Texas Commission on Environmental Quality Response to Public Comments Received on the September 2015 Proposed Ethylene Glycol Development Support Document

The public comment period for the September 2015 Proposed Development Support Document (DSD) for ethylene glycol ended in December 2015. The Toxicology Division (TD) received public comments from the Ethylene Glycols Panel of the American Chemistry Council (ACC) on December 22, 2015. The TD of the Texas Commission on Environmental Quality (TCEQ) appreciates the effort put forth by the ACC to provide technical comments on the proposed DSD for ethylene glycol. The goal of the TD and TCEQ is to protect human health and welfare based on the most scientifically-defensible approaches possible (as documented in the DSD), and evaluation of these comments furthered that goal. A summary of the comments from the ACC and TCEQ responses are provided below. The full comments and cover letter are provided in the Appendix. TCEQ responses indicate what changes, if any, were made to the DSD in response to the comments.

Comment 1:

ACC:

The Panel notes that the key human study selected by TCEQ is Wills et al. (1974). In 2014, the Panel provided detailed comments on the Wills study to ACGIH in response to its TLV Notice of Intended Changes for Ethylene Glycol. In its evaluation it appeared ACGIH applied mean chamber concentration values of 17-49 mg/m^3 to develop its recommended TLV-TWA of 10 mg/m^3. These values, however, were not daily mean values as stated, but weekly mean values. The Panel encouraged ACGIH to report the correct daily mean values from the Wills study, as high as 67 mg/m^3 in the main study and as high as 75 mg/m^3 in the preliminary study. In October 2014, ACGIH proposed a TLV-TWA of 10 mg/m^3, inhalable aerosol, a TLV-TWA of 63.5 mg/m^3, inhalable fraction and vapor, and a TLV-STEL of 127 mg/m^3, inhalable fraction and vapor.

TCEQ Response:

The TCEQ appreciates this background information.

Comment 2:

ACC:

The draft DSD generally reflects the existing studies fairly well. For the acute ReV, the decision to use the LOAEL of 140 mg/m^3 as the POD accurately reflects the Wills study results. From that POD, an acute ReV of 1.5 mg/m^3 is calculated based on UFs that total 90 (10 for intrahuman variability, 3 for LOAEL to NOAEL uncertainty, and 3 for database uncertainty). Based on the Panel's comments to ACGIH, TCEQ could designate a POD as a NOAEL of 67 (or 75) mg/m^3 – from the daily high average concentrations. In this case, the UFs would total 30 and the resulting acute ReV would be 2.2 mg/m^3, slightly higher than the proposed acute ReV of 1.5 mg/m^3.

TCEQ Response:

The acute ReV was derived using the LOAEL of 140 mg/m^3 as the POD along with a LOAEL to NOAEL uncertainty factor of 3, rather than a NOAEL of 67 (or 75) mg/m^3 as the POD, as there was some uncertainty associated with the reported daily high concentrations. The duration of exposure to these daily high exposure concentrations was unknown, and an instantaneous reading would not accurately represent a 1-hour exposure at this concentration. Therefore, the LOAEL of 140 mg/m^3 was used as the POD. However, as pointed out by this reviewer, using the daily high as a NOAEL results in an acute ReV only slightly higher than when calculating the ReV using the LOAEL.

Comment 3:

ACC:

For the proposed chronic ReV, TCEQ selected Coon et al. (1970), with a POD of 12 mg/m^3 as a LOAEL for ocular irritation and lung inflammation. The Panel is not aware of sufficient data from that study to argue for a NOAEL, so the POD is reasonable. The choice of the various UFs also appear to be reasonable – no PK uncertainty and a 12 mg/m^3 HEC. Thus, the UFs are 10 for intrahuman variability, 3 for interspecies variability, 3 for LOAEL to NOAEL uncertainty, 3 for subchronic to chronic uncertainty (Coon was a 90 day study) and 3 for database uncertainty. The resulting chronic ReV is 15 μg/m^3.

TCEQ Response:

The TCEQ acknowledges your concurrence with the critical study selected and derivation of the chronic ReV.

Comment 4:

ACC:

TCEQ should also review the toxicology information on ethylene glycol that is contained in the ECHA database. Information in the database supplements information previously compiled for the OECD High Production Volume initiative.

TCEQ Response:

The TCEQ has reviewed this information and appreciates the reference.

Comment 5:

ACC:

There appears to be an error on p. 24 (p. 31 of the pdf) of the draft DSD, lines 27-28, which states "The margin of exposure between the observed adverse effect level (12 mg/m^3) and the chronic ReV (0.0045 mg/m^3) is a factor of approximately 2700." The Panel believes the chronic ReV of 0.015 mg/m^3 results in a margin of exposure of 800.

TCEQ Response:
Consistent with the comment, this error has been corrected.

Appendix – Comments received from the American Chemistry Council (ACC) on December 22, 2015.

December 22, 2015

Via E-Mail

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Texas Commission on Environmental Quality
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Austin, Texas 78711-3087
E-Mail: tox@tceq.texas.gov

Re: American Chemistry Council Comments on Draft Development Support Document (DSD) for Ethylene Glycol

To Whom It May Concern:

The Ethylene Glycols Panel[1] (The Panel) of the American Chemistry Council appreciates the opportunity to provide comments on the draft DSD for ethylene glycol, dated September 2015. The Panel notes that the key human study selected by TCEQ is Wills et al. (1974).[2] In 2014, the Panel provided the attached detailed comments on the Wills study to ACGIH in response to its TLV® Notice of Intended Changes for Ethylene Glycol. In its evaluation it appeared ACGIH applied mean chamber concentration values of 17-49 mg/m^3 to develop its recommended TLV-TWA of 10 mg/m^3. These values, however, were not daily mean values as stated, but weekly mean values. The Panel encouraged ACGIH to report the correct daily mean values from the Wills study, as high as 67 mg/m^3 in the main study and as high as 75 mg/m^3 in the preliminary study. In October 2014, ACGIH proposed a TLV-TWA of 10 mg/m^3, inhalable aerosol, a TLV-TWA of 63.5 mg/m^3, inhalable fraction and vapor, and a TLV-STEL of 127 mg/m^3, inhalable fraction and vapor.[3]

The draft DSD generally reflects the existing studies fairly well. For the acute ReV, the decision to use the LOAEL of 140 mg/m^3 as the POD accurately reflects the Wills study results. From that POD, an acute ReV of 1.5 mg/m^3 is calculated based on UFs that total 90 (10 for intrahuman variability, 3 for LOAEL to NOAEL uncertainty, and 3 for database uncertainty). Based on the Panel's comments to ACGIH, TCEQ could designate a POD as a NOAEL of 67 (or 75) mg/m^3 – from the daily high average concentrations. In this case, the UFs would total 30 and the resulting acute ReV would be 2.2 mg/m^3, slightly higher than the proposed acute ReV of 1.5 mg/m^3.

[1] The EGs Panel is comprised of Celanese, The Dow Chemical Company, Eastman Chemical Company, Huntsman Corporation, LyondellBasell Industries N.V., and Shell Chemical LP.
[2] Wills, J.H., Coulston, F., Harris, E.S., McChesney, E.W., Russell, J.C., and Serrone, D.M. 1974. Inhalation of aerolized ethylene glycol by man. Clinical Toxicology. 7(5): 463-476.
[3] Draft Documentation- Ethylene Glycol, ACGIH 2015 (attached).

For the proposed chronic ReV, TCEQ selected Coon et al. (1970),[4] with a POD of 12 mg/m^3 as a LOAEL for ocular irritation and lung inflammation. The Panel is not aware of sufficient data from that study to argue for a NOAEL, so the POD is reasonable. The choice of the various UFs also appear to be reasonable – no PK uncertainty and a 12 mg/m^3 HEC. Thus, the UFs are 10 for intrahuman variability, 3 for interspecies variability, 3 for LOAEL to NOAEL uncertainty, 3 for subchronic to chronic uncertainty (Coon was a 90 day study) and 3 for database uncertainty. The resulting chronic ReV is 15 µg/m^3.

TCEQ should also review the toxicology information on ethylene glycol that is contained in the ECHA database.[5] Information in the database supplements information previously compiled for the OECD High Production Volume initiative.[6].

Finally, there appears to be an error on p. 24 (p. 31 of the pdf) of the draft DSD, lines 27-28, which states "The margin of exposure between the observed adverse effect level (12 mg/m^3) and the chronic ReV (0.0045 mg/m^3) is a factor of approximately 2700." The Panel believes the chronic ReV of 0.015 mg/m^3 results in a margin of exposure of 800.

If you have any questions about the foregoing, please contact me at (202) 249-6714 or at bill_gulledge@americanchemistry.com.

Sincerely yours,

William Gulledge

William P. Gulledge
Senior Director
Chemical Products & Technology Division

[4] Coon, R.A., Jones, R.A., Jenkins Jr., L.J., and Siegel, J. 1970. Animal inhalation studies on ammonia, ethylene glycol, formaldehyde, dimethylamine, and ethanol. Toxicology and Applied Pharmacology. 16: 646-655.
[5] http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d87859b-95d3-6682-e044-00144f67d249/AGGR-9aa60c92-0658-424a-9db8-b2f57398d285_DISS-9d87859b-95d3-6682-e044-00144f67d249.html#AGGR-9aa60c92-0658-424a-9db8-b2f57398d285
[6] http://webnet.oecd.org/hpv/ui/ChemGroup.aspx