Texas Commission on Environmental Quality (TCEQ) Response to Public Comments Received on the Proposed Development Support Document for Hydrogen Fluoride and Other Soluble Inorganic Fluorides October 8, 2009

The public comment period for the proposed Development Support Document (DSD) for hydrogen fluoride and other soluble inorganic fluorides ("HF") ended in July 2009. The American Chemistry Council's Hydrogen Fluoride Panel ("ACC") and Dydek Toxicology Consulting ("Dr. Dydek", on behalf of Acme Brick Company, Boral Bricks, Inc., Hanson Brick East, L.L.C., and American Marazzi Tile, Inc.) submitted comments. The Toxicology Division (TD) of the Texas Commission on Environmental Quality (TCEQ) appreciates the effort put forth by these commentators to provide technical comments on the proposed DSD for HF. 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 comments from each commentator is provided below, followed by TCEQ responses. The full comments are provided in Appendices. 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.

Upon further review, the TD has included the Lund et al. (2002) study as an additional key study, and developed the acute toxicity values. It turned out that the derived toxicity values are similar to those derived based on the Lund et al. (1999) study. The TD also agrees with ACC that the severity of plant injury by HF is related to both concentration and duration of exposure. As discussed in Section 3.2.2.2 of DSD, F injury to plants commonly results from gradual accumulation of F in the plant tissue over a period of time, so a longer averaging time, such as 24-hour (h) is more appropriate for the HF $^{acute}ESL_{veg}$. Therefore, the proposed 1-h $^{acute}ESL_{veg}$ has been deleted.

Dydek Toxicology Consulting ("Dr. Dydek")
Comments Regarding the TCEQ Development Support Document for HF ESL Values
(Appendix 1)

I. Derivation of a New Short-term ESL

Comment No. 1:
Dr. Dydek had concerns about the validity of using the Lund et al. (1999) study as the key study to derive the acute ReV and ESL. He indicated that while numbers of CD3-positive cells were significantly increased in the "intermediate" and "high" exposure group, the authors did not state whether there were statistically significant differences between the CD3-positive cell levels in the three exposure groups. Thus, it is not known if a true dose-response relationship was demonstrated. Dr. Dydek further commented that lymphocyte and neutrophil percentages in the

BAL fluid were significantly higher in the "intermediate" exposure group, however, no dose-response relationship was shown for these parameters.

TCEQ Response:

The TD appreciates Dr. Dydek's comments. However, the DSD was not revised based on these comments. While the Lund et al. (1999) study did not clearly demonstrate a dose-response relationship for the parameters examined in the BAL fluid, the study showed that the exposure of healthy subjects to HF in the " intermediate" (0.7-2.4 mg/m³) and the "high" (2.5-5.2 mg/m³) exposure groups can induce an inflammatory reaction in the airways 24 h after the exposure. Lund and colleagues concluded that the exposure of healthy subjects to HF concentrations above 0.6 mg/m³ may induce an inflammatory response in the airways 24 h after the exposure. The range of concentrations (0.2-0.6 mg/m³) has been considered a NOAEL by the Swedish National Institute for Working Life (NIWL 2005) while the American Governmental Industrial Hygienists Association (ACGIH 2005) considered 0.6 mg/m³ a NOAEL for airway inflammation. The TD's selection of a NOAEL of 0.6 mg/m³ identified from the 1999 Lund et al. study was further supported by the American Chemistry Council's Hydrogen Fluoride Panel ("ACC") (see Comment No. 14 below). ACC indicated that the Lund et al. (1999) study is consistent with other Lund et al. papers that have shown some mild irritation associated with exposures above 0.6 mg/m^3. ACC further pointed out that other agencies have also developed their toxicity values based on the Lund et al. (1999) study.

Comment No. 2:

Dr. Dydek stated that it was curious that no increase in neutrophil and macrophage percentages were seen in the Lund et al. (1999) study because neutrophil and macrophage usually show up in the greatest numbers at the site of injury. While Lund and colleagues explained that neutrophil numbers may have peaked at a much earlier time point and then gone back down 24 hours after HF exposure, Dr. Dydek indicated that the explanation was a somewhat speculative observation.

TCEQ Response:

The DSD was not revised based on this comment. The TD concurs with Lund and colleagues' explanation. Please also see Response to Comment No. 1 above.

Comment No. 3:

Dr. Dydek commented that the increased CD3-postitive cells seen in the 1999 Lund et al. study would definitely be sub-clinical effects. He further commented that since the study did not see significant increases in other inflammatory markers, the adaptive effect of inflammation was very mild. In addition, no mention was made of any symptoms the subjects might have reported in the 1999 study whereas the symptoms reported in human volunteers exposed to identical levels of HF were addressed in the 1997 Lund et al. study.

TCEQ Response:

The TD acknowledges that the increase in CD3-postitive cells was sub-clinical effects and the adaptive effect of inflammation was very mild. However, the DSD was not revised based on this comment. Please see Response to Comment No. 1 above.

Comment No. 4:

Dr. Dydek stated that according to TCEQ's guidelines to develop ESLs and US EPA guidance for establishing inhalation reference concentrations, a key study should be the one that "contributes most significantly" to the assessment of the human risk of exposure to a chemical.

Based on this and Comment No. 3 above, he indicated that the 1999 Lund et al. study should be considered more a Supporting Study than a Key Study.

TCEQ Response:

The DSD was not revised based on this comment. The TD believes that the selection of the Lund et al. (1999) study as key study is appropriate. Please see Response to Comment Nos. 1 above and 7 below.

Comment No. 5:

Dr. Dydek commented that the 1997 Lund et al. study would be a better choice for the Key Study. He indicated that while the exposure regime was the same as in the 1999 Lund et al. study, the health endpoints used in the 1997 study (frank upper and lower respiratory tract symptoms, eye irritation symptoms, and lung function measurements) are more pertinent to the assessment of human health risk embodied in an ESL determination.

TCEQ Response:

The TD agrees that the health endpoints used in the 1997 study are more pertinent to the assessment of human health risk embodied in an ESL determination. However, as indicated in Section 3.1.3.1.1 of the DSD, the TD concurs with the ACGIH and NIWL that the results of the Lund et al. (1997) study for (1) symptom scores from the eyes and upper and lower airways, (2) total symptom scores and (3) pulmonary function decrements failed to identify a reliable NOAEL or LOAEL. The total symptom scores were significantly increased in the "low" exposure group ($p=0.04$) and the "high" group ($p=0.02$), but not in the "intermediate" exposure group ($p=0.67$). There was no clear dose-response relationship for symptoms involving upper and lower airways, eye irritation, or total symptom scores. Additionally, significant reduction of FVC was seen in the low-exposure group, but not observed in the other groups. The pulmonary function decrements observed in the Lund et al. (1997) study did not show an evident dose-response relationship. NIWL further indicated that since there were few subjects in the Lund et al. (1997) study, and they were not given a null exposure to allow them to become accustomed to the exposure chamber, it is difficult to assess the effect of the lowest exposure. NIWL further indicated that the most probable LOAEL was estimated to be 0.7-2.4 HF/m³ and the 0.2-0.6 HF/m³ was the NOAEL (NIWL 2005). The estimated LOAEL for upper respiratory symptoms and/or lung function supported the LOAEL for airways inflammation identified from the Lund et al. (1999) study (see Section 3.1.2.1).

Comment No. 6:

Dr. Dydek indicated that the only statistically significant symptomatic changes seen in the Lund et al. (1997) study were increased upper airway symptoms in the "high" exposure group (2.5 to 5.2 mg/m^3). However, he indicated that total symptomatic changes were only seen in the "low" and "high" exposure groups; and that no dose-response relationship for actual symptoms experienced by the subjects could be shown. Dr. Dydek also indicated that changes in forced expiratory volume capacity (FVC) after exposure were only significant in the "low" exposure group and thus, no dose-response relationship for effects on FVC was found either.

TCEQ Response:

The DSD was not revised based on this comment. While the TD acknowledges that statistically significant increased upper airway score was only seen in the "high" exposure group, the same trend was found in the "low" ($p=0.06$) but not in the "intermediate" ($p=0.10$) exposure group. As indicated in the Response to Comment No. 5 above, there was no clear dose-response

relationship for symptoms involving upper and lower airways, eye irritation, or total symptom scores.

Comment No. 7:
Dr. Dydek commented that the results of a follow-up study by Lund et al. (2005) fail to replicate the findings in the 1999 Lund et al. study because no effects on lung function and no evidence of inflammation in the lung were observed in BAL fluid measurements taken 2 h after HF exposure. He indicated that the 2005 Lund et al. study showed evidence that the 1999 Lund et al. study may not be the best choice for the Key Study in the ESL determination process.
TCEQ Response:
The DSD was not revised based on this comment. The TD notices that the results of BAL fluid measurements taken 2 hours after HF exposure in the Lund et al. (2005) did not show effects on lung function and no evidence of inflammation in the lung. However, the TD does not agree with Dr. Dydek that the Lund et al. (2005) failed to replicate the findings in the 1999 Lund et al. study and that the 1999 Lund et al. study may not be the best choice for the Key Study in the ESL determination process.

While the results of the 2005 study were different from the 1999 study which demonstrated airway inflammation in healthy volunteers 24 h after exposure to HF (Section 3.1.3.1.2 of DSD), the unexpected findings of this study indicate that the development of inflammation following HF exposure follows different time courses in the nose (Lund et al. 2002) compared to that found in the lungs (Lund et al. 1999, 2005). Lund and colleagues suggested that because HF is very hydrophilic and will effectively be absorbed in the nasal epithelium and upper airways, the higher deposition of HF in the nasal region may account for some of the difference in mucosal response.

As indicated in Response to Comment Nos. 1, 5, 6, and 8, the TD concurs with other agencies that the Lund et al. (1999) study was a well-conducted acute inhalation study with an adequate number of healthy human subjects at 1-h exposure duration and demonstrated dose-related responses for airway inflammation. The key observation of the 1999 study was that significant increases in the percentage of CD3-positive cells (a marker of T-lymphocytes) were found in the *bronchial portion* of BAL fluid individually before and 24 h after exposure to HF in the "intermediate" and "high" exposure group ($p=0.03$), and in the bronchoalveolar portion in the "high" exposure group ($p=0.04$). The authors indicated that inflammatory responses seemed to be prominent in the more proximal airways due to the high water solubility of HF leading to a higher absorption rate with a concomitant cellular response. The results were further supported by the Lund et al. (2002) study which demonstrated nasal inflammatory and antioxidant responses in nasal lavage performed immediately after and 1.5 h after the end of a 1-h exposure to HF (3.3-3.9 mg/m^3). Because the observed critical effects, such as immediate inflammatory responses in nasal tissues, "contributed most significantly" to the assessment of the human health risk of exposure to HF, the Lund et al. (2002) study was chosen as another key study. Thus, the LOAEL of 3.3 mg HF/m^3 (4 ppm) (the highest concentration) for nasal inflammatory and antioxidant responses from Lund et al. (2002) was also used as the POD to develop the acute ReV and ESL (see Section 3.1.2.2 of DSD). It appears that the derived ReV and ESL based on the LOAEL from the Lund et al. (2002) study are consistent with those derived from the NOAEL identified in the 1999 Lund et al. study (see Section 3.1.7.1 of DSD).

In summary, the studies by Lund et al. (1997, 1999, 2002 and 2005) have shown that acute upper respiratory tract irritation and inflammation were the most prominent effects on human volunteers after 1-h exposure to HF. The TD believes that the Lund et al. (1999 and 2002) studies are the best choices for the key studies and the Lund et al. (1997 and 2005) are good supporting studies (see Section 3.1.2 and 3.1.3 of DSD, for details).

Comment No. 8:
Dr. Dydek commented that based on Comment No. 7 above, a NOAEL of from 0.7 to 2.4 mg/m^3 and a LOAEL of from 2.5 to 5.2 mg/m^3 from the Lund et al. (1997) study are reasonable choices for a point of departure (POD) to be used in the determination of a short-term ESL for HF. He further commented that this was the conclusion reached by California EPA when they set an acute reference exposure limit (REL) for HF. Dr. Dydek indicated that California EPA did not use the data from the 1999 Lund et al. study in their acute REL.

TCEQ Response:
The DSD was not revised based on this comment. While the NOAEL and LOAEL from the Lund et al. (1997) study are appropriate for the critical effects of upper respiratory tract membrane irritation, as indicated in Response to Comment Nos. 5 and 6, the TD does not agree that the NOAEL and LOAEL are a reasonable choice for a POD to be used in the determination of a short-term ESL for HF. The TD believes that the use of a NOAEL for upper airway score as a POD without considering results observed in other Lund et al. (1997, 1999 and 2002) studies may not be protective against acute HF toxicity. For example, Lund and colleagues observed the following:

- significant increases in concentration of F in plasma were observed in the "intermediate" and "high" exposure group;
- that the exposure of healthy subjects to HF concentrations above 0.6 mg/m^3 may induce an inflammatory response in the airways 24 h after the exposure (Lund et al. 1999);
- and that exposure to HF (3.3-3.9 mg/m^3) induced immediate nasal inflammatory responses (Lund et al. 2002).

As indicated in Comment No. 14 below, the range of concentrations (0.2-0.6 mg/m^3) based on the Lund et al. (1999) study have been considered a NOAEL to develop their acute toxicity values by agencies such as the NIWL (NIWL 2005), ACGIH (ACGIH 2005), National Academy of Science (NAC) acute exposure guideline level (AEGL) (NAC 2004), and American Industrial Hygiene Association (AIHA) emergency response planning guideline (ERPG). The midpoint of the range of concentrations (0.2-0.6 mg/m^3) has also been considered a LOAEL based on the Lund et al (1997) study by the Agency for Toxic Substances and Disease Registry (ATSDR 2003) to develop its acute minimal risk level (MRL). Please also see Response to Comment No. 7 above.

Dr. Dydek commented that California EPA used the NOAEL and LOAEL from the Lund et al. (1997) study and did not use the data from the 1999 Lund et al. study to set its acute REL for HF. However, the Lund et al. (1999) study might not have been available to California EPA when it published the acute REL in March 1999 (OEHHA 1999). Hopefully, an updated acute REL will be developed by California EPA in the near future.

Comment No. 9:
Dr. Dydek proposed using the midpoint of the NOAEL of 0.7 to 2.4 mg/m^3 from the 1997 Lund et al. study, 1.55 mg/m^3, as the POD for an acute ESL determination. He explained that while he suggested that the Lund et al. (1999) study be used as a Supporting Study, since some mild, sub-clinical effects were seen in the "intermediate' exposure group, it would be defensible to use a measure of conservatism in using the NOAEL from the Lund et al. (1997) study.

TCEQ Response:
The DSD was not revised based on this comment. Please see Response to Comment Nos. 1, 5, 6, 7, and 8 above.

Comment No. 10:
Dr. Dydek further indicated that the choice of the NOAEL of 1.55 mg/m^3 for the POD was supported by the results of another human study which found a NOAEL of 1.18 mg/m^3 (Largent 1961). Dr. Dydek stated that Lund and co-investigators also did two follow-up studies (Lund et al. 2002 and 2005) using greater HF exposure levels (3.3 to 3.9 mg/m^3) than their earlier work. The Lund et al. (2002) found inflammatory responses in nasal tissues 1.5 h after 1-h exposure. The Lund et al. (2005) did not find evidence of lung inflammation 2 h after 1-h exposure.

TCEQ Response:
The DSD was not revised based on this comment. Please see Response to Comment No. 7 above.

Comment No. 11:
By using the NOAEL of 1.55 mg/m^3 as a POD and dividing it by an uncertainty factor of 10 which accounts for intra-human variability, Dr. Dydek proposed a ReV of 155 µg/m^3 and an ESL of 46.5 µg/m^3 for HF.

TCEQ Response:
The DSD was not revised based on this recommendation. Please see Response to Comment Nos. 1, 5, 6, 7, and 8.

II. Derivation of a New Long-term ESL

Comment No. 12:
Dr. Dydek agreed that the choices made in the determination of a new long-term ESL for HF seem to be appropriate.

TCEQ Response:
The TD appreciates Dr. Dydek's agreement with the agency's proposed long-term ReV and ESL values for HF.

III. Summary and Conclusions

Comment No. 13:
Dr. Dydek commented that, based his analysis; a more scientifically supported choice for the Key Study in the derivation of a short-term ESL for HF would be that of Lund et al. (1997) rather than that of Lund et al. (1999). The latter study would be better used as a Supporting Study. Accordingly, he recommended that the TD uses a short-term ESL of 46.5 µg/m^3 for HF rather than the 18 µg/m^3 value which was proposed by the TD.

TCEQ Response:
The TD appreciates Dr. Dydek's recommendation for the derivation of the above short-term proposed ESL. However, the DSD was not revised based on this recommendation. Please see Response to Comment Nos. 1, 5, 6, 7, 8, and 9 above.

American Chemistry Council's Hydrogen Fluoride Panel ("ACC")
Comments Regarding the TCEQ Development Support Document for HF ESL Values
(Appendix 2)

I. Acute ReV and ^{acute}ESL [1 hr]

Comment No. 14:
The ACC stated that it agrees with the selection of the Lund et al. (1999) study as the key study for the acute toxicity study. It indicated that the results of the key study have shown a clear dose-response relationship on transitory effects of respiratory tract irritation and inflammation in healthy human volunteers exposed to three different exposure levels of HF. ACC further indicated that the Lund et al. (1999) study is consistent with other Lund et al. papers that have shown some mild irritation associated with exposures above 0.6 mg/m^3. ACC pointed out that the recently revised ACGIH threshold limit value (TLV), NAC AEGL and AIHA ERPG, were also based on the data from Lund et al. (1999).
TCEQ Response:
The TD appreciates ACC's comments and agreement with the agency's selection of the Lund et al. (1999) study as the key study for the development of acute toxicity values for HF. The TD also appreciates ACC's acknowledgment that other agencies have also developed their toxicity values based on the Lund et al. (1999) study.

Comment No. 15:
While the ACC agrees with the use of the NOAEL of 0.6 mg/m^3 as a POD to set TCEQ's acute toxicity values for HF, it considers the uncertainty factor (UF) of 10 for intra-human variation unnecessary. ACC argues that the NOAEL of 0.6 mgHF/m^3 is similar to the ACGIH TLV of 0.5 ppm (0.41 mgF/m^3) for HF. It indicated that other studies have shown no effect on respiratory parameters in healthy adults at concentrations up to 7.8 ppm or in healthy but atopic individuals at concentrations up to 6.3 ppm (5.2 mg/m^3) (Lund et al. 1997 and 1999). ACC further argued that data in the literature have shown atopic individuals to be no more sensitive to the irritation of HF than their healthy counterparts so an additional safety factor for those with asthma is not necessary. ACC commented that as described by TCEQ methods, a hazard quotient (HQ) of 0.3 should be used for the development of the Acute ESL to protect the general population. It indicated that the HQ value of 0.3 should be sufficient to protect the general population including sensitive subpopulations such as children, elderly, and people with pre-existing health conditions.
TCEQ Response:
The TD appreciates ACC's agreement with the agency's use of the NOAEL of 0.6 mg/m^3 as a POD to set TCEQ's acute toxicity values for HF. However, the TD disagrees with ACC's comment that it was not necessary to apply an UF of 10 to the POD for intra-human variation because the NOAEL is similar to the ACGIH TLV of 0.5 ppm (0.41 mgF/m^3) for HF. Both the

Lund et al. (1997 and 1997) studies were conducted in healthy but *not* atopic, nonsmoking men, aged 21-44 years. Therefore, in order to protect the general population including sensitive subpopulations, it is necessary to add an UF of 10 to a POD identified from healthy human subjects. The application of a UF of 10 to account for intra-human variation is commonly accepted in developing toxicity values such as US EPA reference concentration (RfC), California EPA REL, ATSDR MRL, NAC AEGL, or TCEQ ReV. As indicated by ACC, other agencies have also developed their toxicity values based on the Lund et al. (1999) study. However, except for ACGIH, all other agencies, have applied a UF of 10 to the aforementioned NOAEL when developing acute toxicity values for HF. Since the ACGIH TLV for HF was set to protect against the potential for respiratory tract effects in workers, it may not be necessary to apply an additional UF to a NOAEL identified from studies conducted in the healthy human subjects to protect workers. But the toxicity values developed by other agencies, including the TCEQ, are to protect the general public so it is necessary to apply an additional UF of 10 for intra-human variation.

The TD does not agree with ACC that a HQ of 0.3 should be used to develop the acute ESL. The use of a HQ of 0.3 is a policy decision to account for cumulative and aggregate impacts. A policy-based HQ is different than use of UFs to develop a ReV. According to the 2006 TCEQ ESL Guidelines, a ReV is derived by adjusting a selected POD with appropriate UFs to protect the most sensitive individuals in a population. ReVs are the health-based toxicity values used in the evaluation of ambient air monitoring data. However, ESLs are primarily used as guideline concentrations, *not* ambient standards, for the review of predicted maximum off-property ground level concentrations ($GLCs_{max}$) in the air permitting process. In order to account for the potential cumulative and aggregate impacts in an area where multiple permitted sources may be emitted simultaneously and different chemicals are emitted simultaneously, chemical-specific ESLs are derived from ReVs by applying a HQ value of 0.3. The TD believes it may not be sufficient to protect the general public to derive an acute ESL for HF just by applying a HQ of 0.3 to a POD.

II. $^{acute}ESL_{veg}$ [1 hr]

Comment No. 16:
The ACC commented that it is more appropriate to have the vegetation ESL values dependent on the time of year (i.e., growing season) than to have the same value year round. It further commented that it seems overly conservative to base the $^{acute}ESL_{veg}$ [1 hr] on the lowest LOEL following 2 h exposure because the severity of plant injury is related to both concentration and duration of exposure. ACC urged that TCEQ limit this value for use in agricultural areas where susceptible plants are grown (alfalfa, barley, and soybeans) and also consider whether the value should be used only during growing seasons rather than year round.

TCEQ Response:
The TD agrees that no adjustment for the exposure duration from 2-h to 1-h is conservative. The TD also agrees with ACC that the severity of plant injury is related to both concentration and duration of exposure. Upon further review, as indicated in Section 3.2.2.2 of DSD, F injury to plants commonly results from gradual accumulation of F in the plant tissue over a period of time, so a longer averaging time, such as 24-h, would be more appropriate for setting the HF ^{acute} ESL_{veg}. Therefore, the proposed 1-h ^{acute} ESL_{veg} has been deleted. The 24-h HF ^{acute} ESL_{veg} is the only acute vegetation-based ESL for HF.

The TD acknowledges ACC's suggestion to limit the use of the $^{acute}ESL_{veg}$ for sensitive species during the growing season. The HF vegetation ESLs are used for air permit evaluations limited to facilities located in agricultural areas where the most sensitive plant species may be impacted. However, the suggestion to limit the use of the $^{acute}ESL_{veg}$ only during the growing season may not be practical for air permit reviews. ESLs are primarily used as guideline concentrations, *not* ambient standards, for the review of predicted maximum off-property ground level concentrations ($GLCs_{max}$). If the predicted GLC_{max} for a chemical exceeds the respective ESL, adverse effects would not necessarily be expected to result, but a more in-depth case-by-case review would be conducted follow the air permitting effects evaluation procedure. When an impacts review is conducted, the TD will evaluate whether or not any sensitive species (alfalfa, barley, and soybeans) are grown in the surrounding area where $GLCs_{max}$ are predicted to occur during the growing season. Higher predicted impacts for HF may be considered allowable if there are no sensitive plant species grown in an agricultural area. The TD believes that the case-by-case impacts review process is flexible and protective. Therefore, it is not necessary to limit the use of the $^{acute}ESL_{veg}$ only during the growing season.

III. $^{acute}ESL_{veg}$ [24 hr]

Comment No. 17:

The ACC commented that the $^{acute}ESL_{veg}$ [24 hr] is based on the threshold level of trace foliar injury leaf necrosis in conifers. However, conifers are not a feed crop and the effects observed are mild. TCEQ should consider using the lowest calculated no observed effect concentrations (NOEC) of 0.76 mg/m3 for all plant species, including sensitive species following a one hour exposure as reported in the European Union's risk assessment report on HF. ACC suggested that the NOEC be considered for the setting the $^{acute}ESL_{veg}$ [24 hr] rather than the studies summarized by McCune (1963).

TCEQ Response:

While the TD acknowledges the ACC's suggestion that the NOEC be considered for the setting the 24-h $^{acute}ESL_{veg}$, the DSD was not revised. According to the 2006 TCEQ ESL guidelines, vegetation-based ESLs are set at the lowest threshold concentration for adverse effects that won't significantly affect species survival or plant yield (TCEQ 2006). Furthermore, based on available data on vegetation effects, the TD believes that the NOEC of 0.76 mg/m^3 for setting the 24-h $^{acute}ESL_{veg}$ as suggested by ACC may not be protective for sensitive plant species (see Section 3.2 of DSD). Therefore, the 24-h $^{acute}ESL_{veg}$ for HF and soluble F was set based on the lowest observed effects level (LOEL) of 3.0 $\mu g/m^3$ (3.7 ppb) for a 24-h averaging time for foliar injury on conifers reported by McCune (1969a, 1969b). The 24-h $^{acute}ESL_{veg}$ is consistent with the secondary standards set by some other states (Table 6 of DSD). While the TD acknowledges that the 24-h $^{acute}ESL_{veg}$ is conservative, as indicated in Response to Comment No. 16 above, when impacts reviews are conducted in the air permitting process, the TD will evaluate whether or not any sensitive species are grown in the surrounding area where $GLCs_{max}$ are predicted to occur during growing seasons. Higher predicted impacts for HF may be considered allowable if there are no sensitive plant species grown in an agricultural area.

IV. $^{chronic}ESL_{veg}$

Comment No. 18:
ACC commented that the proposed $^{chronic}ESL_{veg}$, which was based on the most sensitive lowest LOEL of the most sensitive of 10 plant species, is conservative. It suggested that the $^{chronic}ESL_{veg}$ be based on the individual specific sensitive species rather than all species and consideration be given for having different limits during the growing season.
TCEQ Response:
The DSD was not revised based on this suggestion. See Response to Comment No. 16 above,

V. $^{chronic}ESL_{cattle}$ [30 days]

Comment No. 19:
The ACC stated that it agreed the Bunce regression equation is more appropriate because the data were derived from longer term studies than those described by Van der Erden. However, it commented that the Bunce regression analysis which was conducted using some data from laboratory and/or controlled field conditions may lead to unrealistically high HF concentration exposure. ACC stated that the amount of fluoride in forage is highly variable and can vary as much as 10 fold from season to season. Therefore, the approach used by the TCEQ seems overly conservative. ACC recommend that TCEQ consider removing the $^{chronic}ESL_{cattle}$ [30 days] value and replace it with the National Academy of Science (NAS) annual average tolerance level of 40 ppm fluoride in forage.
TCEQ Response:
The DSD was not revised based on this comment. The TD does not agree with ACC's comment that the use of the Bunce regression analysis to derive the $^{chronic}ESL_{cattle}$ is overly conservative. The TD believes that the size of data collected from laboratory or controlled field conditions, as well as field measurements in industrial areas, was sufficient to develop a regression equation which adequately expressed the relationship between fluorides in air and in grass. The TD disagrees with ACC's recommendation to consider removing the ^{chronic}ESLcattle [30 days] value and replace it with the NAS tolerance level of 40 ppm fluoride in forage. As indicated in Response to Comment No. 16 above, ESLs are primarily used as guideline concentrations, *not* ambient standards, for the review of predicted $GLCs_{max}$ in air permitting process. It is not possible for the TD to conduct the effects evaluation of cattle fluorosis based on the level of fluoride in forage because most facilities are not even constructed before permits are authorized. Therefore, the $^{chronic}ESL_{cattle}$ is required for the evaluation of potential for cattle F poisoning in agricultural areas. However, the suggested annual average tolerance level of 40 ppm fluoride in forage, which has been adopted as regulatory standard in several states, may be used for post-permit enforcement.

VI. $^{chronic}ESL_{nonlinear(nc)}$ and Chronic ReV

Comment No. 20:
ACC commented that the results of the key study (Derryberry et al.1963) showed only 17 of 74 workers with questionable or minimally increased bone density (Grade 1 Fluorosis). These data were analyzed by California's OEHHA but showed no apparent threshold based on the logistic regression. These data were then grouped into quintiles by OEHHA to calculate the NOAEL,

LOAEL, and $BMCL_{05}$. ACC indicated that this amount of data manipulation is not appropriate for a study where the maximum effect observed was only grade 1 fluorosis. It further indicated that while TCEQ considered increased bone density a severe effect, grade 1 fluorosis does not result in medically recognized dysfunction. ACC stated that the toxicity of HF and fluorides has been extensively reviewed by several expert panels (ATSDR, ACGIH, WHO). These groups did not consider the available data, including the Derryberry study, of sufficient quality to be used to derive a chronic inhalation exposure values. ACC commented that there are not sufficient data available to calculate a chronic health ESL value for fluorides and suggested that TCEQ consider removing the proposed $^{chronic}ESL_{nonlinear(nc)}$.

TCEQ Response:

While the TD may not necessarily agree with the comments, the TD does appreciate ACC's comments. The TD noticed the maximum effect observed in 17 of 74 workers in the Derryberry et al. 1963 study was grade 1 fluorosis. However, according to the TCEQ ESL Guidelines, the use of benchmark concentration (BMC) as a POD is a better approach over the NOAEL/LOAEL approach (TCEQ 2006). Nevertheless, upon further review, considering the maximum effect observed in the Derryberry et al. 1963 study was grade 1 fluorosis (i.e., the severity of response is considered minimal to low), the TD has modified the level of the benchmark response (BMR) from 5% to 10%. Therefore, the corresponding $BMCL_{10}$ of 0.756 mg F/m^3, instead of $BMCL_{05}$ 0.374 mg F/m^3, was used as a POD to develop the chronic ReV and $^{chronic}ESL_{nonlinear(nc)}$. The final chronic ReV and $^{chronic}ESL_{nonlinear(nc)}$ are higher than the proposed ones (see Section 4.1.5 of DSD).

APPENDIX 1

Dydek Toxicology Consulting ("Dr. Dydek")
Comments Regarding the TCEQ Development Support Document for HF ESL Values

Dydek Toxicology Consulting

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Chemical Toxicology and Engineering | Expert Witness Testimony | Risk Assessment and Health Effects Evaluations

June 15, 2009

Dr. Jong-Song Lee
Toxicology Division
Mail Code 168
Texas Commission on Environmental Quality
Post Office Box 13087
Austin, Texas 78711-3087

Re: Comments on Draft Development Support Document (DSD)
Effects Screening Levels for Hydrogen Fluoride

Dear Dr. Lee:

I am hereby submitting comments on the proposed new ESLs for hydrogen fluoride on behalf of Acme Brick Company; Boral Bricks, Inc.; Hanson Brick East, L.L.C.; and American Marazzi Tile, Inc. I have put these comments in the form of a report that is attached to this letter.

If you have any questions on this, please feel free to contact me.

Sincerely,

Thomas Dydek

Dr. Thomas Dydek, Ph.D., D.A.B.T., P.E.
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Enclosures

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Comments on the TCEQ Draft Development Support Document for Hydrogen Fluoride

A. Derivation of a New Short-term ESL

1. The Key Study chose in the draft DSD was that of Lund, et al. (1999). I have some concerns about the validity of using that work as the Key Study in the evaluation of a new short-term ESL for HF. In the Lund, et al. study, human volunteers were exposed to three different ranges of hydrogen fluoride in the air (less than 0.6 mg/ m^3, 0.7 to 2.4 mg/ m^3, and 2.5 to 5.2 mg/ m^3) for a one-hour time period. Bronchoalveolar lavage (BAL) was performed for each subject three weeks before and 24 hours after exposures began.

Markers of inflammatory response such as CD3 positive T-cells, lymphocytes, macrophages, and neutrophils were measured in the BAL fluid taken pre- and post-exposure. Numbers of CD3 positive T-cells were significantly increased in both the intermediate and highest exposure level groups. The paper by Lund, et al. did not state whether there were statistically significant differences between the CD3+ cell levels in the three exposure level groups, however. Thus it is not known if a true dose-response relationship was demonstrated. Normally, that would be noted by the investigators if it did exist.

Lymphocyte and neutrophil percentages in the BAL fluid were significantly higher post-exposure only in the intermediate HF exposure level group. No dose-response relationship was shown for these parameters. The percentage of macrophages in the BAL fluid was actually lower post-exposure to HF in the study subjects.

2. To assess the significance of these results, it is instructive to consider some basic toxicological aspects of inflammation. A recent review of this topic (Medzhitov, 2008) clearly states that inflammation is an adaptive effect. Its function is to "allow the host to adapt to the abnormal conditions and, ultimately, to restore functionality and homeostasis to the tissue". Chronic inflammation is, on the other hand, a condition that can lead to frank tissue injury. The short-term ESL, however, considers only acute exposures and chronic inflammation is not an issue.

In general, the main contributors to inflammatory responses are macrophages, neutrophils, and T-cells. Neutrophils usually show up first and in the greatest numbers at the site of injury (Kaminski, et al., 2008). It is curious that no increase in neutrophil percentage was seen in the 1999 study by Lund, et al. This may be, as the authors point out starting on page 331 of their article, that neutrophil numbers may have peaked and then have gone back down before the post-exposure bronchoalveolar lavage was performed 24 hours after the start of the HF exposures. The same idea could explain the absence of an increase in

the amounts of macrophages post-exposure. While these explanations are possible, this is a somewhat speculative observation.

3. In any case, the increased CD3+ T-cells seen in the 1999 Lund, et al. study would definitely be a sub-clinical effect. Furthermore, Lund did not see significant increases in other inflammatory markers, indicating the even the adaptive effect of inflammation was very mild under the exposure conditions in that study. No mention was made of any symptoms the subjects might have reported in the 1999 study. The symptoms reported in human volunteers exposed to identical levels of HF exposure were addressed in an earlier study by the same group of investigators (Lund, et al., 1997).

4. According to TCEQ's guidance document for developing ESLs (TCEQ, 2006) and U.S. Environmental Protection Agency guidance for establishing Inhalation Reference Concentrations (EPA, 1994), a Key Study should be the one that "contributes most significantly" to the assessment of the human health risk of exposure to a chemical. Supporting studies contain information that is "useful for providing insight and support for conclusions". Based on these definitions, it seems that the Lund, et al. 1999 study should be considered more as a Supporting Study than a Key Study.

5. It is my opinion that the earlier study by Lund and colleagues (Lund, et al., 1997) would be a better choice for the Key Study for the determination of a short-term ESL for hydrogen fluoride. While the exposure regimen was the same as in the 1999 work, the health endpoints used in the 1997 study (frank upper and lower respiratory tract symptoms, eye irritation symptoms, and lung function measurements) are more pertinent to the assessment of human health risk embodied in an ESL determination.

6. In the Lund, et al. study from 1997, the only statistically significant symptomatic changes seen upon HF exposure were increased upper airway symptoms in the subjects exposed to the highest HF level (2.5 to 5.2 mg/m^3). Even when symptom scores were totaled up to provide greater statistical power, effects were only seen in the lowest and the highest exposure levels, not in the intermediate exposure level. Thus no dose-response relationship for actual symptoms experienced by the subjects could be shown. No changes were seen in forced expiratory volume for one second (FEV_1) after HF exposure. Changes in forced ventilatory capacity (FVC) after exposure were only significant in the subjects in the lowest exposure level, not at the intermediate or the highest HF levels. Thus, no dose-response relationship was found for effects on FVC either.

7. In a follow-up study by the same investigators (Lund, et al., 2005), human volunteers were exposed to between 3.3 to 3.9 mg/m^3 of HF for one hour. No evidence of inflammation in the lung was found when BAL contents measurements were taken two hours after the cessation of exposure. No effects on the lung function of the study subjects were seen either. These results fail to

replicate the findings in the Lund, et al., 1999 study. This is further evidence that the 1999 study may not be the best choice for the Key Study in the ESL determination process.

8. Based on this information, a NOAEL of from 0.7 to 2.4 mg/m^3 and a LOAEL of from 2.5 to 5.2 mg/m^3 from the Lund, et al. 1997 study are reasonable as possible choices for a Point of Departure to be used in the determination of a short-term ESL for HF. This was the conclusion reached by the California Environmental Protection Agency when they set an Acute Reference Exposure Limit (AREL) for HF. They did not use the data from the Lund, et al. 1999 study in their AREL determination (Cal EPA, 2008).

9. If the Lund, et al. 1999 study were used instead as a Supporting Study, data from that work could be used to "provide insight" into the choice of a Point of Departure. Since some mild, subclinical effects were seen in the intermediate exposure group, this would imply the need for some measure of conservatism in using the NOAEL from the Lund, et al. 1997 study. Accordingly, I propose using the midpoint of that exposure range, 1.55 mg/m^3, as the POD for this ESL determination.

10. Support for this choice for the POD can be found in the results of another human exposure study which found a NOAEL of 1.18 mg/m^3 for HF (Largent, 1961). Lund and co-investigators also did two follow-up studies of hydrogen fluoride exposure (Lund, et al., 2002; Lund, et al., 2005). Both of these studies used greater HF exposure levels (3.3 to 3.9 mg/m^3) than their earlier work. One of these studies found inflammatory responses in nasal tissues at the end of and 1.5 hours after cessation of exposures (Lund, et al., 2002). The other study, as mentioned above, did not find evidence of lung inflammation even at these higher HF exposure levels.

11. I agree with the conclusion reached in the draft DSD for HF that it is appropriate to use only one uncertainty factor, intraspecies variability, in this analysis. Using 1.55 mg/m^3 as a Point of Departure and dividing it by 10 yields a Reference Value (ReV) of 0.155 mg/m^3 or 155 µg/m^3. Applying a Hazard Quotient of 0.3, this would result in a short-term health-based ESL of 46.5 µg/m^3.

B. Derivation of a New Long-term ESL

The choices made in the determination of a new long-term ESL for HF seem to be appropriate and thus I have no concerns or further comments on this aspect of the draft DSD.

C. Summary and Conclusions

This analysis has shown that a more scientifically supported choice for the Key Study in the derivation of a short-term ESL for hydrogen fluoride would be that of Lund, et al. (1997) rather than that of Lund, et al. (1999). The latter study would better be used as a Supporting Study in my opinion. Using the Point of Departure from the 1997 study yields to a proposed short-term ESL of 46.5 $\mu g/m^3$ rather than the 18 $\mu g/m^3$ value found in the draft DSD. I am in agreement with the agency's choice for a long-term ESL (4.1 $\mu g/m^3$).

We urge the agency staff to consider these comments and their rationale in their deliberations concerning the setting of a new short-term ESL for hydrogen fluoride. Thank you for the opportunity to make these comments.

Respectfully submitted,

Thomas Dydek

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June 15, 2009

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APPENDIX 2

American Chemistry Council's Hydrogen Fluoride Panel ("ACC") Comments Regarding the TCEQ Development Support Document for HF ESL Values

July 9, 2009

Via email at Tox@tceq.state.tx.us

Texas Commission on Environmental Quality
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RE: Comments on the Effects Screening Level Development Support Document for Hydrogen Fluoride

Dear Sir or Madam:

On behalf of the American Chemistry Council's Hydrogen Fluoride Panel[1] (Panel), these comments are submitted in response to the Texas Commission on Environmental Quality's (TCEQ) request for public comments on its Effects Screening Level (ESL) Development Support Document (DSD) concerning hydrogen fluoride (HF).

In summary, while we agree with the selection for the acute toxicity study identified as the key study, we consider the uncertainty factor to be excessive based on the available data. For the chronic ESL, we do not believe there are any studies that are of sufficient quality to be used as the basis for the chronic ESL. The study identified by TCEQ as the key study was not sufficiently robust for the data manipulation that was conducted in order to derive the chronic ESL. For the vegetative ESL values, we suggest TCEQ consider the vegetative limits be based on the sensitive species rather than all species and consideration be given for having different limits during the growing season. Below are our comments on the specific values noted in Table 1.

Table 1: Health and Welfare-Based Values

Short-Term Values	Concentration	Notes	ACC recommendation
^{Acute} ESL[1hr] (HQ=0.3)	18 µg HF/m^3 (22 ppb) or 17 µg F/m^3 **Short term ESL for Air Permit Reviews**	Critical Effect: upper respiratory tract and eye irritation; respiratory tract inflammation in human volunteers	Revise based on Acute ReV below ^{Acute} ESL[1hr] = 180 µg HF/m^3
Acute ReV (HQ=1)	60 µg HF/m^3 (73 ppm) or 57 µg F/m^3		Remove uncertainty factor of 10 Acute ReV = 600 ug HF/m^3
^{Acute} ESL_{veg} [1hr]	12 µg HF/m^3 (15	Threshold value for	Consider values for species

[1] The members of the Hydrogen Fluoride Panel are Arkema, Inc.; Daikin America, Inc.; DuPont; Honeywell; Mexichem Fluor; and Solvay Fluorides LLC.

	ppb) or 11 µg F/m^3 **Short-term ESL for air permit reviews in agricultural areas**	trace of leaf necrosis in Alfalfa and Barley	and growing season rather than generic short term ESL
$^{Acute}ESL_{veg}$ [24hr]	3.0 µg HF/m^3 (3.7 ppb) or 2.8 µg HF/m^3 **Short-term ESL for air permit reviews in agricultural areas**	Threshold level for a trace of foliar injury/leaf necrosis in Conifers	Consider permit reviews based on species grown and season rather than generic short term ESL
$^{Chronic}ESL_{nonlinear(NC)}$	4.1 µg HF/m^3 (5 ppb) or 3.9 µg HF/m^3 **Long term ESL for Air Permit Reviews**	Critical effect: Increased bone density and skeletal fluorosis in workers	Remove - Data insufficient to derive chronic $ESL_{nonlinear(NC)}$ value.
Chronic REV	14 µg HF/m^3 (17 ppb) or 3.9 µg F/m^3		Remove - Data insufficient to derive chronic REV value.
$^{Chronic}ESL_{linear}$		Data inadequate	
$^{Chronic}ESL_{cattle}$ [30 days]	0.75 µg HF/m^3 (0.91 ppb) or 0.71 µg F/m^3	Critical Effect: fluoride poisoning, dental lesions, osseous lesions, lameness and stiffness in cattle and other livestock	Data inconsistent. Replace $^{Chronic}ESL_{cattle}$ air value with the National Academy of Science annual average tolerance level of 40 ppm fluoride in forage
$^{Chronic}ESL_{veg}$	0.60µg HF/m^3 (0.73 ppb) or 0.57 µg F/m^3 **Long-term ESL for air permit reviews in agricultural areas**	Threshold level for decrease in yield of bean, decrease in number of fruit per pot, dry weight of stems and leaves, and stem length of soybean	Consider permit reviews based on species grown and season rather than generic long term ESL

Acute REV and ^{Acute} ESL[1hr]

The acute REV and ^{Acute} ESL[1hr] limits are based on the 1999 Lund paper. In the Lund study, bronchoalveolar lavage fluid analyses combined with bronchoscopy were conducted as indicators for lower respiratory tract irritation. In this study, 19 healthy, nonsmoking, men were exposed for 1 hour to $\leq$0.6 mg/m^3, 0.7-2.4 mg/m^3, or 2.5-5.2 mg/m^3 of HF. There was a significant increase in the number of CD3 cells in the two higher exposure level groups but not in the group exposed to $\leq$0.6 mg/m^3. There was also a clear difference between the intermediate and high level exposure groups. Two hours after the end of the exposure changes in some protein levels were seen. By 24-hours post-exposure most had returned to normal indicating that these changes were transitory. This study is consistent with other papers that have shown some mild irritation associated with exposures above 0.6 mg/m^3. Given the sensitivity of the parameters measured, the effects appear to be mild especially for the 0.7 to 2.4 mg/m^3 exposure level group. There did not appear to be any significant effects associated with exposures below 0.6 mg/m^3. The recently revised ACGIH threshold limit value (TLV), acute exposure guideline level (AEGL) and American Industrial Hygiene Association (AIHA) Emergency Response Planning Guideline (ERPG), were also based on the data from Lund (1999). We agree that this should be the critical paper for the derivation of the acute values. However, an uncertainty factor of 10 is not necessary. The NOAEL value of 0.6 mg/m3 in the study is similar to the recently revised ACGIH threshold limit value of 0.5 ppm (0.535 mgF/m3) for HF. Irritation is not dependent on duration of exposure. Therefore the values do not have to be scaled for extended exposure times. An additional uncertainty factor for pre-existing conditions is unnecessary. Other studies have shown no effect on respiratory parameters in healthy adults at concentrations up to 7.8 ppm or in healthy but atopic individuals at concentrations up to 6.3 ppm (Lund 1997, 1999).

As described by TCEQ methods, a hazard quotient of 0.3 should be used for the development of the ^{Acute} ESL[1hr] to protect the general population including sensitive subpopulations such as children, elderly, and people with pre-existing health conditions. The HQ value of 0.3 should be sufficient to protect these populations. As noted above, data in the literature have shown atopic individuals to be no more sensitive to the irritation of HF than their healthy counterparts so an additional safety factor for those with asthma is not necessary.

^{Acute} ESL$_{veg}$ [1hr]

Fluoride uptake in plants is predominately from aerial deposition on plant surfaces. As noted in the TCEQ documentation, there is much variation in susceptibility of plants to fluoride toxicity. For the vegetation ESL values, it is more appropriate to have values dependent on the time of year (*i.e.*, growing season) than to have the same value year round. Most of the data on fluoride's toxicity to plants is from fumigation studies that were conducted many years ago. The fumigation systems used do not represent realistic exposure scenarios. The amount of fluoride in the air will be dependent on atmospheric conditions. HF is highly water soluble and will be incorporated into rain thereby reducing the amount of HF in the air. As noted in the TCEQ report, the severity of plant injury is related to both concentration and duration of exposure. Therefore, it seems overly conservative to base the ^{Acute} ESL$_{veg}$ [1hr] on the lowest LOEL

following 2 hour exposure. Rather than use the $^{Acute}ESL_{veg}$ [1hr] for the short term ESL review for agricultural areas, we urge you to limit this value for use in agricultural areas where susceptible plants are grown (alfalfa, barley, soybeans) and also consider the value be used only during growing seasons rather than year round.

$^{Acute}ESL_{veg}$ [24hr]

The $^{Acute}ESL_{veg}$ [24hr] is based on the threshold level of trace foliar injury leaf necrosis in conifers. Conifers are not a feed crop and the effects observed are mild. TCEQ should consider using the data published in the European Union's risk assessment report on hydrogen fluoride. As noted in the report, the studies evaluating the effects of fluoride on vegetation were fumigation studies. Sloof *et al*., 1988 evaluated the available data and derived a relationship between the no-effect concentration and exposure times. The German authorities also derived a calculation to estimate the no observed effect concentrations (NOEC) for plants. The European risk assessment included the calculated NOEC for all plant species over different exposure times using both models. Interestingly, the data were similar. The lowest calculated NOEC for all plant species, including sensitive species following a one our exposure was 0.76 mg/m^3. These data should be considered for the setting the $^{Acute}ESL_{veg}$ [24hr] rather than the studies summarized by McCune (1963).

$^{Chronic}ESL_{veg}$

TCEQ based the proposed $^{Chronic}ESL_{veg}$ on the most sensitive lowest observed effect level (LOEL) of the most sensitive of 10 plant species as reported by Pack and Sulzbach (1976). These were fumigation studies. As noted in Table 8 of the TCEQ's documentation, the toxicity varies depending on the species tested. We suggest the $^{Chronic}ESL_{veg}$ be based on the individual specific sensitive species rather than all species and consideration be given for having different limits during the growing season.

$^{Chronic}ESL_{cattle}$ [30 days]

As noted in section 4.3.2.4, the relationships between F in air and in the forage have been described in several studies but the relationships described have not been consistent. We agree the Bunce regression equation is more appropriate because the data were derived from longer term studies than those described by Van der Erden. The Bunce regression analysis was conducted using some data from laboratory and/or controlled field conditions. As noted above, laboratory and controlled conditions may lead to unrealistically high HF concentration exposure. As noted by the NRC, the amount of fluoride in forage in areas prone to air pollution is highly variable and can vary as much as 10 fold from season to season. In general, when forage is growing quickly such as in the summer, the amount of fluoride accumulated is less compared to later in the fall or during a drought (NRC 1971). As noted in the vegetation section above, the main process by which the fluoride content in grass decreases is by dilution by plant growth but additional decreases can occur due to desorption and death. In addition, rain can cause a rapid fall in the fluoride content of grass (Sloof *et al*., 1989). Based on all these events, the approach used by TECQ seems overly conservative. Therefore, we recommend TCEQ consider removing the $^{Chronic}ESL_{cattle}$ [30 days] value and replace it with the National Academy of Science annual average tolerance level of 40 ppm fluoride in forage.

$^{Chronic}ESL_{nonlinear(NC)}$ and Chronic REV

TCEQ set the $^{Chronic}ESL_{nonlinear(NC)}$ based on the skeletal fluorosis observed is workers as reported by Derryberry *et al.*, (1963). The data used by TCEQ was taken from California's chronic toxicity summary of fluorides including hydrogen fluoride (2003). This study evaluated the health effects of 74 male workers in a fertilizer manufacturing plant. Only 17 of 74 workers showed questionable or minimally increased bone density. The data collected included bone density, years exposed, maximum and minimum urine F concentration, age and F concentration in the air (average time weighted average). These data as analyzed by California's OEHHA showed a statistically significant relationship between mean air fluoride concentrations and bone density. A threshold was not apparent based on the logistic regression so OEHHA grouped the data into quintiles. Based on this analysis, a no-observed effect level (NOEL) of 1.07 mg/m^3 was calculated. The lowest observe effect level (LOAEL) was calculated to be 1.89 mg/m^3. The data were also evaluated using EPA's BMDS software. This amount of data manipulation is not appropriate for a study where the maximum effect observed was grade 1 fluorosis (minimally increased bone density). While TCEQ considered this to be a severe effect because it was in bones, ACGIH did not consider these data in the development of the TLV for HF because "grade 1 fluorosis does not result in medically recognized dysfunction" (ACGIH, 2005). The authors of the original paper reported "radiologist has stated that none of the radiographs showed sufficient increase in bone density to be recognized as such in routine radiological practice. In this study, therefore, the term "increased bone density" refers to questionable or minimal changes recognized with prior knowledge that the individual had a potential fluoride exposure" (Derryberry *et al.*, 1963). The toxicity of HF and fluorides has been extensively reviewed by several expert panels (ATSDR, ACGIH, WHO). These groups did not consider the available data, including the Derryberry study, of sufficient quality to be used to derive a chronic inhalation exposure values. We agree with these groups that there are not sufficient data available to calculate a chronic health ESL value for fluorides and suggest TCEQ consider removing the $^{Chronic}ESL_{nonlinear(NC)}$.

We appreciate the opportunity to comment on this important document and look forward to future discussions with TCEQ. If further information is needed with respect to these comments, please feel free to contact me at (703) 741-5614 or via email at Kristy_Morrison@americanchemistry.com.

Sincerely,

Kristy L. Morrison

Kristy L. Morrison
Manager, Hydrogen Fluoride Panel
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Cc: Mike McMullen, Texas Chemical Council

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