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

The public comment period for the proposed Development Support Document (DSD) for isobutene ended in March 2008. The Texas Chemical Council (TCC) and ExxonMobil Refining & Supply Company submitted 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 isobutene. The goal of the Toxicology Section 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 and ExxonMobil comments are provided below, followed by TCEQ responses. The full comments of TCC and ExxonMobil are in Appendices 1 and 2, respectively. 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.

A new section entitled *Comparison of ^{acute}ESL to Generic ESL* was added to the DSD since the ESL Guidelines suggest that when a subacute study is used to derive the ^{acute}ESL, a comparison to a generic ESL should be made to determine whether the ^{acute}ESL based on the subacute study is too conservative.

Texas Chemical Council (TCC) Comments Regarding the Isobutene DSD

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

   Response: The DSD has been updated to reflect a UF_D of 1 and the database quality to high. The following information has been added to the DSD:

   > "A UF_D of 1 was used because toxicity data from a reproductive/developmental study in rats as well as a 14-week study and a chronic study investigating a wide range of endpoints is available in both rats and mice (NTP 1998). The free-standing NOAEL from each of these studies is 8,000 ppm and supports the acute study NOAEL. The confidence in the acute database is high."

2. **Comment:** TCEQ should consider a hazard quotient of 1.0 in developing an acute ESL for isobutene.

   Response: The DSD was not revised based on this comment. The TCEQ applied a total uncertainty factor of 30 to account for uncertainties in using animal data to predict the

human response and to account for variability of the human response. 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 442 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."

3. **Comment:** TCEQ should reconsider the appropriateness of using 50% odor detection thresholds in the development of ESLs. . . . Often the test methods and conditions are not reported in detail making it difficult to choose the most reliable value. In the case of isobutene, TCEQ references two 50% odor threshold values (3,000 and 22,900 ug/m^3) both of which meet the criteria for acceptable odor threshold measurement techniques developed by the American Industrial Hygiene Association and the USEPA. While both values meet "accepted criteria" they differ from one-another by nearly 8-fold. This difference clearly demonstrates the lack of precision involved in the estimation of odor threshold and thus the lack of reliability for using reported odor threshold values in the calculation of ESLs.

   Response: The DSD was not revised based on this comment. **I**sobutene's proposed odor-based ESL adheres to TCEQ's 2006 regulatory guidance document, *Guidelines to Develop Effects Screening Levels, Reference Values, and Unit Risk Factors* (RG-442), that underwent external scientific peer review and two rounds of public comment. Furthermore, development of isobutene's odor-based ESL included a comprehensive literature search, consideration of all available isobutene odor studies, and selection of the lowest 50% odor detection threshold among the approved studies that meet the American Industrial Hygiene Association and USEPA odor evaluation criteria. Isobutene's odor-based ESL is considered a useful tool in the air permit review process, and addresses the Commission's mandate to protect public welfare and public enjoyment of air resources.

4. **Comment:** TCC believes that, if TCEQ continues to rely on odor thresholds as a basis for ESLs, it is extremely important to indicate that these values are not based on anticipated health effects but rather simply represent a conservative estimate of a "nuisance" level.

Response: The DSD was not revised based on this comment. The fact that odor-based ESLs are not derived on anticipated health effects is clear in the DSD. ESLs, including odor-based ESLs, are intended to be guidelines and not strict standards. For example, when applying the odor-based ESL in an air permit application review, consideration of the nature of the odor, the surrounding land use, the frequency of odor-based ESL exceedance, and the odor complaint history at the site, all play a role in allowing off-site concentrations that exceed the odor-based ESL. Isobutene is odorous at a concentration much lower than the concentration which could cause an adverse health effect. Because of this, if the permit applicant's predicted or monitored isobutene concentrations are allowable from an odor perspective, they are allowable from a health perspective as well.

5. **Comment:** The available data do not support an uncertainty factor of greater than 3 to account for differences between animals and humans (UF_A) in deriving the health-based chronic ReV and chronic ESL for isobutene

   Response: The DSD has been changed based on a reevaluation of the UF_A. The $UF_A = 3$ and Section 3.1.5.2 *Default Dosimetry Adjustments from Animal-to-Human Exposure* has been updated so that isobutene is considered to be a category 3 gas (i.e., producing systemic effects). The reasons that TCC provided in their comments mainly pertained to the database quality for isobutene. However, TS staff reevaluated the animal-to-human dosimetric adjustment and updated this section to be consistent with information in the acute section.

6. **Comment:** TCEQ should consider a hazard quotient of 1.0 in developing a health-based chronic ESL for isobutene.

   Response: The DSD was not revised based on this comment. Refer to Response to comment #2.

ExxonMobil
Comments Regarding the Isobutene DSD

7. **Comment:** It is clear that the RG-442 guidelines were fully implemented as designed by the TERA group.

   Response: It is unclear what ExxonMobil meant by the reference to the TERA group, although this acronym is used by Toxicology Excellence for Risk Assessment. Although TERA organized the peer-review of the ESL Guidelines, the Toxicology Section wrote the guidelines.

8. **Comment:** ExxonMobil's general comment on the 5 DSD documents (list above) pertains to the development and/or application of the odor threshold value as the basis of

short-term ESL permit review values. . . ExxonMobil offers that the body of data and information surrounding the very important odor limit values are not very robust, and the primary documents from Katz and Talbert (1930's) with updates from Nagata (2002) should be investigated with more current and technically precise methods.

Response: The DSD was not revised based on this comment. If more current and technically precise methods are developed and used to evaluate 50% odor detection thresholds, the Toxicology Section will consider the updated odor studies. Please refer to Response to Comments # 3 and 4.

APPENDIX 1

Texas Chemical Council (TCC)
Comments on TCEQ's Proposed Developmental Support Document for Isobutene 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 Isobutene 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 isobutene.

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 isobutene. 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 isobutene is scientifically sound and demonstrates the diligence of TCEQ in developing supportable values. However, TCC believes that, based on the weight of the evidence, TCEQ was overly conservative on a few key scientific issues which affect the acute ReV and ESLs for isobutene. The attached document briefly discusses TCC's comments, as stated below:

- In deriving the health-based acute ReV and acute ESL for isobutene, an uncertainty factor for database deficiencies (UF_D) is not justified based on the robust database for isobutene
- TCEQ should consider a hazard quotient of 1.0 in developing an acute ESL for isobutene
- TCEQ should reconsider the appropriateness of using 50% odor detection thresholds in the development of ESLs

- TCC agrees with TCEQ's selection of the NTP (1998) studies as the key studies for developing a health-based chronic ReV and ESL for isobutene
- The available data do not support an uncertainty factor of greater than 3 to account for differences between animals and humans (UF_A) in deriving the health-based chronic ReV and chronic ESL for isobutene
- TCEQ should consider a hazard quotient of 1.0 in developing a health-based chronic ESL for isobutene

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

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 Isobutene dated January 2008

In general, TCC believes the Proposed Development Support Document for Isobutene 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 Isobutene, an Uncertainty Factor for Database Deficiencies (UF_D) is Not Justified Based on the Robust Database for Isobutene

TCC agrees with TCEQ's choice of the CTL (2002) and the NTP (1998) studies as the key studies for developing an acute ESL and with the choice of 8,000 ppm as the point of departure. However, the choice of uncertainty factors is unnecessarily conservative and results in an acute ReV value of 150 ppm. This level is derived from a study in which there were no reported adverse effects at doses as high as 8,000 ppm from exposure to isobutene.

The use of an uncertainty factor of 3 for database limitations is not supported by the available evidence. While there are only a few acute toxicity studies for isobutene, the overall health effects database for isobutene is robust. Four additional studies (NTP 1998), two 14-week studies (one each in rat and mouse) and two 2-year bioassay studies (one each in rat and mouse), showed no adverse effects following exposures up to 8,000 ppm isobutene for either 14 weeks or 2 years (*Hyaline degeneration in the respiratory and olfactory epithelia in rats and mice after two years exposure and slight weight loss in female mice in the second year of exposure were not considered adverse effects*). In addition, there is a prenatal developmental effects study available (CTL 2002) showing no adverse effects up to 8,000 ppm isobutene exposure on gestation days 5-16 (16 days). The existence of this large database helps to illustrate that isobutene is not acutely toxic at relatively high exposure levels (8,000 ppm for 14-weeks, for example). Thus, based on these studies, TCC urges TCEQ to consider the confidence in its acute ReV as "high" rather than "medium to high" and use a database uncertainty factor of 1.0.

TCEQ Should Consider a Hazard Quotient of 1.0 in Developing an Acute ESL for Isobutene

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 isobutene, TCEQ incorporates an uncertainty factor of 100. Health protective assumptions have been considered and built into the derivation of the acute ReV for isobutene, such that the available evidence does not support the need for additional factors for health protection. In the case of isobutene, exposure to rats and mice of 8,000 ppm, 6 hours per day, 5 days per week for a period of 14 weeks did not result in any significant adverse effects. Based

on consideration of all the data, it is, therefore, likely that a short-term (hourly average) ESL of 150 ppm (500 if one includes an UF of 30 rather than 100) would be appropriate in regard to any potential acute effects of short-term isobutene exposures.

TCEQ Should Reconsider the Appropriateness of Using 50% Odor Detection Thresholds in the Development of ESLs.

The TCC believes that it is inappropriate to use odor thresholds in the development of ESLs. Published odor thresholds for a given material can vary dramatically; in some cases by several orders of magnitude. This variability has been attributed to a number of factors including but not limited to reliance on different test methods, trained versus untrained test subjects or "sniffers," purity of the test sample, differences in test environment conditions such as temperature and humidity and human variability. Often the test methods and conditions are not reported in detail making it difficult to choose the most reliable value. In the case of isobutene, TCEQ references two 50% odor threshold values (3,000 and 22,900 ug/m^3) both of which meet the criteria for acceptable odor threshold measurement techniques developed by the American Industrial Hygiene Association and the USEPA. While both values meet "accepted criteria" they differ from one-another by nearly 8-fold. This difference clearly demonstrates the lack of precision involved in the estimation of odor threshold and thus the lack of reliability for using reported odor threshold values in the calculation of ESLs. Furthermore, simply relying on the lowest values without further justification is likely to result in an unnecessarily low and overly conservative ESL value. In summary, TCC believes that given the high variability of existing threshold values, and the apparent absence of a method capable of generating a reproducible result, TCEQ should not rely on odor thresholds in the development of ESLs for isobutene.

TCC believes that, if TCEQ continues to rely on odor thresholds as a basis for ESLs, it is extremely important to indicate that these values are not based on anticipated health effects but rather simply represent a conservative estimate of a "nuisance" level.

TCC Agrees with TCEQ's Selection of the NTP (1998) Studies as the Key Studies for Developing a Health-Based Chronic ReV and ESL for Isobutene

The NTP (1998) studies are well-conducted, comprehensive studies in which rats and mice were exposed to isobutene at concentrations up to 8,000 ppm, 5 days per week, for 2 years. There were no adverse findings in these studies (*Hyaline degeneration in the respiratory and olfactory epithelia in rats and mice after two years exposure and slight weight loss in female mice in the second year of exposure were not considered adverse effects*). TCC supports TCEQ's use of 7,960 ppm (analytical) as the point of departure in determining the chronic ReV and ESL for isobutene. The no adverse effect levels from the 14-week rat and mouse studies were also 8,000 ppm, the highest dose tested.

The Available Data Do Not Support an Uncertainty Factor of Greater than 3 to account for differences between animals and humans (UF_A) in Deriving the Health-Based Chronic ReV and Chronic ESL for Isobutene

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 greater than 3 to account for differences between animal and humans. As stated previously, the data base for isobutene is robust, consisting of two 14-week (rat and mouse) and two 2-year toxicity studies (rat and mouse) and a repeat dose developmental effects study. No adverse effects of isobutene exposure were reported in any of the studies noted above. In addition, a number of genetic toxicology studies have been conducted for isobutene, all of which appear to be negative (OECD 2004). Most importantly, reports of an association between chronic exposure (for example occupational exposure) to isobutene and adverse effects in humans are lacking (the lack of adverse effects in animal models likely explains the absence of reported effects in humans). TCC urges TCEQ to consider the robust database that exists for isobutene and the lack of reported adverse effects in humans and therefore to consider the use of a UF_A of 3.0 in developing the health-based chronic ReV and ESL for isobutene.

TCEQ Should Consider a Hazard Quotient of 1.0 in Developing a Health-Based Chronic ESL for Isobutene

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 isobutene, TCC agrees with TCEQ's use of uncertainty factors for potential species differences, and intraspecies variability. As noted above, the database for isobutene is robust. Health protective assumptions have been considered and built into the derivation of the chronic ReV for isobutene, and thus the weight of the evidence supports a HQ of 1.0 for the derivation of the chronic ESL for isobutene.

References

Central Toxicology Laboratory (CTL). 2002. Isobutylene: Prenatal Developmental Toxicity Study in the Rat. CTL/RR0907/Regulatory Report. Chelshire, UK.

National Toxicology Program (NTP). 1998. Toxicology and Carcinogenesis studies of isobutene (Cas No. 115-11-7) in F344/N rats and B6C3F1 mice (inhalation studies), Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Services, National Institutes of Health. NTP TR 487, NIH Publication No. 99-3977.

Organization for Economic Cooperation and Development (OCED). 2004 SIDS Initial Assessment Report for SIAM 19, Berlin Germany -19-22 October 2004.

Appendix B

ExxonMobil Comments on Proposed DSDs

From: <judy.m.bigon@exxonmobil.com>
To: <tox@tceq.state.tx.us>
Date: Mon, Mar 24, 2008 8:51 AM
Subject: ExxonMobil Comments on Proposed DSDs

ATTN: Dr. Michael Honeycutt and Roberta Grant

ExxonMobil Downstream & Chemical Safety Health and Environmental (SHE) submits comments on the latest list of Development Support Documents (DSD) for Effects Screening Level (ESL) development. The chemicals of interest to ExxonMobil are 1) Butene-1; 2) Butene-2; 3) Ethylene; 4) Isobutene; and 5) Toluene. Our understanding is the DSD is the summary document of available technical health and environmental information and the DSD's were developed according to RG-442 Guidelines to Develop Effects Screening Levels, Reference Values and Unit Risk Factors.

ExxonMobil congratulates the TCEQ on the thorough and complete preparation of these DSD's, and it is clear that the RG-442 guidelines were fully implemented as designed by the TERA group. The RG-442 guidelines appear to be a significant procedure that allows the TCEQ to craft a whole, complete technical dossier on individual chemicals in order to arrive at technically sound and defensible Effects Screening Levels that are protective of public health and welfare. ExxonMobil especially applauds the TCEQ on the open and transparent processes that were used to develop the DSD's, to include the public discussions that TCEQ staff offered for individual DSD review as well as data solicitation early in the process. ExxonMobil provided information and data to the TCEQ staff early in the process, and was engaged as one of the many stakeholders in the ESL development. We want to encourage TCEQ to continue this progressive and open scientific development process, guided by RG-442 and a cooperative spirit.

ExxonMobil's general comment on the 5 DSD documents (list above) pertains to the development and/or application of the odor threshold value as the basis of short-term ESL permit review values. We believe that the TCEQ has essentially done its best with respect to evaluation and implementation of an odor threshold value to describe the short-term ESL permit targets, and those targets are uniformly lower than both Acute and Chronic health values such that the public can and should feel confident that TCEQ ESL values are conservative in a manner to protect against human health effects. As well, the information with respect to odor thresholds used to develop these latest DSD's allowed a general relaxation of earlier (i.e., 2003) acute odor limit values, which had obviously been set using quite conservative values and techniques. ExxonMobil offers that the body of data and information surrounding the very important odor limit values are not very robust, and the primary documents from Katz and Talbert (1930's) with

updates from Nagata (2003) should be investigated with more current and technically precise methods. Since these odor values essentially take precedence over all the very sophisticated acute/chronic ReV's and URF's, the TCEQ should encourage the more complete and accurate development of these values in the future.

A specific comment on the proposed odor ESL value for toluene, the selection of the lowest value of the three studies (i.e., 170 ppb from Hellman, 1974) over more recent values and those chosen as the basis for other chemicals (i.e., 330 ppb from Nagata, 2003) is tenuous, however it is consistent with the RG-442 guidelines to use the lowest value from an appropriate study as you explain in the DSD for toluene. We feel that TCEQ will be challenged in areas such as this, for example with respect to the chronic ESL/ReV values for both 1-butene and 2-butene. TCEQ carefully followed the guidelines laid out by TERA in the 2006 RG-442 document, and properly chose to not establish the chronic ReV as the minimum data sets were not met.

ExxonMobil supports the values developed by TCEQ with respect to Acute and Chronic ESL values for health and welfare for the 5 chemicals listed above. ExxonMobil wants to reiterate the significant effort and collegial approach that TCEQ has employed in this latest set of DSD's. Overall, the current Acute and Chronic ESL proposed values were developed in a documented scientific manner, with clear and transparent methods, and include the maximum amount of actual published data and methods to interpret those data based on the publically reviewed and agreed upon approaches laid out in RG-442. ExxonMobil would very much like to continue to be included in these processes and offer our technical services whenever TCEQ and the public feel they are necessary.

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