Charles Eirkson, Roanan Bloom, and Erik Silberhorn. In their comments they recommended that EPA work cooperatively with FDA to obtain data for deriving aquatic life criteria for CECs. They stated that: 1) FDA had worked with EPA to develop an aquaculture effluent guideline and best management practice, 2) FDA had worked with EPA to assist in the development of water quality benchmarks for aquaculture drug ingredients, 3) FDA had worked with EPA on developing methods for predicting environmental concentrations for terrestrial veterinary products, 4) FDA had worked with EPA on a *Pharmaceuticals in the Environment Working Group* to develop a research agenda. They stated that FDA data collection for drug development under the Federal Food, Drug, and Cosmetic Act and the national Environmental Policy Act was relevant to the development of water quality criteria.

The Chair thanked those who provided comments and called for discussion of the first charge question

### **Discussion of Charge Question #1a**

Dr. Schoenfuss led the discussion of charge question 1a, which focused on the relevance of acute toxicity effect concentrations in setting aquatic life criteria for CECs. Members agreed in principle with the recommendation in the White Paper to derive aquatic life criteria directly from criteria continuous concentrations when sufficient information

demonstrated a negligible risk of acute lethality for a CEC. However, the Committee discussed the following caveats to be considered by EPA.

- Some CECs (e.g., nanoparticles) did not fit the effect model of endocrine disrupting chemicals or were not well enough understood to allow a judgment of their mode of action.
- For some CECs the lowest observed effects concentrations and LC50s (test concentrations that result in mortality to 50% of the test population) were within one order of magnitude, indicating that acute toxicity may occur in environmental settings.
- Some compounds had differing modes of action for acute and chronic toxicity. In these cases it may be appropriate to derive both a criterion continuous concentration and a criterion maximum concentration.
- The pulsed nature of some CEC releases (e.g., pulsed industrial discharge, tidal action in the marine environment, and recurring natural events such as hurricanes) may result in short-term concentrations of CECs that could exceed what would generally be considered environmentally relevant concentrations.
- Consideration of mixture effects was important. Members stated that mixture effects of compounds with similar modes of action should be taken into account in determining whether acute toxicity may occur in environmental situations.

A member stated that the process of criteria development should not be truncated. Others noted that implementing the recommendations in the White Paper would not truncate the process because it would still be necessary to review data to determine the risk of acute lethality.

A member stated that the bulleted list on page 28 of the White Paper identified the kinds of information to be reviewed to determine the risk of acute lethality. He stated that this list was useful and should be expanded to take into consideration factors discussed by the committee.

Another member noted that EPA should use information available from FDA to assist in determining the mode of action of CECs.

Following discussion of these points the Chair stated that she would like move to the discussion of charge question 1b.

### **Discussion of Charge Question #1b**

Drs. Benfield and Mihaich led the discussion of charge question 1b, which focused on defining minimum data requirements for taxonomic coverage. The Committee discussed EPA's recommendation to interpret minimum requirements for taxonomic coverage as

information requirements instead of toxicity test requirements. A number of members supported consideration of the unique properties of CECs and the use of expert judgment and weight of evidence to determine appropriate taxonomic coverage. However, members discussed the following concerns:

- There was a need to maintain broad taxonomic coverage for development of aquatic life criteria in order to account for differences in sensitivity among various taxa. A member noted, for example, that studies of the compound bisphenol A had demonstrated sensitivity of vertebrates and invertebrates.
- Little was known of chronic effects of CECs on “wild type” species. There was some probability that criteria protecting “lab species” might not protect species of special concern (e.g., threatened and endangered species).
- Modes of action were not known for some CECs. Different organisms may be affected in different ways by the same compound both as adults and at earlier stages of development.

A member stated that EPA needed to define what constituted a sufficiently robust set of chronic data for criteria development and a reasonable understanding of the mode of action for a chemical that would allow inferences about the insensitivity of certain taxa.

Another member stated that EPA might consider emphasizing information needed to develop criteria rather than just toxicity test requirements.

A member noted that it was important to consider the unanticipated effects of CECs on non-target organisms, such as the impact of antibiotics on plants and atrazine effects on the quality of algae.

A member stated that it was important to expand the discussion in the White Paper to include specific recommendations concerning the marine environment.

Following this discussion the Chair stated that the Committee would break for lunch.

### **Discussion of Charge Question #1c**

Following lunch, Dr. Burton led the discussion of charge question 1c, which focused on use of non-resident species in criteria development. Members supported the use of non-resident species data in developing aquatic life criteria for CECs but discussed the following concerns:

- Non-resident species data should not be the sole basis for driving aquatic life criteria.
- The non-resident species data to be used should be high quality data.

- Variation among strains of test organisms used in laboratory studies was often unknown. In addition, differences in husbandry, test organism health, and parasite and pathogen load contributed to response variation. Therefore, it was difficult to understand whether the variation observed between native and non-native species was within the uncertainty of the test data for either species.
- Because of the relatively large amount of available non-resident species data, such data could dominate the criteria derivation process and lead to inappropriately biased criteria in certain sensitive geographic areas.

A member recommended amphibian testing. EPA staff stated that the Guidelines allowed amphibian testing. The Committee discussed amphibian tests.

The Committee discussed the usefulness of data available from the Food and Drug Administration and the U.S. Department of Agriculture.

Chair next called for discussion of the response to Charge Question 1d.

### **Discussion of Charge Question #1d**

Dr. Van Der Kraak led the discussion of charge question 1d, which focused on defining appropriate chronic toxicity data. A number of members expressed support for the recommendation in EPA's White Paper to require at least one full life-cycle test for a fish unless there was a compelling body of information indicating that life processes outside the early life stage or partial life-cycle exposure/observation window were not critical to capturing the biologically important effects of chronic exposure to a CEC. Other members supported use of a full life cycle test but viewed EPA's proposed "guilty until proven innocent" approach as extremely precautionary. The following issues were discussed.

- Transgenerational effects of CECs were potentially important and should be considered in developing aquatic life criteria for these chemicals.
- Test guidelines should have the flexibility to include assessment of key developmental events (e.g., metamorphosis in amphibians, acquisition of saltwater tolerance, or smolting).
- There was a need to ensure that test methods included provisions to consider non-traditional endpoints such as immune function and behavior.
- Surrogate test species may be needed in the case of: 1) Long-lived species with delayed sexual maturity; 2) organisms of large size which precluded their suitability as test species in the laboratory, 3) endangered species, and 4) species for which there is little knowledge of the husbandry conditions or background biology.

- Although the Committee supported EPA’s recommendation concerning the use of life cycle tests, some members of the committee viewed EPA’s statement describing when full life cycle test would be required (i.e., unless there is an affirmative reason to believe that it is not necessary) as extremely precautionary, while others viewed it as appropriate.

A member commented that EPA needed to clearly indicate how the White Paper would ultimately be used.

The Chair next called for the discussion of charge question 1e.

### **Discussion of Charge Question #1e.**

Dr. Schlenk led the discussion of charge question 1e, which focused on selection of effect endpoints for criteria development. A number of Committee members agreed with EPA’s recommendation to continue exploring the possibility of using sublethal endpoints to help set aquatic life criteria. The Committee discussed the following points concerning the use of sublethal endpoints.

- Contaminants effects should be linked to different levels of biological organization. Definitions of “biologically important effect” were needed. Linkages to effects on such endpoints as reproduction, growth, and survival were needed. A member stated that it was difficult to define what a population should look like.
- Activational biological effects could provide useful information, particularly regarding mode of action. It would be important to consider how mixtures of CECs with comparable modes of action may result in higher environmental concentrations than expected for any single compound.
- Members stated that the use of non-traditional endpoints held promise but further validation was needed.
- The Committee discussed how research and development could be undertaken to obtain mode of action “fingerprints” for a CEC or other compound through combined sublethal endpoints. Committee members suggested that these data could be integrated with fingerprints of other compounds with different modes of action and used to help address mixture issues or potential indirect effects.
- Members discussed the need for additional research to link biomarkers with effects.
- The Committee discussed the use of vitellogenin production as a biomarker of exposure to feminizing chemicals. It was noted that while the linkage of vitellogenin to exposure was reasonably solid, linkages of vitellogenin in males

and juveniles to higher biological effects such as altered reproduction, survival, and growth were limited, even though the relationship may make sense.

The Chair then called for a break before beginning the discussion of the response to Charge question 1f.

### **Discussion of Charge Question #1f**

Following a break, Drs. Allen-King and Sanders led the discussion of charge question 1f, which focused on involvement of an expert panel in the process of developing aquatic life criteria for contaminants of emerging concern. A number of Committee members stated that they agreed with EPA's recommendation to use expert panels to provide professional judgment during the process of developing aquatic life criteria for CECs. Several members commented that EPA should develop a transparent process to select and use expert panels. Members stated that this would be necessary in order to avoid inconsistency in the criteria derivation process.

A member stated that panels needed to include toxicologists and ecologists and also include members with different perspectives (e.g., industry and academia). Another member stated that it would be important to have a diverse group of people on the panel that could offer a balanced perspective. Committee members also recommended that the charge to the panel and end product be clearly defined and that EPA take advantage of similar panel processes that might be occurring in Europe and Asia.

The Chair then called for discussion of charge question 3.

### **Discussion of Charge Question #3**

Drs. Chapman, Rabeni, and Rodewald led the discussion of charge question 3, which focused on suggestions to improve the utility of Part II of EPA's White Paper. Members commented that Part II of the White Paper, which was intended to illustrate application of EPA's recommendations using the synthetic estrogen ethynylestradiol (EE2) as an example, was a well-written and thorough review of the literature. The Committee discussed recommendations to improve the usefulness of this part of the White Paper. The discussion focused on the following areas:

- There was a need to recognize that EE2 had unique properties and considerable data were available to describe these properties.
- Part II of the White Paper failed to address a number of issues such as multiple stressors and how the influence of EE2 might be affected by mixtures of compounds with similar modes of action.
- The Committee discussed the choice of taxa noting that, the White Paper should state that resident species data, especially life-cycle tests from resident species, remain extremely valuable. The Committee also noted that results from non-

resident species tests, while useful, should not be generalized to resident species unless data were available to compare sensitivities. Committee members also commented on the lack of amphibian data.

- Committee members commented that Part II of the White Paper did not address transgenerational effects.
- Committee members commented that a broader array of endpoints should be included in Part II of the White Paper, noting that genomic or physiologically-based pharmacokinetic modeling studies might be considered.
- The use of weight of evidence was implicit in the evaluation in Part II but it needed to be explicitly included as part of the documentation.
- Interactions between weight of evidence and the Precautionary Principle (i.e., appropriate levels of uncertainty) should be clarified.
- When appropriate data were available, EC<sub>x</sub> values (i.e., concentration causing an effect in x percent of the test organisms) should be used rather than no observed effect/lowest observed effect concentrations.

Members discussed whether Part II should be integrated with Part I or possibly included in the White Paper as a case study appendix. EPA staff commented that Part II was considered to be an illustrative example but not a case study.

A member stated that it would be useful to integrate Parts I and II of the White Paper and include detailed information in text boxes. Another member commented that he thought Part II was a useful “stand alone” example and should not be integrated with Part I. A member suggested including a discussion of other chemicals in Part II. Another member stated that the discussion of the criteria derivation process that was based on expert opinion could be included in Part I and the analytical work included in Part II.

The Chair next called for discussion of the response to charge question 2.

### **Discussion of Charge Question #2**

Drs. Dickson, Kidd, and Landis led the discussion of the response to charge question 2, which focused on identification of appropriate issues to be addressed in deriving aquatic life criteria for CECs. The Committee discussed the question of whether EPA had identified the appropriate issues in the White paper and whether there were additional issues that should be considered. Members commented that appropriate technical issues had been identified in the White Paper. The Committee discussed the following additional issues to be considered.

- Members commented that EPA should articulate principles that could be applied when modifying the 1985 Guidelines to develop water quality criteria for CECs.

It was suggested that these principles include seeking a wide range of inputs from diverse perspectives, determining receptors of concern, developing a robust conceptual model, developing multiple lines of evidence, and identifying uncertainties associated with criteria development. A member stated that the conceptual model should address more than the fate and direct effects of CECs. It should include consideration of probable direct or indirect impacts on food webs; ecological processes and services; and unique, endangered, or keystone species of concern.

- Committee members commented that it would be particularly important to consider uncertainty and multiple modes of action of contaminants.
- Committee members discussed the importance of other issues such as change in gene frequencies, antibiotic resistance, how life history could reduce the impacts of toxicants, application of quantitative structure activity relationships, how to address non-linear responses, biomagnification, and the need for flexibility to address specific questions.

The Committee further discussed the need to consider mixtures of contaminants with similar modes of action.

EPA staff commented that it was important to consider what a conceptual model meant and how it could be used. Staff commented that the original 1985 Guidelines contained a good discussion of their intended purpose. Staff stated that the Guidelines were intended to provide fairly broad guidance.

A Committee member stated that the 1985 Guidelines document was based on a conceptual model but the model was not clearly described.

A member stated that, while he did not disagree with the points that had been discussed by other members, he did not see how some of the points specifically addressed adaptation of the existing guidelines to develop criteria for CECs. Another member responded that the existing Guidelines did not offer much to address ecology. He stated that a reasonable conceptual model was needed to address ecology.

A member stated that as a toxicologist, he thought it would be important to further consider how mechanisms of action could be used in developing aquatic life criteria. He noted that mode of action studies were very important, and that it would be helpful to use available human health effects data and adapt it to look at non-human endpoints.

A member questioned where the points discussed would fit into the White Paper. He asked whether there could be a section in the paper to address mode of action and how it should be applied.

Another member stated that she had not seen any recommendations to prioritize CECs for setting aquatic life criteria. She asked EPA staff whether the Agency was seeking advice to do that.

EPA staff responded that process of prioritizing CECs for criteria development would be separate from the process of developing the White Paper and that many factors would be considered in prioritizing chemicals. Staff stated, however, that expert panels might have an opportunity to offer input in the prioritization process.

The Chair then called for discussion of the response to charge question 4.

#### **Discussion of Charge Question #4**

Drs. Scott and Thompson led the discussion of the response to charge question 4, which focused on additional suggestions to assist EPA in implementing the proposed recommendations discussed in the White Paper. The following points were discussed by the Committee.

- It would be important to prioritize the list of CECs for which aquatic life criteria should be developed and leverage research and development activities to develop the necessary data to needed to derive aquatic life criteria.
- Leveraging research efforts of other agencies was essential in a time of decreasing research funds within the federal government.
- The linkages between ecological risk assessment and development of aquatic life criteria needed to be articulated.
- Tissue based criteria should be considered for bioaccumulative CECs where food chain transfer was a concern.
- Quantitative linkages were needed between mode of action indicators and population-level endpoints and it would be important to set priorities for technical research that addresses significant knowledge gaps in this area.
- Additional factors might need to be considered to protect endangered, highly managed, protected, and “charismatic” species (e.g., marine mammals, eagles, polar bears, sturgeon). Such factors included consideration of different lag times for sexual differentiation and different CEC uptake characteristics.
- There was a need for continued development of analytical capabilities to measure levels of CECs in the environment.
- Input into the aquatic life criteria development process was needed from private industry and state government. The perspective of these important stakeholders was needed before finalizing the White Paper.

- It would make sense to consider using parallel processes to develop aquatic life criteria for compounds with similar modes of action.
- As EPA developed a research plan to support derivation of CECs, it might be useful to consider questions such as: How could aquatic life criteria be developed to take into account the fact that aquatic organisms are exposed to mixtures of CEC, other contaminants, and other stressors? What were the likely modes of action of CECs that were known to be present in the environment? and How could field study results be used to inform the derivation of an aquatic life criterion for a CEC?

Following the discussion of charge question 4, the chair reviewed plans for the next day. She stated that in the morning the Committee would have a writing session to develop written responses to the questions. She asked members assigned to each of the questions to develop the responses. The Committee would then convene as a group to discuss the written responses. The Chair asked members to prepare summary bullets of the written responses to assigned questions so they could be discussed by the entire Committee. She stated that the writing session would begin at 8:00 a.m. the following day and the charge question responses would be reviewed from 10:15 a.m. – 12:15 p.m. The Chair then recessed the meeting for the day.

## **Tuesday, July 1, 2008**

The Chair convened the meeting at 8:00 a.m. for a writing session to develop responses to the charge questions.

### **Discussion of the Responses to the Charge Questions**

At 10:00 a.m. the Committee summarized and discussed the responses that had been developed for each of the charge questions. Highlights of the responses to each of question are presented in Appendix G.

Following the discussion of charge question responses, the Chair thanked the Committee members for their comments and also thanked EPA staff for responding to the Committee's questions. She then reviewed the schedule for developing the Committee report. She noted that members had given the DFO the initial drafts of the charge question responses and requested that members send any additional information to the DFO within the next week. The Chair stated that she and the DFO would develop the first draft of the report send it to the Committee for review by the end of July. The DFO would then work with the Chair to incorporate member comments and send the second draft to the Committee by the end of August. The Committee would hold a teleconference in mid-September to discuss the report, and a final draft would be sent to the Committee with a request for concurrence to send it to the Chartered Science Advisory Board in early October for quality review. She stated that the DFO would contact members to schedule the September teleconference.

The Chair then thanked members for their participation and adjourned the meeting.

Respectfully Submitted:

Certified as True:

*/Signed/*

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Dr. Thomas Armitage  
Designated Federal Officer

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Dr. Judith L. Meyer, Chair  
SAB Ecological Processes and Effects  
Committee

## **APPENDICES**

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Appendix A: Committee Roster

Appendix B: Meeting Agenda

Appendix C: Charge to the Committee

Appendix D: Ohanian Presentation Slides

Appendix E: Beaman Presentation Slides

Appendix F: Erickson Presentation Slides

Appendix G: Highlights of Responses to the Charge Questions

## Appendix A – Committee Roster

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### **U.S. Environmental Protection Agency Science Advisory Board Ecological Processes and Effects Committee Augmented for the Advisory on EPA's Aquatic Life Water Quality Criteria**

#### **CHAIR**

**Dr. Judith L. Meyer**, Distinguished Research Professor Emeritus, Odum School of Ecology, University of Georgia, Athens, GA

#### **MEMBERS**

**Dr. Richelle Allen-King**, Professor and Chair, Department of Geology, University at Buffalo, Buffalo, NY

**Dr. Fred Benfield**, Professor of Ecology, Department of Biological Sciences, Virginia Tech, Blacksburg, VA

**Dr. Ingrid Burke**, Professor, Department of Forest, Rangeland and Watershed, Stewardship, Colorado State University, Fort Collins, CO

**Dr. G. Allen Burton**, Professor and Director, Cooperative Institute for Limnology and Ecosystems Research, University of Michigan, Ann Arbor, MI

**Dr. Peter Chapman**, Principal and Senior Environmental Scientist, Environmental Sciences Group, Golder Associates Ltd, North Vancouver, BC, Canada

**Dr. Loveday Conquest**, Professor and Associate Director, School of Aquatic and Fishery Sciences, University of Washington, Seattle, WA

**Dr. Kenneth Dickson**, Regents Professor, Department of Biological Sciences, University of North Texas, Aubrey, TX,

**Dr. Karen Kidd**, Canada Research Chair and Professor, Biology Department, University of New Brunswick, Saint John, NB, Canada

**Dr. Wayne Landis**, Professor and Director, Institute of Environmental Toxicology, Western Washington University, Bellingham, WA

**Dr. Ellen Mihaich**, President, Environmental and Regulatory Resources, LLC, Durham, NC

**Dr. Charles Rabeni**, Leader of Missouri Cooperative Fish and Wildlife Research Unit, U.S. Geological Survey, University of Missouri, Columbia, MO

**Dr. Amanda Rodewald**, Associate Professor of Wildlife Ecology, School of Environment and Natural Resources, The Ohio State University, Columbus, OH

**Dr. James Sanders**, Director and Professor, Skidaway Institute of Oceanography, Savannah, GA

**Dr. Daniel Schlenk**, Professor, Department of Environmental Sciences, University of California, Riverside, Riverside

**Dr. Heiko Schoenfuss**, Professor of Aquatic Toxicology, Department of Biological Sciences, Aquatic Toxicology Laboratory, St. Cloud State University, St. Cloud, MN

**Dr. Geoffrey Scott**, Director, Center for Coastal Environmental Health and Biomolecular Research, National Ocean Services, National Oceanic and Atmospheric Administration, Charleston, SC

**Mr. Timothy Thompson**, Senior Environmental Scientist, Science, Engineering, and the Environment, LLC, Seattle, WA

**Dr. Glen Van Der Kraak**, Professor and Associate Dean, Integrative Biology, College of Biological Science, University of Guelph, Guelph, Canada

**Dr. Ivor van Heerden**, Associate Professor and Director, Department of Civil and Environment Engineering, LSU Hurricane Public Health Research Center, Louisiana State University, Baton Rouge, LA

## Appendix B – Meeting Agenda

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### U.S. ENVIRONMENTAL PROTECTION AGENCY SCIENCE ADVISORY BOARD

#### Ecological Processes and Effects Committee Augmented for Advisory on EPA's Aquatic Life Water Quality Criteria

Public Meeting, June 30 – July 1, 2008

SAB Conference Center, Suite 3700  
1025 F Street NW, Washington DC

#### AGENDA

##### Monday, June 30, 2008

8:30 - 8:40 a.m.

##### **Meeting Convened by the Designated Federal Officer**

Dr. Thomas Armitage  
EPA Science Advisory Board Staff Office

##### **Welcome**

Dr. Anthony Maciorowski, Deputy Director  
EPA Science Advisory Board Staff Office

8:40 - 8:50 a.m.

##### **Purpose of the Meeting and Review of the Agenda**

Dr. Judith Meyer, Chair

8:50 – 10:20 a.m.

##### **Remarks from EPA**

- Regulatory framework for aquatic life water quality criteria for contaminants of emerging concern.
- EPA's white paper on aquatic life water quality criteria for contaminants of emerging concern.
- Technical issues for deriving aquatic life water quality criteria for contaminants of emerging concern.

- Charge to the SAB.

Dr. Edward Ohanian, Director  
Health and Ecological Criteria Division  
EPA Office of Water

Mr. Joseph Beaman  
Health and Ecological Criteria Division  
EPA Office of Water

Dr. Russell Erickson  
Mid Continent Ecology Division  
EPA Office of Research and Development

Dr. Dale Hoff  
Mid Continent Ecology Division  
EPA Office of Research and Development

10:20 – 10:35 a.m.

**Break**

10:35 – 10:50 a.m.

**Public Comments**

10:50 – 12:00 p.m.

**Committee Response to the Charge Questions 1a and 1b**

Dr. Meyer and Committee

- Charge Question 1a. Comments on recommendations concerning relevance of acute toxicity data.
- Charge Question 1b. Comments on recommendations concerning minimum taxonomic coverage required.

12:00 – 1:00 p.m.

Lunch

1:00 – 3:15 p.m.

**Committee Response to the Charge Questions 1c, 1d, and 1e**

Charge Question 1c. Comments on recommendations concerning use of non resident species

Charge Question 1d. Comments on recommendations concerning appropriate chronic toxicity data.

Charge Question 1e. Comments on recommendations concerning selection of endpoints.

3:15 – 3:30 p.m.

**Break**

- 3:30 – 5:00 p.m.      **Committee Response to the Charge Questions 1f, 3, 2, and 4**
- Charge Question 1f. Comments on the use of an expert Panel.
  - Charge Question 3. Does the Committee have suggestions that may improve the utility of the case study in the white paper for illustrating the technical issues presented and for providing a basis for understanding the issues?
  - Charge Question 2. Please comment on whether EPA has identified the appropriate issues to be addressed in deriving water quality criteria for contaminants of emerging concern. Are there additional important issues that EPA has not addressed?
  - Charge Question 4. Does the Committee have additional suggestions to assist EPA in implementing the proposed recommendations discussed in the white paper?

5:00 – 5:15 p.m.      **Plans for the Following Day**  
 Dr. Judith Meyer, Chair

5:15 p.m.              **Recess for Day**

**Tuesday, July 1, 2008**

- 8:00 – 10:00 a.m.      Writing Session to Synthesize and Edit Responses to Charge Questions
- 10:00 – 10:15 a.m.      Break
- 10:15 – 12:15 p.m.      Review Responses to the Charge Questions  
 Dr. Meyer and Committee
- 12:15 – 12:30 p.m.      Summary of Discussion and Next Steps  
 Dr. Meyer
- 12:30 p.m.              Adjourn

## Appendix C – Committee Charge

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### Charge to the SAB Ecological Processes and Effects Committee for the advisory on Aquatic Life Criteria for Contaminants of Emerging Concern

#### Background

The U.S. Environmental Protection Agency (EPA), Office of Water, is charged with protecting aquatic life, wildlife and human health from adverse anthropogenic, water-mediated effects under the purview of the Clean Water Act (CWA). In support of this mission, the Office of Water's Office of Science and Technology (OST) develops ambient water quality criteria (AWQC) that serve as guidance to states and tribes to assist them in their adoption of water quality standards. In 1985, EPA published *Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses* or "Guidelines" (Stephan, C.E., D.I. Mount, D.J. Hansen, J.H. Gentile, G.A. Chapman and W.A. Brungs, PB85-227049, National Technical Information Service, Springfield, VA). The majority of EPA's currently recommended AWQC for aquatic life (aquatic life criteria or ALC) have been derived using the methods outlined in the *Guidelines*, which specify various data and procedural recommendations for criteria derivation, and also define general risk management goals for criteria. Section 2 in Part I of the white paper provides a brief description of the *Guidelines* procedures and identifies several areas particularly relevant to this advisory.

The Agency's Emerging Contaminants workgroup has prepared the accompanying white paper to address some of the challenges facing the development of ALC for contaminants of emerging concern (CECs). The term CEC has been used to identify chemical compounds that have no regulatory standard (e.g., ambient water quality criteria), have been recently "discovered" in the natural environment because of improved analytical chemistry detection levels, and potentially cause deleterious effects in aquatic life at environmentally relevant concentrations. In general, widespread uses, some indication of chemical persistence, effects found in natural systems, and public concerns over some CECs, have made clear the need for EPA to develop criteria that can be used to help assess and manage their potential risk in the aquatic environment. The Agency is particularly concerned about pharmacologically active ingredients and personal care products commonly discharged at wastewater treatment plants that are designed to stimulate a physiological response in humans, plants, and animals. Many of these compounds are known (or suspected) to disrupt endocrine function in animals, and thus are referred to as endocrine disrupting chemicals, or EDCs. The synthetic hormone ethynylestradiol used for birth control is an example of one such EDC that demonstrates a reasonable potential to adversely affect aquatic life.

EPA is seeking advice from the Science Advisory Board (SAB) Ecological Processes and Effects Committee (*Committee*) regarding the technical soundness of the white paper as the basis for future development of water criteria for CECs. The white paper discusses how principles in the *Guidelines* could be interpreted and adapted to develop ALC for

CECs. Technical challenges and recommendations are described in the first part of the white paper (Part I), entitled "General Challenges and Recommendations." The second part of the white paper (Part II), "*Illustration of Recommendations Using Data for 17 $\alpha$  – Ethynylestradiol (EE2)*," explores the workgroup recommendations in the context of an example CEC, ethynylestradiol (EE2), a synthetic pharmaceutical estrogen.

### **Charge to SAB**

1. The following recommendations have been developed to address important technical challenges and issues in deriving water quality criteria for CECs. Please comment on the technical merit, practicality, and implementability of the recommendations addressing the following issues as described in Part I of the white paper and the EE2 Case study in Part II .
  - a. *Relevance of Acute Toxicity Effect Concentrations in Setting ALC for CECs:* Criteria consist of a Criterion Maximum Concentration (CMC), intended to address acute lethality and a Criterion Continuous Concentration (CCC), intended to address effects of chronic exposures on survival, growth, and reproduction. Many CECs are physiologically active at concentrations orders of magnitude lower than those causing acute lethality, and the high concentrations sufficient to cause lethality may never occur in the environment. Rather than rotely require a robust acute toxicity data set for such chemicals, the workgroup recommends that aquatic life criteria consist of only a CCC and that no CMC be derived, w hen sufficient information demonstrates risks of acute lethality are negligible.
  - b. *Defining Minimum Data Requirements Regarding Taxonomic Coverage:* If an acute criterion is not calculated, then the CCC cannot be calculated using the acute to chronic ratio (ACR) approach and must be instead calculated directly from chronic toxicity data. Procedures for this are included in the *Guidelines* (pages 40-42), but they require that acceptable chronic toxicity tests be conducted for a broad range of taxonomic groups. In the case of many CECs, toxicological research tends to focus on organisms for which the MOA is most relevant (e.g., vertebrates for estrogen mimics) and may have limited data coverage for other taxonomic groups that will likely be less sensitive. To avoid generation of resource-intensive chronic toxicity data for insensitive species that will have little impact on the final criterion, the workgroup recommends interpreting the minimum data requirements for taxonomic coverage as information requirements instead of toxicity test requirements. By this we mean that, rather than requiring an acceptable chronic toxicity test, the data requirement for certain taxonomic group expected to be insensitive might be met by a body of information demonstrating insensitivity of the taxon.
  - c. *Use of Non-Resident Species in Criteria Development:*

Historically, EPA has not used data derived from toxicity testing with non-resident species in the actual criteria derivation process. Excluding species simply because they are not resident may be unnecessarily restrictive for the purposes of deriving national criteria, and may actually increase rather than decrease uncertainty. The workgroup recommends that non-resident species be considered for use in criteria derivation calculations, focusing on those species with widely used and standardized test methods and for which there is no reason to believe would misrepresent the sensitivity of comparable resident species. Furthermore, the workgroup specifically suggest accepting data for zebrafish (*Danio rerio*) and Japanese medaka (*Oryzias latipes*), to reflect international efforts toward data equivalency.

- d. *Defining Appropriate Chronic Toxicity Data:*  
For fish, the *Guidelines* allow the use of early life stage (ELS; egg to juvenile) exposures in lieu of full life-cycle (F<sub>0</sub> egg to F<sub>1</sub> offspring) or partial life-cycle (F<sub>0</sub> adult to F<sub>1</sub> juvenile) exposures for determining chronic toxicity of chemicals, unless there is reason to believe this is inappropriate. Current understanding of many CECs, particularly EDCs, is that important effects of these chemicals may not occur, or at least not be expressed, until after the ELS exposure window; in fact, partial life-cycle exposures may also miss important effects, such as those on sexual development. For such chemicals, it is clear that the definition of an acceptable chronic test must include consideration of key windows of exposure and effect (e.g., to include sexual development and reproduction in assessments of steroid hormone agonists/antagonists). However, even more broadly, the workgroup recommends that the Office of Water consider amending the chronic data acceptability requirements in the *Guidelines* to require at least one full life-cycle test for a fish (for invertebrates, life-cycle tests are already required) unless there is a compelling body of information indicating that life processes outside the early life stage or partial life-cycle exposure/observation window are not critical to capturing the biologically important effects of chronic exposure to the chemical. This amended requirement would include all chemicals, not just EDCs/CECs.
- e. *Selection of Effect Endpoints Upon Which to Base Criteria:*  
Aquatic life criteria typically are based on direct measures of survival, growth, and reproduction; other measures of response are generally not included unless they can be shown to be closely linked to expected changes in population dynamics. The workgroup supports this existing guidance, but recognizes that many CECs, particularly those with very specific modes of action like steroid hormone agonists/antagonists, will have data for a wide variety of histological, biochemical, physiological, or behavioral endpoints that may warrant consideration as measures of biologically important effects. The degree to which such measures can be used to infer population level effects is likely endpoint-, chemical-, and/or

organism-specific, and developing a universal list of recommended endpoints is therefore beyond the scope of the workgroup to make specific, comprehensive recommendations. Rather, the recommendation here is simply that criteria development more thoroughly explores such possibilities.

*f. Involvement of an Expert Panel:*

While not addressed explicitly in the *Guidelines*, the complexities involved in the assessment of many CECs, and the reliance on professional judgment in making some of the determinations required under the workgroup's recommendations, make clear the need to bring the best scientific knowledge to bear in the development of criteria for CECs, as well as other chemicals. The workgroup supports the recommendation from a SETAC Pellston workshop (2003) that criteria development involve recruitment of an expert panel early in the process to insure that all relevant issues are considered during initial development of the criterion and to provide scientific perspective on decisions that are made as part of the process. Such a panel would not undermine the authority of the Agency to make policy decisions regarding criteria, but would ensure that such policy decisions are made from the best possible technical foundation. It is envisioned that expert panels would be formed around specific chemicals, or perhaps groups of chemicals with chemical or toxicological similarities (e.g., same MOA).

2. Please comment on whether EPA has identified the appropriate issues to be addressed in deriving ALC for CECs. Are there additional important issues that EPA has not identified?
3. Part II of this white paper was specifically developed as a companion to Part I and focuses on the use of ethynylestradiol as a model chemical to illustrate the technical issues presented by the workgroup, as well as providing a basis for understanding the recommendations. Does the *Committee* have suggestions that may improve the utility of Part II of this white paper for the purposes stated above?
4. Does the *Committee* have suggestions that would assist EPA in implementing the proposed recommendations discussed in the white paper, particularly with respect to developing the necessary scientific data and information and/or providing expert scientific input at the appropriate stages of the risk assessment process?

## USEPA Aquatic Water Quality Criteria and Chemicals of Emerging Concern: The Challenges Ahead

Edward V. Ohanian, Ph.D., Director  
Health and Ecological Criteria Division  
Office of Science and Technology/Office of Water  
U.S. Environmental Protection Agency  
Washington, DC

SAB/EPEC Meeting  
Washington, DC  
June 30 – July 1, 2008



## Clean Water Act

➤ Objective: “restore and maintain the chemical, physical and biological integrity of the Nation’s waters”

➤ §304(a) of the Clean Water Act:

The Administrator, after consultation with appropriate Federal and State agencies and other interested persons, shall develop and publish, within one year after the date of enactment of this title (and from time to time thereafter revise) criteria for water quality accurately reflecting the latest scientific knowledge (A) on the kind and extent of all identifiable effects on health and welfare including, but not limited to, plankton, fish, shellfish, wildlife, plant life,...



## Goals of White Paper

- Workgroup Recommendations act as a “Supplemental Interpretation” of the 1985 Guidelines for CECs:
  - Recommendations emphasize
    - technical rigor,
    - use of the "good science" clause,
    - maintain the level of protection and the amount of uncertainty.
- The white paper shows how criteria can be derived for CECs in a way that is explicitly consistent with the 1985 Guidelines.



## Aquatic Life Criteria Derivation: The Current Guidelines

- The methodology by which EPA derives AWQC for aquatic life protection was published in 1985:

*Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses* (Stephan, Mount, Hansen, Gentile, Chapman, and Brungs 1985)

- Referred to as the “Guidelines”



## Contaminants of Emerging Concern (CECs)

- Chemicals and other substances that have no regulatory standards, recently “discovered” in natural waters
- Potentially cause deleterious effects in aquatic life at environmentally relevant concentration
- May be candidates for future regulation depending on their toxicity and occurrence
- Frequently have insufficient toxicity data for aquatic life criteria development under the Guidelines



## CECs Challenges

- Often detected in the environment at very low concentrations
- May cause sublethal effects that are more difficult to detect
- May cause effects in particular taxa but not others
- May cause effects only during particular exposure windows (life stages)



## Relationship of work to ongoing *Guidelines* Revisions

- Proposed *Guidelines* Revisions presented to SAB in 2005
- Current efforts regarding CECs not addressed in 2005
- National focus on CECs allowed OST to prioritize these efforts
- Our efforts begin to address 2005 SAB comments concerning:
  - non-traditional endpoints, sublethal/subchronic endpoints,
  - delayed effects, and
  - compounds such as EDCs

## White Paper: General Overview

Joseph Beaman,  
Office of Science and Technology

### Purpose of the White Paper

- The information contained in this document will serve as the foundation for decision-making for the subsequent development of AWQC for CECs when the need arises.
- This white paper and the recommendations it contains does not supersede the *Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses or "Guidelines"* (Stephan, C.E., D.I. Mount, D.J. Hansen, J.H. Gentile, G.A. Chapman and W.A. Brungs,
- Document intended to serve as supplemental information to guide the problem formulation and effects characterization of the ecological risk assessment paradigm as applied to ambient water quality criteria development for aquatic life.

## Focus of the White Paper

- This white paper discusses some of the major technical issues that challenge development of AWQC for contaminants of emerging concern (CECs) specific to the use of the current *Guidelines*
- The paper also presents specific technical recommendations reflecting best available science that address those issues and may allow progress with respect to derivation of AWQC for CECs with same technical rigor currently achieved using the *Guidelines*.

## Additional Considerations

- The workgroup realizes that there are other concerns inherent to the criteria derivation process that have been identified, but these concerns are not specific to CECs, nor do the recommendations presented here preclude other efforts to address these issues.
- Some of these issues are currently being addressed under separate criteria derivation or guidelines revisions efforts;
- Other issues may require additional information so that scientifically defensible methods can be developed to address them.

## Acknowledgements

- Office of Research and Development
  - NHEERL (Mid Continent Ecology Division) – Duluth, Minnesota
    - Dale J. Hoff, Workgroup Co-chair\*
    - Gerald T. Ankley\*
    - Russell J. Erickson\*
    - David R. Mount\*
    - Richard Bennett
    - Joseph Tietge
  - NHEERL (Gulf Ecology Division) – Gulf Breeze, Florida
    - Geraldine Cripe
  - NERL (Ecological Exposure Research Division) – Cincinnati Ohio
    - James Lazorchak\*
    - Mitchell Kostich
    - David Lattier

## Acknowledgements

- Office of Water; Office of Science and Technology (HQ)
  - Immediate Office
    - Ephraim King, Director, Office of Science and Technology
    - Suzanne Rudzinski, Deputy Director, Office of Science and Technology
  - Health and Ecological Criteria Division
    - Joseph Beaman, Workgroup Co-chair\*
    - Diana Eignor
    - Lisa Huff
  - Standards and Health Protection Division
    - Janita Aguirre
- Office of Pollution Prevention and Toxics (HQ)
  - Les Touart
- Office of Pesticide Programs (HQ)
  - Jean Holmes

# Acknowledgements

- Technical Support (Great Lakes Environmental Center)
  - Tyler K. Linton\*
  - Gregory J. Smith

## Technical Issues and Workgroup Recommendations Regarding Criteria Derivation for Contaminants of Emerging Concern (“CECs”)

Russell Erickson, Ph.D  
ORD (NHEERL-MED) - Duluth, MN  
SAB Advisory, June 30, 2008

### *1a. Relevance of Acute Toxicity Effect Concentrations in Setting ALC for CECs:*

Many chemicals of emerging concern are physiologically active at concentrations orders of magnitude lower than those causing acute lethality, and the high concentrations sufficient to cause lethality may never occur in the environment  
.....the workgroup recommends that aquatic life criteria consist of only a CCC and that no CMC be derived, when sufficient information demonstrates risks of acute lethality are negligible.

*1a. Relevance of Acute Toxicity Effect Concentrations in Setting ALC for CECs:*

“Except possibly where a very sensitive species is important at a site, aquatic life should be protected if: The four-day average concentration does not exceed the Criterion Continuous Concentration (CCC) more than once every three years on the average, And the one-hour average concentration does not exceed the Criterion Maximum Concentration (CMC) more than once every three years on the average.”

*1a. Relevance of Acute Toxicity Effect Concentrations in Setting ALC for CECs:*

(1) Are CVs for sensitive taxa 100X or more below AVs for sensitive taxa? If so, when exposures are managed to satisfy the CCC, then exposures can never be high enough to reach the CMC.

(2) Does available exposure information demonstrate that maximum concentrations will be far below those eliciting acute effects?

(3) Can acute toxicity information for other chemicals inform this evaluation?

(Note – the elimination of the CMC precludes deriving the CCC based on acute-chronic ratios.)

*1a. Relevance of Acute Toxicity Effect Concentrations in Setting ALC for CECs:*

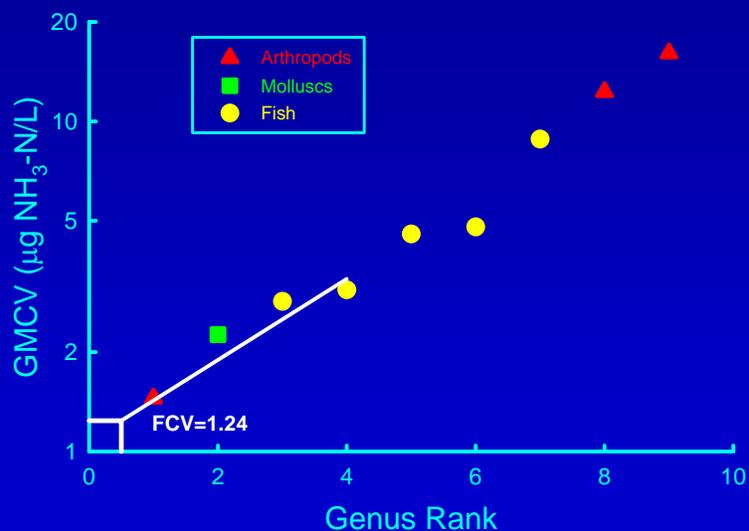
*Acute Toxicity of Ethynylestradiol*

Genus	GMAV (ng/L)	Comments
<i>Gammarus</i>	>840,000	10-d test
<i>Rana</i>	>850,000	14-d test
<i>Medaka</i>	>1,000,000	
<i>Danio</i>	1,700,000	
<i>Ceriodaphnia</i>	1,800,000	
<i>Hydra</i>	3,800,000	
<i>Sida</i>	>4,100,000	24-h test
<i>Daphnia</i>	>5,000,000	24-h test
<i>Chironomus</i>	9,100,000	24-h test

*1b. Defining Minimum Data Requirements Regarding Taxonomic Coverage:*

In the case of many CECs, toxicological research tends to focus on organisms for which the MOA is most relevant (e.g., vertebrates for estrogen mimics) and may have limited data coverage for other taxonomic groups that will likely be less sensitive ..... rather than requiring an acceptable chronic toxicity test, the data requirement for certain taxonomic group expected to be insensitive might be met by a body of information demonstrating insensitivity of the taxon.

1b. Defining Minimum Data Requirements  
Regarding Taxonomic Coverage:



1b. Defining Minimum Data Requirements  
Regarding Taxonomic Coverage:

Chronic Toxicity of Ethynylestradiol

Genus	Chronic Value(s) (ng/L)	Notes
<i>Danio</i>	0.6, 1.5, <1.1	Life-cycle tests
<i>Pimephales</i>	<0.32, 1.5	Life-cycle tests
<i>Oryzias</i>	3.2	F0 from 1 d through spawning
<i>Oncorhynchus</i>	<16	Adult exposure, fertilization success
<i>Potamopyrgus</i>	50	Adult exposure; embryo production
<i>Gammarus</i>	>7600	100 d test, population size
<i>Daphnia</i>	45,000	Life-cycle test
<i>Tisbe</i>	>100,000	Saltwater copepod
<i>Chironomus</i>	320,000	Larval growth and molting schedule
<i>Brachionus</i>	800,000	72 h test, intrinsic rate of increase

### 1c. Use of Non-Resident Species in Criteria Development:

Excluding species simply because they are not resident may be unnecessarily restrictive for the purposes of deriving national criteria, and may actually increase rather than decrease uncertainty. The workgroup recommends that non-resident species be considered for use in criteria derivation calculations, focusing on those species with widely used and standardized test methods and [if] there is no reason to believe [that these species] would misrepresent the sensitivity of resident species.

### 1c. Use of Non-Resident Species in Criteria Development:

Chronic Toxicity of Ethynylestradiol

Genus	Chronic Value(s) (ng/L)	Notes
<i>Danio</i> **	0.6, 1.5, <1.1	Life-cycle tests
<i>Pimephales</i>	<0.32, 1.5	Life-cycle tests
<i>Oryzias</i> **	3.2	F0 from 1 d through spawning
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<i>Chironomus</i>	320,000	Larval growth and molting schedule
<i>Brachionus</i>	800,000	72 h test, intrinsic rate of increase

### *1c. Use of Non-Resident Species in Criteria Development:*

#### *Sex Reversal, Intersex for EE2*

<i>Genus</i>	<i>LOECs (ng/L)</i>
<i>Danio**</i>	0.10 - >25
<i>Pimephales</i>	1.0 - 12
<i>Oryzias**</i>	2.9 - 100
<i>Margariscus</i>	3.5
<i>Gobiocypris**</i>	5.0
<i>Gasterosteus</i>	50
<i>Poecilia</i>	110

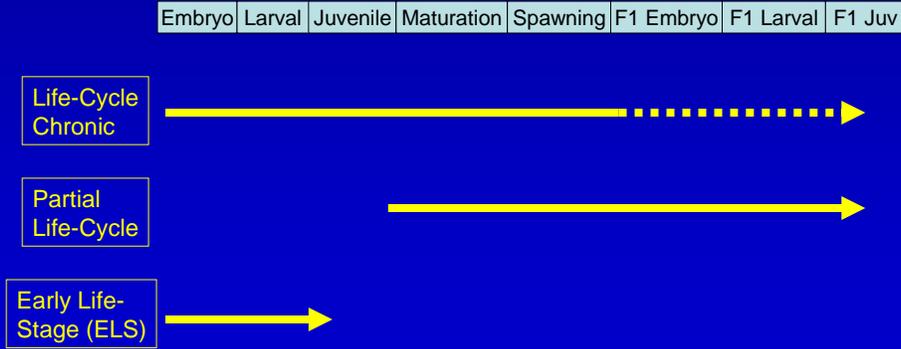
### *1d. Defining Appropriate Chronic Toxicity Data:*

.....important effects of these chemicals may not occur, or at least not be expressed, until after the ELS exposure window; in fact, PLC exposures may also miss important effects, such as those on sexual development ..... the workgroup recommends that the Office of Water ..... require at least one full life-cycle test for a fish unless there is a compelling body of information indicating that life processes outside the ELS or PLC exposure/observation window are not critical to capturing the biologically important effects of chronic exposure to the chemical.

## 1d. Defining Appropriate Chronic Toxicity Data

### Sources of Chronic Data for Fish

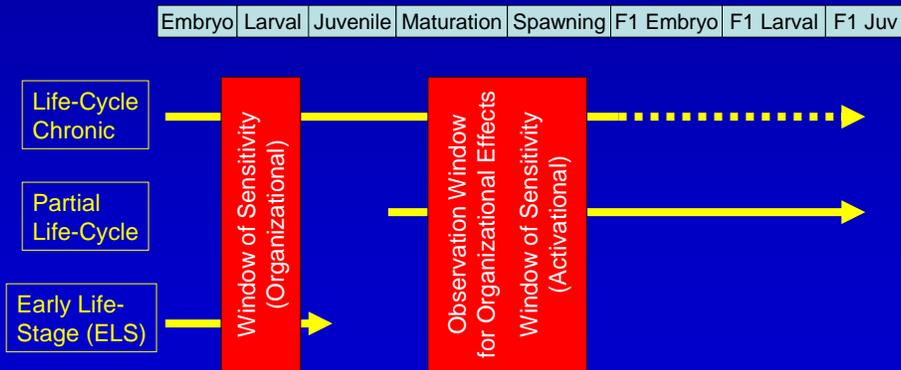
Life Stages (not to scale)



## 1d. Defining Appropriate Chronic Toxicity Data

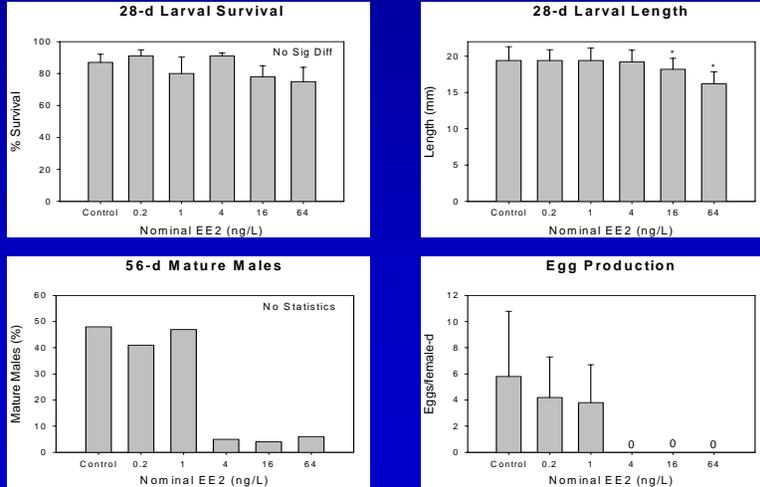
### Windows of Sensitivity for EE2

Life Stages (not to scale)



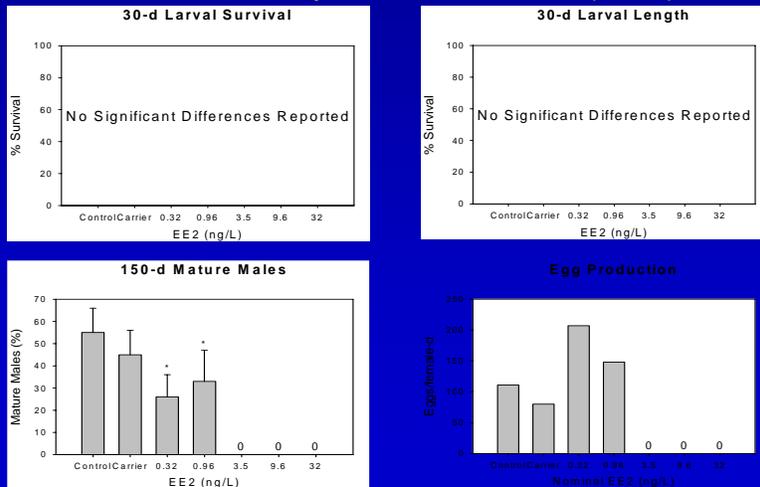
## 1d. Defining Appropriate Chronic Toxicity Data

### FHM Chronic by Länge et al. (2001)



## 1d. Defining Appropriate Chronic Toxicity Data

### FHM Chronic by Parrott and Blunt (2005)



*1e. Selection of Effect Endpoints  
Upon Which to Base Criteria:*

.....many CECs, particularly those with very specific modes of action like steroid hormone agonists/ antagonists, will have data for a wide variety of histological, biochemical, physiological, or behavioral endpoints ..... The degree to which such measures can be used to infer population level effects is likely endpoint-, chemical-, and/or organism-specific, and developing a universal list of recommended endpoints is beyond the scope of the workgroup ..... the recommendation here is simply that criteria development more thoroughly explores such possibilities.

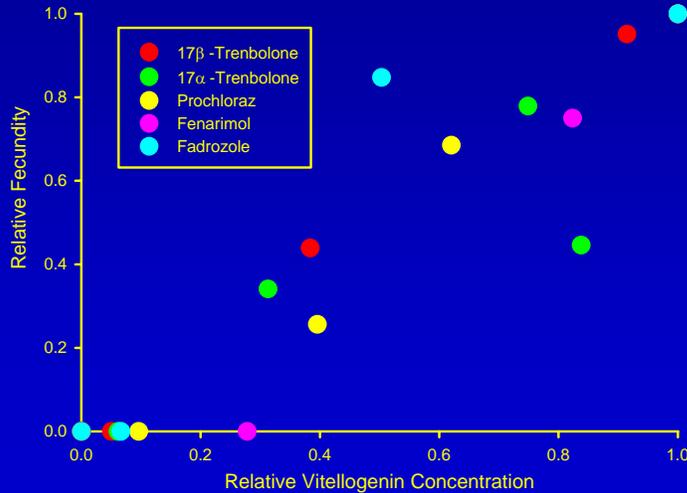
*1e. Selection of Effect Endpoints  
Upon Which to Base Criteria:*

(1) Endpoint important in its own right? Or used for interchemical, interspecies extrapolations based on established correlations to important endpoints?

(2) EE2 Effects Discussed in White Paper, Part II:

- Vitellogenin in males
- Sex ratios
- Intersex/testis-ova

*1e. Selection of Effect Endpoints  
Upon Which to Base Criteria:*



*1f. Involvement of an Expert Panel:*

.....the complexities involved in the assessment of many CECs, and the reliance on professional judgment in making some of the determinations required under the workgroup's recommendations, make clear the need to bring the best scientific knowledge to bear in the development of criteria  
.....The workgroup supports the recommendation from a SETAC Pellston workshop (2003) that criteria development involve recruitment of an expert panel early in the process to insure that all relevant issues are considered during initial development of the criterion and to provide scientific perspective on decisions that are made as part of the process.

## Appendix G – Highlights of Responses to the Charge Questions

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### Charge Question #1a - Relevance of Acute Toxicity Effect Concentrations in Setting ALC for CECs

- The committee, in principle, supports the suggestion to derive ALCs solely from CCCs for CECs.
- However, several caveats were noted:
  - Not enough is known for some classes of CECs (e.g., nanoparticles) to determine whether acute toxicity needs to be taken into account in deriving ALCs.
  - Some CECs appear to have differing MOAs for acute toxicity vs. chronic toxicity.
  - LOECs and LC50s are within one order of magnitude for some CECs, making acute toxicity relevant in deriving ALC.
  - Pulsatility of some CECs may result in exceedingly high concentrations of CECs in specific circumstances (natural disasters – spills).
  - Mixtures of CECs with comparable MOAs may result in higher environmental concentrations than would be expected for any single compound.
- The committee suggested several amendments to the white paper’s suggestion regarding the relevance of acute toxicity to ALC development for CECs:
  - All available data on any new class of CECs should be used in determining whether acute toxicity is likely to occur in environmentally relevant settings.
  - CMCs should be derived for compounds where LOECs are found to be within one order of magnitude of LC50s or where MOAs for acute and chronic toxicity differ.
  - Pulsatility needs to be considered in determining the range of environmentally relevant concentrations.
  - Mixture effects of compounds with similar MOAs need to be considered when determining the range of environmentally relevant concentrations.
  - A summary of all available data speaking to the relevance of acute toxicity should be included in any ALC document to maintain transparency when CMCs are not used in ALC development.☐

Together, these considerations should allow a robust determination on whether CMC are necessary or can be discharged off in the derivation of ALC.

### Charge Question #1b - Defining minimum data requirements regarding taxonomic coverage.

Current taxonomic coverage requirements are:

- Salmonid
  - Rainbow trout
- Second fish family
  - Medaka, zebrafish, fathead, bluegill, catfish
- Third fish or non-fish chordate
  - Same as above for fish, frog
- Planktonic crustacea
  - Daphnid, copepod
- Benthic crustacea
  - Amphipod, copepod
- Aquatic insect
  - Chironomid
- Non-arthropod, non-Chordata
  - Rotifer, sponge, hydra, algae
- Any phylum not represented
  - Mollusk, algae, sponge, hydra

Committee recommendations concerning taxonomic coverage are:

- View taxonomic coverage as information requirements not test requirements
  - Best scientific judgment
- Exceptions rather than the rule suggest maintaining broader coverage
  - Don't just assume you know the MOA or the most "sensitive" species
- Check-box versus "weight of evidence"
  - How much is enough - uncertainty
  - Utilize resources and animals wisely
  - Inference from other compounds
- Trophic level versus taxonomic coverage focus
  - Consider ecology
- Laboratory species versus "wild type"
- Freshwater and marine in the white paper
- Additional examples needed
  - Lawton et al., 2006
  - Staples et al., 2008

Charge Question #1c - Use of non-resident species in criteria development.

Recommendations concerning non-resident species are:

- Non-resident species should be used for aquatic life criteria development.
- Non-resident species, such as zebrafish and Japanese madaka, add extremely useful information on modes of action.
- Resident species information is preferable to non-resident species.

- In no case should aquatic life criteria be developed based on non-resident species alone.
- The addition of non-resident species data will allow for a better estimation of species sensitivity distributions.
- The addition of non-resident species to aquatic life criteria development will improve international harmonization and equivalency efforts.
- Differences in strains, husbandry, health, and parasite and pathogen load contributes to response variation and should be considered in the aquatic life criteria development process.
- Issues that should be considered in prioritizing species responses should include their vulnerability, endangerment status, recreational, commercial and ecological value.
- Non-resident species data, as with resident species data, must meet *Guidelines* for data and method validity.

Charge Question #1d - Defining Appropriate Chronic Toxicity Data.

The Committee:

(1) strongly supports EPA's recommendation that at least one full life cycle test for a fish be included in the requirements for testing chemicals when deriving water quality criteria for the protection of aquatic life.

(2) recommends that the EPA critically review data dealing with trans-generational responses of aquatic species and evaluate if this additional testing provides significant new information that informs the evaluation process.

(3) recommends that the EPA supports research that addresses the suitability of the use of surrogate species in assessing the response of aquatic species to CECs/endocrine disrupting chemicals.

Charge Question #1e - Selection of effect endpoints upon which to base criteria.

- EPA should pursue "non-traditional measures", but be sure they can be tied to population
- EPA should use non-traditional measures for MOA confirmation/development
- EPA should use human health information and toxicology tools (genomics/ Physiologically Based Pharmacokinetic [PBPK] models) to reduce uncertainty
- Vitellogenin in male/juvenile is indicator of exposure to feminizing stressor (not directly related to population).
  - Strong correlations in females, but not necessarily tied to altered endocrine MOA
- Intersex is indicative of feminizing stressor (not directly related to population--- depends on species and life history)
- Gender ratio can be indicative of endocrine alteration, but baseline information on appropriate life history necessary

Charge Question #1f - Involvement of an expert panel.

- The committee concurs with strong participation (as reviewers) by outside experts from the early stages of problem formulation throughout the assessment
- Expert advice should provide a balanced range of perspectives, including
  - Mix of sector (academic, business, governmental) representation
  - Mix of disciplines
- White paper should outline who convenes the panel, criteria for membership, and how conflicts of interest will be identified and eliminated, In addition, the charge to the panel and the expected end result must be clearly defined.
- The Committee is concerned that the use of expert panels could lead to less consistency in how aquatic life criteria are determined; therefore specific guidance on expert panel expectations and their roles in problem formulation, data evaluation, and the generation of recommendations will help to alleviate this potential problem

Charge Question #2 – Issues in the White Paper.

The issues in addressed in the White Paper are appropriate but it was recommended that additional topics be addressed

- EPA should develop principles for revising the 1985 Guidelines. These principles should include:
  - Seek a wide range of inputs from diverse perspectives
  - Develop a robust Conceptual Model
  - Develop Multiple Lines of Evidence
  - Identify (quantitative and qualitative) the uncertainties associated with the criterion development
- The conceptual model principle should put criteria development in a cause-effect and ecological context
- Expert system or process should be used
  - Flexibility for answering the specific questions to set a ALC
  - More mechanisms and more consideration of ecology
- Uncertainty should be addressed
  - Describe and use as the basis for future research
  - Explicit and transparent
  - Categories for uncertainty?
  - Uncertainty might be important
  - Should incorporate but not show stoppers
  - Are show stoppers
- Context (substrate, interactions, etc) is needed

- Mixtures (similar and different modes of action)
- Analytical chemistry for context
- Biomagnification-biotransformation-physical(thermodynamic), degradation products
- Bioavailability—trophic status of water bodies and how affect
- Other factors/issues to be considered
  - Natural Selection and indirect effects
  - Phylogenetic, functional and habitat diversity
  - Life history versus toxicity outcome, impacts
  - Timing of breeding
  - Threatened and endangered species
  - multiple modes of action for same compound
  - Genomics and specific receptors-Mode of Action
  - Non-linear responses to contaminates
  - QSAR—lots better modeling
  - Population scale-genetics, dynamics, interactions

Charge Question #3 – Part II of the White Paper

- Part II of the white paper, which is intended to serve as an illustration rather than a comprehensive case-study, provides well-written and thorough review of the existing literature on EE2 and illustrates well the complexities inherent in generating CEC-specific water quality criteria to protect aquatic life.
- However, the document needs to explicitly recognize that EE2 is data-rich compared to other CECs, the Agency’s interest in CECs goes beyond endocrine-active substances, and discuss the manner in which it can be extrapolated to other substances, particularly to data-poor substances.
- Further, the illustrative pieces of Part II would be best presented in Part I in the form of succinct text boxes emphasizing key concepts derived from the various Recommendations, with the more detailed components of Part II relegated to appendices in Part I, which would become the sole document. The text boxes should not be restricted to EE2 but rather included other CECs (e.g., non-endocrine-active compounds, data-poor CECs).
- Recommended improvements to Part II include, in addition to specific recommendations for improving clarity and transparency:
  - Explicitly state the importance of considering multiple stressors as well as synergies among CECs.
  - Include caveats that recognize that generalizing results from non-residents to resident species may not be possible and, as such, data from resident species, especially life-cycle tests, remain extremely valuable.

- Address, in a clear and transparent manner, the possibility of trans-generational effects.
- Include a broader array of MOA-specific and non-traditional endpoints.
- Assess the extent to which population-scale impacts of EE2 can be calculated and how a criterion can be developed that will sufficiently protect populations within a reasonable level of uncertainty per the *Guidelines*.
- Improve clarity regarding interactions between weight of evidence and the Precautionary Principle (i.e., appropriate levels of uncertainty)
- Replace NOECs/LOECs with EC<sub>x</sub> values.

Charge Question #4 – Suggestions to assist in implementing the proposed recommendations in the White Paper.

The Committee recommends that the following issues be addressed:

- Future research funding to identify priority data needs (intramural and extramural help to EPA)
- Focus on ecological risk assessment
- Use of a mode of action (MOA) approach (use molecular fingerprint approach/novel approaches)
- Develop ecosystem based criteria (linking ecological integrators, index of biotic integrity [IBI]).
- Consider tissue residue approach/bioavailability
- Involve state and industry stakeholders
- Develop a list of CECs in priority order for aquatic life criteria development
- Develop a mixture strategy for compounds with similar MOAs and define broad classes of CECs for criteria development
- Develop analytical chemistry methods for detection of low level CECs
  - Help with list so that these analytical challenges can be resolved earlier.
- Focus on special considerations needed for endangered/highly managed (charismatic) species
  - Examples include apex predators and marine mammals.
    - These predators are aquatic
    - These predators eat fish
    - Marine mammals have a dive reflex that forces more contaminant into tissue due to pressure gradients.