Texas Commission on Environmental Quality Response to Public Comments

November 2013 n-Butyraldehyde

Development Support Document

The American Chemistry Council's Oxo Process Panel ("the Oxo Panel") submitted comments dated March 10, 2014 on the November 2013 Development Support Document (DSD) for n-butyraldehyde. The Texas Commission on Environmental Quality (TCEQ) appreciates the effort put forth by the Oxo Panel to provide technical comments on the proposed DSD for n-butyraldehyde. The goal of the 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 comments from the Oxo Panel is provided below, followed by TCEQ responses. The full comments are provided in Appendix 1. Comments on issues that suggest changes in the DSD are addressed whereas comments agreeing with TCEQ's approach are not. TCEQ responses indicate what changes, if any, were made to the DSD in response to the comment.

Upon further review, the DSD has been revised, as indicated below.

Comment No. 1:

There is additional mutagenicity and clastogenicity data available for n-butyraldehyde that could be provided.

The 2009 dossier for n-butyraldehyde developed for the Organization for Economic Cooperation and Development's (OECD) Screening Information Data Set (SIDS) provides additional information on mutagenicity and clastogenicity studies for n-butyraldehyde that TCEQ may want to include and reference in the proposed support document. (See enclosed list of references.) Inclusion of these additional studies does not change the conclusion that the results are mixed for n-butyraldehyde for these types of studies.

TCEQ Response:

The TCEQ appreciates the Oxo Panel's providing these additional references. The DSD was revised to include the Martelli et al. (1994) and the OECD SIDs dossier (2009) references, which were reviewed by the TCEQ, but were not cited in the DSD (see revised Section 5.2). However, the Brambilla et al. (1989) and the Galloway et al. (1987) articles were not reviewed by the TCEQ and were not included in the DSD. The TCEQ did reference NIOSH (1991), USEPA (1994) and HSDB (2012) which provide an overview of a number of references discussing the mutagenicity and clastogenicity data available for n-butyraldehyde. These summary documents are more recent reviews than the Brambilla et al. (1989) and the Galloway et al. (1987) studies. As noted by the Oxo Panel, these additional studies do not change the conclusion that the results are mixed for n-butyraldehyde for these types of studies.

Comment No. 2:

TCEQ should consider using the reproductive and developmental toxicity information from structural analogues such as propionaldehyde and isobutyraldehyde to address this toxicity endpoint.

Within the OECD SIDS Dossier, Initial Assessment Profile (SIAP), and the Initial Assessment Report (SIAR) accepted by the OECD Member States, data from structural analogues such as propionaldehyde and isobutyraldehyde were used to address the reproductive and developmental toxicity endpoint. Inclusion of this information in the DSD would allow TCEQ to lower the uncertainty factor for the uncertainty of the data base (UF_D) from the current proposed value of 6, based upon the inclusion of analogue data for reproductive and developmental toxicity.

TCEQ Response:

The DSD was not revised based on this comment. The main reason the UF_D was 6 was due to other considerations, not solely on the lack of reproductive/developmental studies. The fact that n-buytyraldehyde would not be likely to cause reproductive/developmental effects is discussed in Section 3.1.3 Reproductive/Developmental Toxicity Studies.

Comment No. 3

Finally, the Panel notes that the geometric mean calculation in the proposed document combines data from the traditional method of determining an "absolute" odor threshold (i.e., the average concentration that individual panelists can detect odor on 50% of the trials) with another approach that defines a "population" odor threshold as the concentration where 50% of the panelists can detect an odor. While the apparent differences may be small, the actual difference may be quite large, since the dilution steps in an olfactory study typically occur in log cycles. The difference between these two approaches is described within the publication by Dalton and Smeets (2004), which suggests that combining the two may generate results that are confusion or simply uninterpretable.

TCEQ Response:

The TCEQ appreciates the Oxo Panel's comments. The DSD was not revised based on these comments. As described in the Ruijten et al. (2009) and van Doorn et al. (2002) reports, an individual's odor threshold is usually defined as the concentration where this likelihood is 50%. However, the inter-individual variability of odor detectability is known to be very large. The population odor threshold is the concentration at which 50% of the population can smell the odorant. In odor research, the odor detection threshold (ODT) could be described as the concentration at which 50% of population detects a sensory stimulus. According to the TCEQ 2012 guidelines, ODT is defined as the concentrations at which 50% of the volunteers participating in an odor panel detected the odor. The TCEQ uses all reliable population ODTs (e.g., meet Level 1 or Level 2 criteria), *not* data determined by individual's odor threshold, to set an odor-based ESL for a compound. The TCEQ uses a geometric mean value for a compound with two or more reported Level 1 or Level 2 population ODTs instead of the lowest reported population ODT to set the odor-based ESL following the NAC/AEGL Committee's guidance (TCEQ 2012). Level 1 or 2 ODT are determined by modern olfactometry standards such as the Dutch and Japanese methods reported by Hoshika et al. (1993), van Doorn et al. (2002), van Harreveld et al. (2003), or Nagata (2003). NAC/AEGL indicates that because Level 1 or Level 2

population ODTs are determined by modern standards which require minimum performance criteria, a geometric mean value from the data of one or more laboratories can be used. Odor-based ESL set at a geometric mean ODT can minimize potential variation of ODTs reported from different laboratories. The geometric mean calculation is not likely to yield confusion and/or data that are simply not interpretable.

APPENDIX 1
The American Chemistry Council's Oxo Process Panel Comments

Within the OECD SIDS Dossier, Initial Assessment Profile (SIAP), and the Initial Assessment Report (SIAR) accepted by the OECD Member States, data from structural analogues such as propionaldehyde and isobutyraldehyde were used to address the reproductive and developmental toxicity endpoint. Inclusion of this information in the DSD would allow TCEQ to lower the uncertainty factor for the uncertainty of the data base (UF_D) from the current proposed value of 6, based upon the inclusion of analogue data for reproductive and developmental toxicity.

Finally, the Panel notes that the geometric mean calculation in the proposed document combines data from the traditional method of determining an "absolute" odor threshold (*i.e.*, the average concentration that individual panelists can detect odor on 50% of the trials) with another approach that defines a "population" odor threshold as the concentration where 50% of the panelists can detect an odor. While the apparent differences may be small, the actual difference may be quite large, since the dilution steps in an olfactory study typically occur in log cycles. The difference between these two approaches is described within the publication by Dalton and Smeets (2004), which suggests that combining the two may generate results that are confusion or simply uninterpretable.

Thank you for the opportunity to provide these comments. If you have any questions, please do not hesitate to contact me at (703) 249-6727 or srisotto@americanchemistry.com.

Sincerely,

Steve Risotto

Stephen P. Risotto
Senior Director

Enclosure

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BY ELECTRONIC MAIL

March 10, 2014

Toxicology Division, MC 168
Texas Commission on Environmental Quality
P.O. Box 13087
Austin, TX 78711-3087

Re: Proposed Development Support Document for n-Butyraldehyde, CAS Registry Number 123-72-8 (November 2013)

To Whom It May Concern:

The American Chemistry Council's Oxo Process Panel[1] ("the Panel") appreciates the opportunity to provide the Texas Commission on Environmental Quality (TCEQ) with these comments on the November 2013 proposed development support document (DSD) for effects screening levels (ESL) for n-butyraldehyde. The Panel understands the importance of ESLs in providing TCEQ with guidance to protect human health and welfare. The Panel provides the following comments on the proposed DSD for butyraldehyde.

- **There is additional mutagenicity and clastogenicity data available for n-butyraldehyde that could be provided**

The 2009 dossier for n-butyraldehyde developed for the Organization for Economic Cooperation and Development's (OECD) Screening Information Data Set (SIDS) provides additional information on mutagenicity and clastogenicity studies for n-butyraldehyde that TCEQ may want to include and reference in the proposed support document. (See enclosed list of references.) Inclusion of these additional studies does not change the conclusion that the results are mixed for n-butyraldehyde for these types of studies.

- **TCEQ should consider using the reproductive and developmental toxicity information from structural analogues such as propionaldehyde and isobutyraldehyde to address this toxicity endpoint.**

[1] The "Oxo Process" refers to an industrial synthesis process which is used to produce alcohols and related oxygenated compounds. The Panel members include BASF Corporation, Celanese Limited The Dow Chemical Company, and Eastman Chemical Company.

Reference List

Brambilla G *et al.* Mutagenicity in V79 Chinese hamster cells of n-alkanals produced by lipid peroxidation. *Mutagenesis* 4: 277-279 (1989).

Dalton P and Smeets M. Olfactometry: the Human Nose as Detection Instrument. In Hedge A (Ed.). Handbook of Human Factors and Ergonomic Methods. 1st ed. CRC Press (2004).

Galloway SM *et al.* Chromosome Aberrations and Sister Chromatid Exchanges in Chinese Hamster Ovary Cells: Evaluation of 108 Chemicals, *Environmental and Molecular Mutagenesis* 10 (Supplement 10), pp. 1-175 (1987).

Martelli A et al. Cytotoxic and genotoxic effects of five n-alkanals in primary cultures of rat and human hepatocytes. *Mutat. Res*. 323: 121-126 (1994).

OECD SIDS Dossier for n-butyraldehyde. Final dated May 2009. Available at http://webnet.oecd.org/hpv/ui/SIDS_Details.aspx?id=33040f16-6b76-4482-aa79-68d61cfa5689