



January 7, 2015

Mr. Aaron Y. Yeow  
USEPA Headquarters  
William Jefferson Clinton Building  
1200 Pennsylvania Avenue, N. W.  
Mail Code: 1400R  
Washington, DC 20460

Sent via email to: [Yeow.aaron@Epa.gov](mailto:Yeow.aaron@Epa.gov)

**Re: Comments on the Revised External Review Draft Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide- Inclusion of Additional Epidemiology Data**

Dear Mr. Yeow:

Following the discussions at the November 18-20, 2014, meeting of the SAB Chemical Assessment Advisory Committee (CAAC) augmented for the review of the ethylene oxide revised draft IRIS assessment, the Ethylene Oxide Panel (Panel) of the American Chemistry Council (ACC) noted that several members of the CAAC inquired about the availability of the Union Carbide (UCC) ethylene oxide epidemiology data and other potential epidemiology data sources. The inclusion of the UCC data was specifically noted in the discussion on Charge Question 5b which addressed EPA's responsiveness to the 2007 SAB recommendations.

Panel representatives attending the November meeting reminded the CAAC members that the Dow Chemical Company and the Panel offered to provide EPA the UCC data in 2007- see attached letter of November 16, 2007 and related correspondence. Note that the cohort has been updated with vital status follow up through 2003. The Panel again encourages EPA to include the UCC data with the NIOSH data in deriving unit risk estimates in the revised IRIS assessment.

If you have any questions or require additional information please feel free to contact me by phone (202-249-6714) or by email at [bill\\_gulledge@americanchemistry.com](mailto:bill_gulledge@americanchemistry.com).

Sincerely,

*Bill Gulledge*

Bill Gulledge  
Senior Director, Chemical Products and Technology Division  
Manager, Ethylene Oxide Panel





November 19, 2007

Via Email

Henry D. Kahn, D.Sc.  
Chemical Manager  
National Center for Environmental Assessment  
U.S. Environmental Protection Agency  
Mail Code: 8623D  
Ariel Rios Building  
1200 Pennsylvania Avenue, N.W.  
Washington, D.C. 20460

Re: EPA Draft "Evaluation of the Carcinogenicity of Ethylene Oxide" and Inclusion of Additional Epidemiological Data

Dear Dr. Kahn:

The Ethylene Oxide/Ethylene Glycols Panel (Panel) of the American Chemistry Council, in previous communications, has encouraged the U.S. Environmental Protection Agency (EPA) to work with the Dow Chemical Company (Dow) to include the updated Union Carbide Corporation (UCC) ethylene oxide (EO) worker mortality data in EPA's ongoing evaluation of EO's potential carcinogenicity. (Copies of the Panel's August 31, 2007, and September 27, 2007, correspondence to EPA are appended for your convenience). The Science Advisory Board (SAB) Draft Review Report encourages EPA to "broadly consider all of the epidemiology data in developing its final assessment," and specifically references the UCC EO worker mortality data. The Panel strongly believes that including the updated UCC EO cohort data is critical to ensuring scientific robustness and accuracy of EPA's final evaluation of EO's potential carcinogenicity.

As indicated in the appended August 31, 2007, letter to Dr. George Gray, the mortality of 1,896 UCC EO workers from 1940 to 1978 has been reported through 1988 (Teta MJ, Benson LO & Vitale JN, British Journal of Industrial Medicine 1993, 50:704-709.) Vital status follow-up information is available on the cohort through December 31, 2003. This provides an additional 15 years of observation and approximately 27,000 additional person-years, resulting in the longest and most recent follow-up of all EO epidemiology studies.

In late September, the Panel was pleased to have assisted Dow in responding to the numerous questions posed by EPA regarding the updated UCC EO cohort data. However, to date, the Panel is

Dr. Henry D. Kahn  
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troubled that EPA has not indicated that it will in fact include the UCC EO cohort data in its evaluation of EO's potential carcinogenicity. Based on the presolicitation notice, which included numerous tasks to be completed by Dr. Kyle Steenland, we understand that he may be nearing the critical parts of his evaluation and therefore the Panel respectfully requests that EPA respond with a decision regarding this data by close of business on Friday November 30, 2007.

If you have any questions, please contact me at (703) 741-5614 or via email at [kristy\\_morrison@americanchemistry.com](mailto:kristy_morrison@americanchemistry.com)

Sincerely yours.

Kristy L. Morrison  
Manager, Ethylene Oxide/Ethylene Glycols Panel

Attachments

CC:

George Gray, Ph.D.  
Peter Preuss, Ph.D.  
Paul White, Ph.D.  
Vanessa Vu, Ph.D.  
Sue Shallal, Ph.D.  
Peter Caulkins, OPP SRRD  
Nancy Beck, Ph.D.  
Margo Schwab, Ph.D.



SHARON H. KNEISS  
VICE PRESIDENT  
PRODUCTS DIVISIONS

August 31, 2007

Via E-Mail

Dr. George Gray  
Assistant Administrator for Research and Development  
U.S. Environmental Protection Agency  
1200 Pennsylvania Avenue, NW  
Washington DC 20460

Re: EPA's Draft Assessment, "Evaluation of the Carcinogenicity of Ethylene Oxide"  
and Additional Review of Epidemiology Data

Dear Dr.Gray:

As you are aware, the Science Advisory Board's (SAB) Draft Review Report on the U.S. Environmental Protection Agency's (EPA) Draft Evaluation of the Carcinogenicity of Ethylene Oxide (Draft Report)<sup>1</sup> contained numerous recommendations for EPA's Office of Research and Development's (ORD) consideration. The Ethylene Oxide/Ethylene Glycols Panel (EO/EG Panel) of the American Chemistry Council wishes to draw ORD's attention to several specific SAB recommendations that focus on the need to review all available ethylene oxide (EO) epidemiology data. The EO/EG Panel believes that reviewing these data ensures that the final EPA evaluation of EO's carcinogenicity will be fully reflective of all recent, relevant and available epidemiology data and thereby will fulfill both ORD's scientific and legal mandates in this regard and responds fully to the explicit expectations of the SAB reviewers.

The Draft Report and SAB review process are critically important to EO/EG Panel members because it provides significant consensus recommendations to EPA on revising its assessment of the carcinogenicity of ethylene oxide. When issued in final, EPA's assessment will likely serve as the basis for regulatory determinations that may impact EO/EG Panel members who manufacture or use ethylene oxide produced in the United States.<sup>2</sup> The integrity

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<sup>1</sup> SAB, *Review of Office of Research and Development (ORD) Draft Assessment Entitled, "Evaluation of the Carcinogenicity of Ethylene Oxide"* (undated) (Draft Report), available at [http://www.epa.gov/sab/pdf/draft\\_eto\\_report\\_5-15-07ed.pdf](http://www.epa.gov/sab/pdf/draft_eto_report_5-15-07ed.pdf).

<sup>2</sup> The EO members of the Panel are: 3M, ARC/Balchem Corporation; BASF Corporation; Bayer MaterialScience LLC; Celanese Chemicals, on behalf of itself and Old World Industries; Croda,

of this review process must be maintained and the EO/EG Panel believes that the ORD should make every effort to thoroughly address the SAB's comments and requests. The EO/EG Panel is pleased to offer its assistance in helping ORD achieve this goal.

There are several SAB recommendations that are directly relevant to the scope of ORD's review of epidemiology data. The EO/EG panel notes them below for ORD's convenience and consideration.

**“The Panel concurred that the NIOSH cohort is the best single epidemiological data set with which to study the relationship of cancer mortality to the full range of occupational exposures to EtO. That said, the Panel encouraged the EPA to broadly consider all of the epidemiological data in developing its Draft Assessment. In particular, the Panel encourages the EPA to explore uses for the Greenberg et al. (1990) data on cancer outcomes and EtO exposures for 2174 Union Carbide workers at that firms’ two Kana Valley, West Virginia facilities. (See also Teta et al. 1993; Teta et al., 1999).”<sup>3</sup>**

The use of more than one data set was also expressly addressed in the SAB draft report:

**“The Panel did not believe that it was necessary to use only one study to arrive at a single potency estimate or to limit the assessment to a single modeling approach. Panel members emphasized that the EPA’s own cancer risk assessment guidelines support the consideration of the full range of available data as well as alternatives to the default exposure models. Quoting from the EPA’s Guidelines for Cancer Risk Assessment, Section 1.3, p. 1-8, “[T]hese cancer guidelines view a critical analysis of all of the available information that is relevant to assessing the carcinogenic risk as the starting point from which a default option may be invoked if needed to address uncertainty or the absence of critical information”.<sup>4</sup>**

Finally, the EO/EG Panel notes the following item from the SAB draft report:

**“The Panel understands that these data are available to EPA analysts upon request to the CDC/NIOSH. The Panel recognizes the burden that a reanalysis of the individual data places on the EPA ORD staff but given the importance of a best**

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Inc., The Dow Chemical Company; Eastman Chemical Company; Equistar Chemicals LP; Honeywell; Huntsman; Sasol North America, Inc.; Shell Chemical LP; and Sunoco, Inc.

<sup>3</sup> SAB Draft Report “Review of ORD draft assessment entitled Evaluation of the Carcinogenicity of Ethylene Oxide”, Page 8

<sup>4</sup> SAB Draft Report, Page 27

**scientific and statistical treatment of all the available epidemiological data, it sees no alternative.”<sup>5</sup>**

The EO/EG Panel is encouraged that ORD awarded a contract to Dr. Kyle Steenland to complete several tasks related to assist in its evaluation of EO’s carcinogenicity based on epidemiology data. One task identified in the scope of work is to further analyze the NIOSH data relating to EO worker exposure to haematopoietic cancer and breast cancer but also recommends analyses of other EO study data. The ORD solicitation (number RFQ-DC-07-00150) specifically states that **“Where appropriate, per EPA technical guidance, the contractor may perform analyses of available results from other EtO studies to provide comparisons to these results.”** See Task 3.

The scope of work for Dr. Steenland’s tasks also included the following information:

**“This contract involves the analysis of secondary data. Secondary data are defined in this context as environmental or health data that exist and are available for analysis. That is, epidemiological data on the carcinogenic effects of exposure to ethylene oxide that were collected prior to the issuance of this contract. This includes data from the NIOSH study of workers exposed to ethylene oxide and may include other relevant data from published literature, from hard copies and computer data bases.**

**...determine what, if any, additional analyses should be performed to provide technical support for comment responses to the ACC and /or the Science Advisory Board Panel.”<sup>6</sup>**

To facilitate the work of Dr. Steenland and to further assist ORD, the EO/EG Panel understands that The Dow Chemical Company (Dow) is willing to provide access to the updated Union Carbide (UCC) ethylene oxide worker mortality data<sup>7</sup>. Vital status follow-up and cause of death has been extended 15 years through December 31, 2003, for the data set of 1,896 workers assigned to EO UCC production or use operations in the Kanawha Valley, West Virginia, facility. The data also include exposure estimates at the individual level by time period. As of the 1993 publication (an update of Greenberg *et al.*, 1990), the UCC cohort had an average follow-up of 27 years (Teta MJ, Benson LO and Vitale JN *British Journal of Industrial Medicine* 1993, 50: 704-709). The mortality study of EO workers in chemical manufacturing has a ten year update. The most update will result in an average of approximately 42 years of follow up, the longest of all EO epidemiology studies. This cohort with the vital status update has not yet been statistically analyzed and the cause specific mortality patterns at this point are not known.

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<sup>5</sup> SAB Draft Report, Page 30

<sup>6</sup> See FedBizOpps April 12, 2007

<sup>7</sup> See *Attached* Letter from Carol J. Burns to George Gray dated August 29, 2007.

Dr. Gray  
August 31, 2007  
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The EO/EG Panel urges ORD to accept this offer and take advantage of the opportunity to increase significantly its analysis of available and relevant epidemiology data for EO workers. We believe that in so accepting, ORD will be giving expression to the explicit requests of the SAB reviewers, discharging its legal mandate to utilize the best available data for scientific review of EO's carcinogenicity and fulfilling ORD's commitment to undertake the best and most scientifically defensible analysis of EO's carcinogenicity.

The EO/EG Panel appreciates the opportunity to make ORD aware of the UCC data. If you have any questions or want to meet to discuss these issues further, please contact Kristy L. Morrison, the EO/EG panel Manager, at (703) 741-5614 or via e-mail at [Kristy\\_Morrison@americanchemistry.com](mailto:Kristy_Morrison@americanchemistry.com).

Sincerely yours,

Sharon H. Kneiss  
Vice President  
Products Divisions

Enclosure

CC:  
Peter Preuss, Ph.D.  
Henry Kahn, Ph.D.  
Paul White, Ph.D.  
Vanessa Vu, Ph.D.  
Nancy Beck, Ph.D.  
Margo Schwab, Ph.D.  
Mr. Peter Caulkins, Acting Division Director, OPP SRRD



The Dow Chemical Company  
1921-1983  
1984-1993  
1994-2003  
2004-2007

August 29, 2007

Dr. George Gray  
Assistant Administrator for Research and Development  
U.S. Environmental Protection Agency  
1200 Pennsylvania Avenue, N.W.  
Washington, DC 20460

**Re: ORD Draft Assessment “Evaluation of the Carcinogenicity of Ethylene Oxide”; Availability of Additional Epidemiology Data**

As noted in a letter from the Ethylene Oxide/Ethylene Glycols Panel of the American Chemistry Council (“the Panel”), The Dow Chemical Company (“Dow”) has ethylene oxide (“EO”) worker mortality data from Union Carbide Corporation (“Union Carbide”), which is now a Dow subsidiary. Dow is willing to provide this data to EPA’s Office of Research and Development (“ORD”) or its contractor, Dr. Kyle Steenland, in connection with its evaluation of the draft assessment “Evaluation of the Carcinogenicity of Ethylene Oxide”. Dow would provide the data in a format that redacts individual identifiers.

The mortality of 1,896 Union Carbide EO workers from 1940 to 1978 has been reported through 1988. (Teta MJ, Benson LO and Vitale JN, British Journal of Industrial Medicine 1993, 50:704-709). Vital status follow-up information is available on the cohort through December 31, 2003. This provides an additional 15 years of observation and approximately 27,000 additional person-years, resulting in the longest and most recent follow-up of all EO epidemiology studies. The Union Carbide cohort is also unique as compared to other existing cohorts because of the relatively high exposure to early workers (up to 70 ppm average 8-hour TWA prior to 1940, and up to 21 ppm average 8-hour TWA thereafter and prior to 1956).

To help ORD’s contractor with his evaluation of the draft assessment, Dow is willing to provide a version of the cohort with vital status updated to 2003 and causes of death coded to the revision at the time of death. As required by our contract with the National Death Index, the data would be redacted so that the identity of the participants could not be determined.

Consistent with the Panel’s statements, Dow believes that these data provide an important contribution to the analysis of available and relevant epidemiology data for EO workers, because of its long follow-up and its relatively high exposure concentrations.

Please have an appropriate person contact me to make arrangements for Dow to provide the data.

Sincerely,

Carol J. Burns, Ph.D., MPH  
Epidemiology Department  
The Dow Chemical Company  
1803 Building  
Midland, MI 49674  
Telephone: (989) 636-2278  
E-mail: [cburns@dow.com](mailto:cburns@dow.com)

cc: Peter Preuss, Ph.D.  
Henry Kahn, Ph.D.  
Paul White, Ph.D.  
Vanessa Vu, Ph.D.  
Nancy Beck, Ph.D.  
Margo Schwab, Ph.D.  
Peter Caulkins, Acting Division Director, OPP SRRD



SHARON H. KNEISS  
VICE PRESIDENT  
PRODUCTS DIVISIONS

September 27, 2007

Via E-Mail

Henry D. Kahn, D.Sc.  
Chemical Manager  
National Center for Environmental Assessment  
U.S. Environmental Protection Agency  
Mail Code: 8623D  
Ariel Rios Building  
1200 Pennsylvania Avenue, N.W.  
Washington, D.C. 20460

Re: EPA's Draft "Evaluation of the Carcinogenicity of Ethylene Oxide" and Inclusion of Additional Epidemiological Data

Dear Dr. Kahn:

The Ethylene Oxide/Ethylene Glycols Panel (EO/EG Panel)<sup>1</sup> of the American Chemistry Council was pleased to have assisted Dr. Carol Burns of The Dow Chemical Company in responding to your September 12, 2007, letter in which you listed numerous questions regarding the Union Carbide (UCC) ethylene oxide (EO) worker mortality data.

The EO/EG Panel strongly believes that including the updated UCC EO cohort data is critical to ensuring the scientific robustness of the U.S. Environmental Protection Agency's (EPA) evaluation of EO's carcinogenicity potential. Simply put, EPA's evaluation will not reflect all of the available science and will not fully comport with the Science Advisory Board's (SAB) recommendations if EPA does not include the updated UCC EO cohort data in its ongoing carcinogenicity evaluation of EO.

As I noted in my August 31, 2007, letter to Dr. George Gray (a copy of which was sent to you and appended here for your convenience), the SAB draft report of EPA's evaluation of EO includes numerous statements regarding the need for EPA to assess *all* of the epidemiological data in developing its evaluation of EO's carcinogenicity. Indeed, in the more

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<sup>1</sup> The EO members of the Panel are: 3M, ARC/Balchem Corporation; BASF Corporation; Bayer MaterialScience LLC; Celanese Chemicals, on behalf of itself and Old World Industries; Croda, Inc., The Dow Chemical Company; Eastman Chemical Company; Equistar Chemicals LP; Honeywell; Huntsman; Sasol North America, Inc.; Shell Chemical LP; and Sunoco, Inc.

Henry D. Kahn, D.Sc.  
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recent, August 30, 2007, iteration of its report, SAB underscores the importance of this key recommendation by explicitly including it in the transmittal letter to Administrator Johnson. As you know, transmittal letters typically contain only SAB's most important conclusions and recommendations regarding the subject of its review. Specifically, the transmittal letter states that, "the Panel encouraged the EPA to broadly consider all of the epidemiological data in developing its final Assessment." The letter concludes by encouraging EPA, "to devote sufficient resources to make implementation of these recommendations possible."

The EO/EG Panel looks forward to other opportunities in which it can lend its considerable expertise to further EPA's effort in implementing one of SAB's most important recommendations. If you have any questions, please contact Kristy L. Morrison, the EO/EGs Panel Manager, at (703) 741-5614 or via e-mail at [Kristy\\_Morrison@americanchemistry.com](mailto:Kristy_Morrison@americanchemistry.com).

Sincerely yours,

Sharon H. Kn̄eis   
Vice President, Products Divisions

Attachment

cc: George Gray, Ph.D. (w/attachment) (via e-mail)  
Peter Preuss, Ph.D. (w/attachment) (via e-mail)  
Paul White, Ph.D. (w/attachment) (via e-mail)  
Vanessa Vu, Ph.D. (w/attachment) (via e-mail)  
Margo Schwab, Ph.D. (w/attachment) (via e-mail)  
Mr. Peter Caulkins (w/attachment) (via e-mail)