Texas Commission on Environmental Quality (TCEQ) Responses to Public Comments Received on the Proposed Development Support Document for Ethylene April 15, 2008

The public comment period for the proposed Development Support Document (DSD) for ethylene ended in March 2008. The Texas Chemical Council (TCC) submitted specific comments on ethylene. ExxonMobil submitted general comments on ethylene that were grouped with comments for 1-butene, 2-butene, isobutene, and toluene, but no specific comments relating to ethylene were made, so these comments are not included or addressed. Please refer to the 1-butene response to comments to view the ExxonMobil comments. The Toxicology Section (TS) of the TCEQ appreciates the effort put forth by TCC and ExxonMobil to provide technical comments on the proposed DSD for ethylene. The goal of the TS 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 TCC comments are provided below, followed by TCEQ responses. The full comments of TCC are in Appendix 1. Comments on issues that suggest a change 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.

Texas Chemical Council (TCC) Comments Regarding the TCEQ Development Support Document for Ethylene ESL Values

1. **In deriving the health-based acute ReV and acute ESL for ethylene, an uncertainty factor for database deficiencies (UF) is not justified based on the robust database for ethylene.**

   TCEQ Response: The DSD was not revised based on this comment.The TS concurs with the TCC that ethylene is not acutely toxic at high concentrations. However, the ESL Guidelines (TCEQ 2006) recommends the use of "medium database confidence" when acute inhalation studies are limited to a single species. The available ethylene inhalation studies are limited only to rats. The TS, therefore recommends medium database confidence and attributes a database uncertainty factor of 3.0 in deriving the health-based acute ReV and acute ESL for ethylene.

2. **TCEQ may want to specifically cite the references for the three Conolly et al. publications in Section 3.1.1.2.1**

   TCEQ Response: Suggested changes were incorporated in Sections 3.1.1.2.1 and 3.1.1.2.3 of the ethylene DSD.

3. **TCEQ states erroneously that EPA conducted a repeat dose reproductive and developmental effects screening study on ethylene and incorrectly defined the acronym for OECD.**

   TCEQ Response: Suggested changes were incorporated in the ethylene DSD. However, the TS would like to document that the acronym for OECD was obtained from the ACGIH 2005 publication on ethylene.

4. **TCEQ should use a hazard quotient of 1.0 in developing an acute ESL for ethylene**

   TCEQ Response: The DSD was not revised based on this comment. In order to develop ESLs for use in air permitting that adequately consider the potential for cumulative and aggregate exposures, the TS continues to believe that it is prudent to use an HQ less than 1 for chemical effects whose dose-response relationship is known or assumed to be nonlinear (which generally consist of noncarcinogenic effects). Consideration of cumulative risk is required by the Texas Water Code Subchapter D Section 5.130. Consideration of cumulative and aggregate concerns is also consistent with empirical evidence such as ambient air monitoring data that demonstrate the presence of multiple chemicals in the air at the same time and the repeated presence of the same chemical(s) over time, as well as the fact that multiple sources of the same chemical can contribute to the concentration of that chemical at a single location. At the same time, the TS recognizes that the choice of a specific HQ less than 1 is a policy decision. TCEQ Regulatory Guidance 441 Section 1.4 Specific Risk Management Objectives (No Significant Risk Levels) states: "In consideration of cumulative and aggregate exposure, the Toxicology Section (TS) uses an HQ of 0.3 to calculate short-term and long-term ESLs for chemicals with a nonlinear dose-response assessment."

5. **The available data do not support an uncertainty factor database deficiencies in deriving the health-based chronic ReV and Chronic ESL for ethylene**

   TCEQ Response: The DSD was not revised based on this comment. The TS concurs with the TCC that ethylene is not toxic at high concentrations. However, the ESL Guidelines (TCEQ 2006) recommends the use of “medium database confidence” when chronic inhalation studies are limited to a single species. The available ethylene inhalation studies are limited only to rats. The TS, therefore recommends medium database confidence and attributes a database uncertainty factor of 3.0.

6. **TCEQ should use a hazard quotient of 1.0 in developing a health-based chronic ESL for ethylene**

   TCEQ Response: The DSD was not revised based on this comment. In order to develop ESLs for use in air permitting that adequately consider the potential for cumulative and aggregate exposures, the Toxicology Section continues to believe that it is prudent to use an HQ less than 1 for chemical effects whose dose-response relationship is known or

assumed to be nonlinear (which generally consist of noncarcinogenic effects). Consideration of cumulative risk is required by the Texas Water Code Subchapter D Section 5.130. Consideration of cumulative and aggregate concerns is also consistent with empirical evidence such as ambient air monitoring data that demonstrate the presence of multiple chemicals in the air at the same time and the repeated presence of the same chemical(s) over time, as well as the fact that multiple sources of the same chemical can contribute to the concentration of that chemical at a single location. At the same time, the TS recognizes that the choice of a specific HQ less than 1 is a policy decision. TCEQ Regulatory Guidance 441 Section 1.4 Specific Risk Management Objectives (No Significant Risk Levels) states: "In consideration of cumulative and aggregate exposure, the Toxicology Section (TS) uses an HQ of 0.3 to calculate short-term and long-term ESLs for chemicals with a nonlinear dose-response assessment."

APPENDIX 1

Texas Chemical Council (TCC)
Comments on TCEQ's Proposed Developmental Support Document for Ethylene dated January 2008

TEXAS CHEMICAL COUNCIL
1402 Nueces Street • Austin, Texas 78701-1586 • (512) 646-6400 • Fax (512) 646-6420

March 17, 2008

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

Re: Texas Chemical Council Comments Regarding the Ethylene Effects Screening Level Development Support Document

TCEQ Toxicology Section:

The Texas Chemical Council (TCC) submits these comments in response to the Texas Commission on Environmental Quality's (TCEQ) request for public comments on its Effects Screening Level (ESL) Development Support Document concerning ethylene.

The Texas Chemical Council is a statewide trade association representing approximately 85 chemical manufacturers at over 200 Texas facilities. Our industry has invested more than $50 billion in physical assets in the State and pays over $1 billion annually in state and local taxes. TCC's members provide approximately 70,000 direct jobs and over 500,000 indirect jobs to Texans across the State.

TCC appreciates the opportunity to comment on the ESL values for ethylene. TCC understands the importance of ESLs in providing TCEQ with guidance to protect human health and welfare regarding its authority for air permitting and air monitoring. Air quality is also important to the regulated community, particularly to members of TCC.

In general, TCC believes the Draft Development Support Document for ethylene is scientifically sound and demonstrates the diligence of TCEQ in developing supportable values. However, we do offer the following comments:

- In deriving the health-based acute ReV and acute ESL for ethylene, an uncertainty factor for database deficiencies (UF_D) is not justified based on the robust database for ethylene
- TCEQ should use a hazard quotient of 1.0 in developing an acute ESL for ethylene
- TCC agrees with TCEQ's selection of the Alberta Canada studies as the key studies for developing the ESL for vegetative effects for ethylene
- TCC agrees with TCEQ's selection of the study of Hamm et al. (1984) as the key study for developing a health-based chronic ReV and ESL for ethylene

- The available data do not support an uncertainty factor for database deficiencies (UF_D) in deriving the health-based chronic ReV and chronic ESL for ethylene
- TCEQ should use a hazard quotient of 1.0 in developing a health-based chronic ESL for ethylene
- TCEQ appropriately evaluated the carcinogenic potential for ethylene

By offering the following comments, TCC hopes to provide scientific perspectives to enhance the basis of the ESL values for ethylene.

Again, TCC appreciates the opportunity to comment on this important document and looks forward to future discussions with TCEQ.

Sincerely,

Michael McMullen
Director of Regulatory Affairs
Texas Chemical Council

Texas Chemical Council (TCC)

Comments on TCEQ's Proposed Developmental Support Document for Ethylene dated January 2008

In general, TCC believes the Proposed Development Support Document for Ethylene is scientifically sound and well presented. However, TCC believes that in some areas, TCEQ was overly conservative in its approach. TCC offers the comments below for TCEQ's consideration.

In Deriving the Health-Based Acute ReV and Acute ESL for Ethylene, an Uncertainty Factor for Database Deficiencies (UF_D) is Not Justified Based on the Robust Database for Ethylene

TCC agrees with TCEQ's choice of the Conolly et al. studies (Conolly et al., 1978; Conolly and Jaeger, 1977, 1979) as the key studies for developing an acute ESL and with the choice of 50,000 ppm as the point of departure. However, the choice of uncertainty factors is unnecessarily conservative and results in an acute ESL value of 150 ppm. This level is derived from a study in which there were no reported adverse effects at doses as high as 50,000 ppm from exposure to ethylene alone.

The use of an uncertainty factor of 3 for database limitations is not supported by the available evidence. Although there are only three acute toxicity studies for ethylene, the overall health effects database for ethylene is robust. Two additional studies, a 90-day study and a 2-year bioassay study, (Rhudy et al., 1978 and Hamm et al., 1984) showed no adverse effects following exposures up to 10,000 ppm ethylene for 90 days or 3,000 ppm for 2 years. In addition, there is a repeat dose reproductive and developmental effects screening study available (Corning Hazelton, 1997; published as an abstract by Aveyard and Collins, 1997) showing no adverse effects up to 5,000 ppm ethylene exposure for up to seven weeks. While these studies do not specifically address acute toxicity, the existence of this large database helps to illustrate that ethylene is not acutely toxic at relatively high exposure levels (10,000 ppm for 90 days, for example). Thus, based on these studies, TCC urges TCEQ to consider the confidence in its acute ReV as "high" rather than "medium" and use a database uncertainty factor of 1.0.

TCEQ may want to specifically cite the references for the three Conolly et al. publications in Section 3.1.1.2.1 (*e.g.*, Conolly and Jaeger, 1977 and 1979; Conolly et al., 1978), to better clarify which studies are noted as key studies. TCEQ may want to note that the liver enzyme data from Conolly et al. (1978) stems from exposure of PCB-pre-treated rats to 57,000 ppm ethylene, although the histopathology results reported in this publication are from exposure of PCB-pre-treated rats to 50,000 ppm ethylene.

In Section 3.1.2.1.3 TCC states erroneously that EPA conducted a repeat dose reproductive and developmental effects screening study on ethylene. In fact, the study was conducted by Aveyard and Collins (1997) and is described in the OECD dossier for ethylene (OECD SIDS, 1998). In addition, TCEQ incorrectly defined the acronym for OECD. OECD is the Organization for

Economic Co-operation and Development. OECD is not part of EPA, but is an international organization.

TCEQ Should Use a Hazard Quotient of 1.0 in Developing an Acute ESL for Ethylene

As stated in previous comments submitted to TCEQ, TCC continues to have strong reservations concerning the use of a hazard quotient (HQ) of less than 1.0 for noncarcinogenic effects for any purpose, including consideration of cumulative and aggregate exposures. In deriving the acute ReV for ethylene, TCC agrees with TCEQ's choice of uncertainty factors for potential species differences, and intraspecies variability. Health protective assumptions have been considered and built into the derivation of the acute ReV for ethylene, such that the available evidence does not support the need for additional factors for health protection. In the case of ethylene, there were no adverse effects reported following exposure to rats of 50,000 ppm for 4 hours; 10,000 ppm for 90 days; or 3,000 ppm for 2 years. These were the highest concentrations tested in each case. Based on consideration of all the data, it is, therefore, likely that a short-term (hourly average) ESL of 500 ppm to 1,500 ppm would be appropriate in regard to any potential acute effects of short-term ethylene exposures.

TCC Agrees with TCEQ's Selection of the Alberta Canada Studies as the Key Studies for Developing the ESL for Vegetative Effects

TCC agrees with TCEQ's conclusion that ethylene is a plant hormone and is necessary for the proper growth and development of plants and flowers. TCC also agrees with TCEQ in its selection of the Alberta Canada studies (Archambault et al., 2006; Archambault and Li, 1999a, 1999b, 2001) as the key studies for ESL development because it is a well-conducted series of studies on multiple crop species, including 3 plant categories (cereal, legumes and oilseeds), and 2 tree species. The study included multiple exposures and multiple exposure durations.

TCEQ used a no-effect level as the starting point for acute ReV derivation even though the guidelines suggest setting the acute ESL at a threshold concentration for adverse effects. Because of this choice, the acute ReV for ethylene is more conservative than envisioned by the guidelines and thus is expected to be adequately protective for all plant species.

TCC further supports TCEQ's choice not to select studies based on exposures to excised flowers, as these exposures do not properly reflect the exposure situation of concern, which is crops grown in the vicinity of facilities that might release ethylene.

TCC Agrees with TCEQ's Selection of the Study of Hamm et al. (1984) as the Key Study for Developing a Health-Based Chronic ReV and ESL for Ethylene

The Hamm et al. (1984) study is a well-conducted, comprehensive study in which rats were exposed to ethylene at concentrations up to 3,000 ppm, 5 days per week, for 2 years. There were no adverse findings in this study. TCC agrees with TCEQ's selection of the Rhudy et al. (1978) study as the supporting study. The Rhudy et al. (1978) study is a comprehensive study in which rats were exposed to ethylene at concentrations up to 10,000 ppm, 5 days per week, for 90 days. Again, there were no adverse findings in this study. TCC supports TCEQ's use of 3,000 ppm as the point of departure in determining the chronic ReV and ESL for ethylene. Although there was a higher no adverse effect level from the 90-day study (10,000 ppm), TCC believes it is appropriate to select the no adverse effect level from the 2-year study over the 90-day study for development of a health-based chronic ReV.

The Available Data Do Not Support an Uncertainty Factor for Database Deficiencies (UF_D) in Deriving the Health-Based Chronic ReV and Chronic ESL for Ethylene

TCC supports TCEQ's use of default duration and dosimetry adjustments to develop the POD_{ADJ}. However, in developing the chronic ReV, the available data do not support the need for a safety factor for database deficiencies. As stated previously, the data base for ethylene is robust, consisting of a 90-day rat toxicity study, a 2-year rat toxicity study and a repeat dose reproductive and developmental effects screening study. No adverse effects of ethylene exposure were reported in any of the three studies noted above. In addition, a number of genetic toxicology studies have been conducted for ethylene (Vergnes and Pritts, 1994; Walker et al., 2000) as well as a number of metabolism studies, including metabolism studies in humans (Bolt and Filser, 1983; Bolt et al., 1984; Csanady et al., 2000; Filser and Bolt, 1984). TCC urges TCEQ to consider the robust database that exists for ethylene, to reexamine their confidence based on the chronic database, and to consider the use of a UF_D of 1.0 in developing the health-based chronic ReV and ESL for ethylene.

TCEQ Should Use a Hazard Quotient of 1.0 in Developing a Health-Based Chronic ESL for Ethylene

As stated previously in these comments and in comments submitted by TCC on the draft guidelines, TCC continues to have strong reservations concerning the use of a hazard quotient (HQ) of less than 1.0 for noncarcinogenic effects for any purpose, including consideration of cumulative and aggregate exposures. In deriving the chronic ReV for ethylene, TCC agrees with TCEQ's use of uncertainty factors for potential species differences, and intraspecies variability. As noted above, the database for ethylene is robust. Health protective assumptions have been considered and built into the derivation of the chronic ReV for ethylene, and thus the weight of the evidence supports a HQ of 1.0 for the derivation of the chronic ESL for ethylene.

TCEQ Appropriately Evaluated the Carcinogenic Potential for Ethylene

TCC agrees with TCEQ's evaluation of the carcinogenic potential for ethylene being of negligible concern by recognizing that, although ethylene is metabolized to ethylene oxide, the percentage conversion is insignificant, being limited both by low uptake and saturation kinetics. The International Agency for Research on Cancer (IARC, 1994) classified ethylene as Group 3 or "not classifiable as to its carcinogenicity to humans." Similarly, in 2005, ACGIH designated ethylene as A4 or "Not Classifiable as a Human Carcinogen." In addition to the 2-year rat carcinogenicity study (Hamm et al., 1984), data has been generated to compare the effects of ethylene to ethylene oxide for two endpoints that are related to carcinogenicity; gene (point) mutations and chromosome breaks. Vergnes and Pritts (1994) exposed rats and mice to levels of ethylene up to 3,000 ppm for 4 weeks. No changes in micronucleus formation were seen between exposed and unexposed animals in these studies. Walker et al. (2000) evaluated splenic hprt mutations in animals from these same exposures and found no differences in hprt mutation between exposed and unexposed animals. The studies of Vergnes and Pritts (1994) and Walker et al. (2000) further support the lack of carcinogenic potential for ethylene.

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