

**Summary Minutes of the  
U.S. Environmental Protection Agency (EPA)  
Chemical Assessment Advisory Committee (CAAC)  
Augmented for the Ethylene Oxide (EtO) Review  
Public Teleconference  
September 30, 2014**

Date and Time: Tuesday, September 30, 2014, 3:00 PM – 6:00 PM ET

Location: Telephone only

Purpose: To receive a briefing on the EPA's *Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide (Revised External Review Draft - August 2014)*<sup>1</sup> and to discuss EPA's charge questions<sup>2</sup>.

Participants: Augmented CAAC for EtO (for full Augmented CAAC for EtO, see roster<sup>3</sup>)

Dr. Peter S. Thorne, Chair  
Dr. Henry Anderson  
Dr. William Michael Foster  
Dr. Gary Ginsberg  
Dr. Russ Hauser  
Dr. Steve Herringa  
Dr. Peter Infante  
Dr. Lawrence Lash  
Dr. Maria Morandi  
Dr. Victoria Persky  
Dr. Kenneth Ramos  
Dr. Stephen Roberts  
Dr. Elizabeth (Lianne) Sheppard  
Dr. Daniel Zelterman

Mr. Aaron Yeow, Designated Federal Office (DFO), EPA SAB Staff Office  
Dr. Vincent Cogliano, EPA, Office of Research and Development (ORD)  
Ms. Jennifer Jinot, EPA, ORD

Other Attendees (See Attachment A)

### **Opening Remarks**

Mr. Aaron Yeow, DFO, opened the meeting. He noted that as required under the Federal Advisory Committee Act (FACA), the SAB's deliberations are held in public with advanced notice given in the Federal Register, and the meeting minutes will be made publicly available after the meeting. He noted that there were seven members of the public who registered in advance with the SAB Staff Office to present oral comments. He noted that the Augmented CAAC for EtO received written public comments, which were also posted on the meeting webpage. He stated that the SAB Staff Office determined that there were no issues with conflict of interest nor any issues with an appearance of a lack of impartiality

for any of the Augmented CAAC for EtO members. He then turned the meeting over to Dr. Peter S. Thorne, Chair of the Augmented CAAC for EtO.

Dr. Thorne welcomed everyone, provided an overview of the Agenda<sup>4</sup>, and had the members of the Augmented CAAC for EtO introduce themselves.

Dr. Vincent Cogliano, Acting IRIS Program Director of EPA's National Center for Environmental Assessment (NCEA) provided welcoming remarks, noting that the EtO assessment had been reviewed by the SAB in 2007 and revised based on the SAB's advice. He also noted that because this was an older document, it does not incorporate all of the National Research Council's recommendations for IRIS documents.

Ms. Jennifer Jinot, Assessment Manager, EPA NCEA provided an overview of the Draft Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide. Her presentation<sup>5</sup> covered the recent history of the EtO assessment, general information on EtO, and overview of the carcinogenicity assessment, and major SAB (2007) and public (2013) comments and EPA's responses. There were some clarifications regarding the steepness of the slope for the exposure-response models for lymphoid cancer, which data categories were included in the linear model for lymphoid cancer, the short-term recommendations by NRC, the number of categories examined in the exposure-response models for lymphoid cancer, and fitting of the spline knots.

## **Public Comments**

Registered public speakers made oral statements in the order provided in the List of Public Speakers.<sup>6</sup>

Mr. Jake Vandervort, B&C Consortia Management LLC, on behalf of the Ethylene Oxide Sterilization Association, Inc. (EOSA), stated that EtO is an important chemical used for the sterilization of medical devices and that the IRIS assessment may adversely impact those that use EtO and the medical community at large. He asked the Augmented CAAC to consider whether the data support only presenting the results of non-linear modeling, whether the two-piece spline model for breast cancer incidence is appropriate, whether uncertainties in the NIOSH data have been adequately addressed, and whether there are any scientific issues raised in the public comments that have not been adequately addressed by EPA.

Dr. Nancy Beck, American Chemistry Council and Center for Advancing Risk Assessment Science and Policy (ARASP), noted that the American Chemistry Council had submitted written comments<sup>7</sup> and encouraged the Augmented CAAC to look at those. She presented her oral statement<sup>8</sup> and indicated that because this assessment will be released three years after the NRC's recommendations, the public will perceive that this assessment meets all of the recommendations (even though EPA states that it does not). As the Augmented CAAC looks at modeling issues, she urges them to keep the epidemiology literature and biology in mind. She did not believe that EPA's use of linear modeling is consistent with EPA's Cancer Guidelines and expressed concern that EPA has set too high of a bar for the use of nonlinear modeling.

Dr. Chris Kirman, Summit Toxicology, presented his oral statement<sup>9</sup> to the Augmented CAAC, which focused on EPA's selection of a single long lag term, which he believed was not well supported due to underlying biology, precedents from existing IRIS assessments, and the potential policy implications of using a non-zero lag. For the sake of transparency, he urged considerations of the mode of action (MOA), underlying biology, viable alternatives, and impact of alternative options on resulting unit risks.

An Augmented CAAC member sought clarification regarding the source of Dr. Kirman's statement that some lymphomas have as little as a 1.5 year latency. Dr. Kirman referred the members to the CDC report<sup>10</sup> as the source of the information.

Dr. Robert Sielken, Sielken & Associates Consulting, presented his oral statement<sup>11</sup> which focused on a recommended addition of a charge question, asking the Augmented CAAC to comment on EPA's method of implementing their linear regression of categorical results and EPA's rejection of the recommendations in the Valdez-Flores and Sielken (2013) study. He noted additional material<sup>12</sup> submitted for the Augmented CAAC's consideration. He asked the Augmented CAAC to review EPA's breast cancer incidence modeling and gave his view that EPA's selection of a two-piece spline model is not appropriate.

Dr. Jane Teta, Exponent, presented her oral statement<sup>13</sup> which focused on asking that the charge question related to uncertainty be expanded to include whether EPA has adequately covered the uncertainties of the NIOSH exposure assessment and potential selection biases and inconsistencies in exposure-response trends in the NIOSH breast cancer incidence study.

Dr. Richard Albertini, Genetic Toxicology Consultants, presented his oral statement<sup>14</sup> which focused on the use of data for determining the MOA for EtO. He stated that there was a lack of clarity in the process used in EPA's determination of the MOA and had comments regarding the plausibility of other MOAs. He asked that EPA reconsider their insistence on only a linear, non-threshold extrapolation for risk assessment for all tumors in recognition of biologically plausible pathogenic processes being involved in at least some EtO associated tumors. An Augmented CAAC member sought clarification on which cancers Dr. Albertini thought were not driven by a mutagenic MOA. Dr. Albertini thought that the lymphoid cancers do not have chemical bases and are antigen driven.

Dr. Janet Gray, Vassar College, on behalf of the Breast Cancer Fund, presented her oral statement<sup>15</sup> which focused on supporting EPA's hazard characterization of EtO as "carcinogenic to humans," weight-of-evidence criterion, and model selection and application for breast cancer incidence.

### **Review of Charge Questions and Clarifying Questions**

Dr. Thorne indicated that this portion of the meeting was to give the Augmented CAAC an opportunity to seek clarification regarding the charge questions, or to seek modification or additions to the charge questions. He presented each of the charge questions and then opened the floor to the Augmented CAAC to ask clarifying questions. One member of the Augmented CAAC asked whether the suggestions for modification or additions to the charge questions from the public comments would be discussed. Dr. Thorne indicated that most of the suggestions from the public could be answered within the confines of the existing charge questions and asked the Augmented CAAC to, where appropriate, consider those as they develop the responses to the charge questions. Another member asked whether they could request addition information or data from EPA. Mr. Yeow indicated that they could and to submit these requests to him, which would then be passed on to EPA and any responses from EPA would be posted to the SAB website and distributed to the Augmented CAAC.

### **Additional Clarifying Public Comment**

Dr. Nancy Beck, American Chemistry Council, requested and was granted an opportunity to make a clarifying comment. She expressed her disappointment that the Augmented CAAC did not discuss all of the modifications and additions to the charge questions that were suggested by the public comments.

Dr. Thorne indicated that he looked very carefully at the public comments and that the suggestions and modifications could be answered within the confines of the existing charge questions. He stated that as the members review the charge questions, any comment received regarding the charge question will be an important consideration in the development of their response.

The meeting was adjourned by Mr. Yeow at 5:00 pm.

Respectfully Submitted:

Certified as Accurate:

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Mr. Aaron Yeow  
Designated Federal Officer  
EPA SAB Staff Office

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Dr. Peter S. Thorne  
Chair  
Chemical Assessment Advisory Committee  
Augmented for the Ethylene Oxide Review

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by Panel members during the course of deliberations within the meeting. Such ideas, suggestions and deliberations do not necessarily reflect consensus advice from the Panel members. The reader is cautioned to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final advisories, commentaries, letters or reports prepared and transmitted to the EPA Administrator following the public meetings.

## Materials Cited

The following meeting materials are available on the SAB website: <http://www.epa.gov/sab>, at the [September 30, 2014 SAB Meeting page](#):

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<sup>1</sup> Agency Review Document – *Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide (Revised External Review Draft – August 2014)*

<sup>2</sup> Agency Charge – Charge for IRIS Assessment for Ethylene Oxide (2014) – Evaluation of Inhalation Carcinogenicity

<sup>3</sup> Roster

<sup>4</sup> Agenda

<sup>5</sup> EPA Presentation – Overview of the Draft Carcinogenicity Assessment of Ethylene Oxide

<sup>6</sup> List of Public Speakers

<sup>7</sup> Comments from the American Chemistry Council’s Ethylene Oxide Panel

<sup>8</sup> Oral Statement from Nancy Beck, on behalf of the American Chemistry Council and the Center for Advancing Risk Assessment Science and Policy

<sup>9</sup> Oral Statement from Chris Kirman, Summit Toxicology

<sup>10</sup> Comments from Chris Kirman, Summit Toxicology – CDC Reference

<sup>11</sup> Oral Statement from Robert Sielken, Sielken & Associates Consulting

<sup>12</sup> Comments from Robert L. Sielken, Sielkin & Associates Consulting - Appendix J; Comments from Robert L. Sielken, Sielkin & Associates Consulting - Supplementary Material for Valdez-Flores and Sielken (2013); Comments from Robert L. Sielken, Sielkin & Associates Consulting - Valdez-Flores and Sielken (2013)

<sup>13</sup> Oral Statement from Jane Teta, Exponent

<sup>14</sup> Oral Statement from Richard J. Albertini, Genetic Toxicology Consultants, LLC

<sup>15</sup> Oral Statement from Janet Gray, Vassar College, on behalf of the Breast Cancer Fund

**ATTACHMENT A – Other Attendees  
CAAC EtO Public Teleconference  
September 30, 2014**

The following persons identified themselves as being present on the teleconference or had requested call-in information for the meeting.

| <b>Name</b>         | <b>Affiliation</b>  |
|---------------------|---|
| Albertini, Richard  | Genetic Toxicology Consultants                                |
| Avery, James        | USEPA   |
| Bartow, Susan       | USEPA   |
| Beck, Nancy         | American Chemistry Council                                    |
| Berner, Ted         | USEPA   |
| Bussard, David      | USEPA   |
| Cai, Christine      | USEPA   |
| Choi, Haylie        | RegNet Environmental Services                                 |
| Christensen, Carol  | USEPA   |
| Cogliano, Vincent   | USEPA   |
| DeSantis, Joe       | USEPA   |
| Fensterheim, Robert | RegNet Environmental Services                                 |
| Flowers, Lynn       | USEPA   |
| Gibbons, Catherine  | USEPA   |
| Glenn, Barbara      | USEPA   |
| Gray, Janet         | Vassar College  |
| Gulledge, Bill      | American Chemistry Council                                    |
| Hegstad, Maria      | Inside EPA  |
| Itkin, Cheryl       | USEPA   |
| Jinot, Jennifer     | USEPA   |
| Kent, Ray           | USEPA   |
| Keshava, Channa     | USEPA   |
| Keshava, Nagu       | USEPA   |
| Kirman, Chris       | Summit Toxicology   |
| Miller, David       | USEPA   |
| Newhouse, Katherine | USEPA   |
| Nguyen, James       | USEPA   |
| Olden, Ken          | USEPA   |
| Patton, Eric        | Harcros Chemicals Inc.  |
| Perovich, Gina      | USEPA   |
| Putzrath, Resha     | Navy and Marine Corps Public Health Center;<br>Portsmouth, VA |
| Rausch, Louette     | BA Specialty Chemicals  |
| Rizutto, Pat        | Bloomberg BNA, Inc.   |
| Ross, Mary          | USEPA   |
| Sielken, Robert     | Sielken & Associates Consulting                               |
| Spassova, Maria     | USEPA   |

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|-----------------|------------------------------|
| Strother, Dale  | ToxSolve LLC                 |
| Teta, Jane      | Exponent                     |
| Vandevort, Jake | B&C Consortia Management LLC |
| Walsh, Debra    | USEPA                        |
| Wormell, Lance  | USEPA                        |