MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Acetic Acid (CAS # 64-19-7)

FROM: Keisha Williams, Air Quality Division

DATE: December 28, 2016

SUBJECT: Screening Level Review for Acetic Acid

The initial threshold screening level (ITSL) for acetic acid is 1,200 µg/m^3 (1-hour averaging time). The ITSL was previously 250 µg/m^3 (8-hour averaging time).established on July 14, 1992 and based on the Michigan Department of Environmental Quality, Air Quality Division (AQD) Rule 336.1229 (2) (a) and 336.1232 (1) (c) and (2) (a) (MDNR, 1992) (see attachment).

The following references or databases were searched to identify data to determine the screening level: United States Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS), the Registry of Toxic Effects of Chemical Substances (RTECS), the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLV), National Institute of Occupational Safety and Health (NIOSH) Pocket Guide to Hazardous Chemicals, MDEQ Library, International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) Online (1993- September 2014), National Library of Medicine (NLM), Health Effects Assessment Summary Tables (HEAST), National Toxicology Program (NTP) Status Report, EPA Aggregated Computational Toxicology Resource (ACToR) Database, EPA TSCATS database, EPA Superfund Provisional Peer Reviewed Toxicity Values, EPA Acute Exposure Guideline Levels for Airborne Chemicals, EPA High Production Volume Database, United States Department of Labor Occupational Safety and Health Administration Permissible Exposure Limits, Spacecraft Maximum Allowable Concentrations, California Office of Environmental Health Hazard Assessments Reference Exposure Levels, Chemical Safety Program Protective Action Criteria, Texas Commission on Environmental Quality Effects Screening Levels, and European Chemicals Agency Registered Substances Dossiers.

Background Information

Acetic acid (Figure 1.), also known as ethanoic acid, is used to produce plastics and pharmaceuticals, to generate other chemicals, and for food production. It is a colorless, flammable liquid with a pungent odor. Chemical properties are listed in Table 1.

Figure 1. Chemical structure for acetic acid

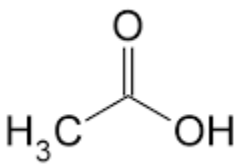

Table 1. Chemical properties of acetic acid

- Molecular weight: 60.05 grams/mole
- Melting point: 16.6 °C
- Boiling point: 117.9 °C
- Vapor pressure: 11 mmHg at 20°C
- Vapor density: 2.07, where air=1

Reference: PubChem database, https://pubchem.ncbi.nlm.nih.gov/compound/176

The American Conference of Industrial Hygienists (ACGIH) has established a Threshold Limit Value (TLV) at 25 mg/m^3, for an 8-hour averaging time (ACGIH, 2004). This value has also been adopted by the National Institute for Occupational Safety and Health, and the Occupational Safety and Health Administration. The Texas Commission on Environmental Quality (TCEQ) has established an interim health effects screening level at 25 µg/m^3 for long-term exposure (TCEQ, 2014).

Evaluation of Cancer Risk

No long-term carcinogenicity studies have been performed by the National Toxicology Program (NTP). Mutagenicity tests with *Salmonella typhimurium* were found to be negative (NTP, 2015). An oral rat study showed that 3% acetic acid alone did not produce an increase in tumors (benign or malignant) (Alexandrov, 1989). However, when given along with a known carcinogen, N-nitrosarcosin ethyl ester (NSEE), there was a significant increase in esophageal carcinomas as compared to NSEE given alone. Thus, this study suggests that acetic acid is a promoter of a cancer causing agent. However, given alone, acetic acid has not been shown to be a carcinogen.

Review of relevant studies

Research previously used to derive the ITSL

In 1992, the screening level was derived from the TLV-TWA to protect against the critical effects of sensory irritation and decreased pulmonary function. The TLV, 25 mg/m^3 (8-hour averaging time) is based on occupational exposure reports as well as controlled animal studies.
Using AQD Rule 336.1232 (1) (c), the screening level was derived as follows:

$$ITSL = \frac{OEL}{100}$$

$$ITSL = \frac{25\frac{mg}{m^3}}{100}\ x\left(10^3\ \frac{\mu g}{mg}\right) = \frac{250\ \mu g}{m^3}$$

Controlled human studies

The TLV, which was established in 1948 and last revisited in 2004, does not take into account two controlled human studies performed in 2005 and 2006. As compared to the case studies and occupational reports used to derive the TLV, controlled human studies are designed to better characterize chemical toxicity. So, the 2005 and 2006 studies are considered here for use in the ITSL derivation.

Shusterman et al. study (2005)

A controlled, human study was performed to determine if acetic acid induced more nasal airflow obstruction in individuals with seasonal rhinitis (N=8) as compared to individuals without seasonal rhinitis (N=8). The average age was 39.5 years old (ranging from 21-63 years), and there were 8 men and 8 women. Nasal airflow obstruction was measured as increased nasal airway resistance (NAR) using a commercially available rhinomanometer. Analysis of variance was used to determine if individuals with seasonal rhinitis had increased acetic acid-induced NAR as compared to individuals without seasonal rhinitis. Each person was exposed to 15 ppm (~36.8 mg/m^3) acetic acid for 15 minutes. The response was measured immediately as well as 15 minutes after exposure. Researchers found that individuals with seasonal rhinitis did have significantly increased nasal resistance as compared to individuals without rhinitis. As this is only a 15 minute study and did not sufficiently describe a dose-response relationship, it was deemed inadequate for use as the key study for ITSL derivation. However, as is assumed with the intraspecies uncertainty factor used for ITSL derivation, this study gives evidence that some groups (specifically those with seasonal rhinitis) are more susceptible to adverse effects from acetic acid exposure.

Ernstgård et al. study (2006)

In this human inhalation study, researchers show nasal irritation after 2 hours of exposure to 10 ppm (~24.6 mg/m^3) acetic acid, but not 5 ppm (~12.3 mg/m^3) acetic acid. Five men and six women ranging from 21 to 41 years of age were exposed to 0, 5 and 10 ppm for two hours. The volunteers reported their symptoms using the 0-100 mm visual analogue scale to answer 10 questions regarding symptoms like discomfort, feeling of intoxication, and smell. Ratings were collected one time before the exposure, three times during the exposure, and two times following the exposure. Pulmonary function measurements for vital capacity, forced vital capacity, forced expiratory volume in one second (FEV1), peak expiratory flow, and forced expiratory flow in 25%, 50% and 75% of forced vital capacity were collected before, immediately after, and three hours after exposure. Nasal swelling, measured by acoustic rhinometry, was also measured before, immediately after, and three hours after exposure. Eye blinking was measured during the exposure via electromyography. Blood was collected before and three hours after the exposure to analyze for inflammatory markers: C-reactive protein and interleukin-6.

Odor detection was the most sensitive response, followed by FEV1/ vital capacity and FEV1 itself. However, FEV1 /vital capacity showed the largest increase, indicative of improved lung function, with the 5 ppm exposure. With the same test, there was a decrease for the 0 and 10 ppm exposed groups. Furthermore, FEV1 showed the largest change in the control group with a 2.1 percent decrease. “Discomfort in the nose” after 118 minutes at the 10 ppm exposure concentration was found to be the only other exposure-related significant adverse effect. Therefore, “discomfort in the nose” was taken as the critical effect, where the no adverse effect level (NOAEL) was 5ppm.

Limitations to this study are the relatively small sample size and inclusion of only healthy individuals. As a result, these results may not be a good representation of health effects that would occur in sensitive populations.

Considering the AQD screening level development rules, a potential acute SL derived from this study would be calculated:

$$Potential\ ITSL = \frac{NOAEL}{Uncertainty\ factors}$$

where uncertainty factor for intraspecies differences would be 10.

$$Potential\ ITSL = \frac{5\ ppm}{10}$$

where 5 ppm is 12,280 µg/m^3 when using the conversion factor for air:

$$concentration\ in\ \frac{\mu g}{m^3} = \frac{5\ ppm\ \frac{10^3 ppb}{ppm} x\ molecular\ weight_{acetic\ acid}}{24.45}$$

$$concentration\ in\ \frac{\mu g}{m^3} = \frac{5\ ppm\ \frac{10^3 ppb}{ppm} x\ 60.05\ \frac{grams}{mole}}{24.45} = 12,280.16 \frac{\mu g}{m^3}$$

$$Potential\ ITSL = \frac{12,280.16 \frac{\mu g}{m^3}}{10} = 1,228.016\ \frac{\mu g}{m^3} \approx 1{,}200\ \frac{\mu g}{m^3}$$

Thus, the potential ITSL would be 1,200 µg/m^3, 1-hour averaging time.

When considering whether the TLV-derived ITSL or the Ernstgård et al. study-derived ITSL is more appropriate, both would make defensible acute ITSLs. The Ernstgård et al. study reports a NOAEL of 5 ppm that is consistent with the data used to generate the TLV which is "based on older human studies indicating that exposures less than 10 ppm were relatively nonirritating." However, the TLV is primarily derived from case reports and epidemiological studies. Neither the controlled human study nor the occupational exposure limit are inclusive of sensitive populations, and the TLV derivation document for acetic acid notes, "…unacclimatized individuals have experienced eye irritation at concentrations below 10 ppm." However, the method for ITSL derivation for both includes an uncertainty factor for sensitive populations. With this in mind, the ITSL derived from the controlled human study is both supported by previous studies and is the best available study from which to derive an ITSL. As a result, the ITSL will be 1,200 µg/m^3 with a 1-hour averaging time.

References

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Michigan Department of Natural Resources

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Interoffice Communication

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July 14, 1992

To: Acetic Acid File (CAS# 64-19-7)

From: Gary Butterfield

Subject: ITSL for Acetic Acid

The ACGIH TLV for acetic acid is 25 mg/m^3.

Based on the July 1992 Interim Process for Developing Screening Levels, the ITSL for this material is based on one percent of the ACGIH TLV. Under the Interim Process, the ITSL will continue to be based on 1% of the TLV if there is no EPA RfC, there is no EPA RfD or it is not appropriate to convert the RfD to an ITSL, the TLV is based on data other than acute exposure data, the TLV is based on health effects information, and the TLV is not included on the list of TLV's intended to be updated.

Therefore the ITSL is calculated by:

ITSL= 0.01 x (25 mg/m^3) = 250 $\mu g/m^3$ with an 8 hour averaging tim