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July 7, 2017

Response to Public Comments for
Methyl Mercaptan (CAS # 74-93-1)

Summary:

Based on public comments, the Air Quality Division (AQD) has reviewed the Initial Threshold Screening Level (ITSL) for methyl mercaptan. As a result of that review, the AQD does not agree with the commenter. The ITSL of 10 µg/m^3 was calculated using Rule 232(1)(c) and continues to be appropriate and defensible to protect public health as an AQD screening level. The available animal toxicity data do not appear to be sufficiently robust to support a more appropriate and defensible ITSL. Therefore, the ITSL is 10 µg/m^3 (1-hour averaging time).

Background:

Revisions to the Air Pollution Control Rules[1] were promulgated December 22, 2016. Subsequently, the Michigan Department of Environmental Quality (MDEQ), Air Quality Division (AQD) published toxic air contaminant screening levels and their basis as required by Rule 230(1). Pursuant to Rule 230(2), the AQD solicited and received public comments on these screening levels for 60 days: February 14 through April 14, 2017. The AQD must respond to these comments within 180 days; the latest date for response is October 11, 2017.

[1] Air Pollution Control Rules in Michigan Administrative Code promulgated pursuant to Article II Pollution Control, Part 55 (Sections 324.5501-324.5542), Air Pollution Control, of the Natural Resources And Environmental Protection Act, 1994.PA 451, as amended (NREPA).

Comments and Responses:

Comment:

One commenter provided comments on the methyl mercaptan (CAS # 74-93-1) Initial Threshold Screening Level (ITSL), which is set at 10 µg/m^3 with a 1-hour averaging time. The commenter requested that the ITSL should be set at 200 µg/m^3 with a 1-hour averaging time. The commenter discussed a 3-month rat inhalation study with an identified NOAEL of 17 ppm (33.5 mg/m^3). Though no citation was provided for this study, it is assumed based on the NOAEL that the commenter is referring to the Tansy et al. (1981) study. The commenter stated that an ITSL of 200 µg/m^3 (1-hour averaging time) would be more than 1,000 times below the LOAEL of 250 ppm in rats from an acute rat inhalation study (as cited in NRC (2008). The commenter suggested that the current ITSL of 10 µg/m^3 (1-hour averaging time) may be based on the odor threshold for methyl mercaptan. The commenter listed four references:

1. ATSDR, 2014, Addendum to The Toxicological Profile for Methyl Mercaptan, https://www.atsdr.cdc.gov/toxprofiles/methyl_mercaptan_addendum.pdf
2. NIOSH, https://www.osha.gov/dts/chemicalsampling/data/CH_254300.html
3. NRC 2008, Acute Exposure Guideline Levels for Selected Airborne Chemicals: Volume 15, https://www.nap.edu/read/18449/chapter/6#47
4. RTECS: https://www.cdc.gov/niosh-rtecs/pb42c1d8.html

Response:

The AQD's Toxics Unit staff have reviewed the basis for the initial threshold screening level (ITSL) for methyl mercaptan (CAS # 74-93-1), which was originally set in 1995 at 10 µg/m^3 (1-hour averaging time). The ITSL was based on the National Institute for Occupational Safety and Health (NIOSH) (1978) recommended exposure limit (REL) of 0.5 ppm (1 mg/m^3) (15-minute ceiling level) to be protective against acute irritant effects, which appears to be the most sensitive endpoint caused by inhalation of methyl mercaptan.

NIOSH RELs are generally designed to prevent significant toxic effects from occupational exposure for healthy workers during an 8- to 10-hour work shift. NIOSH (1978) derived a 15-minute ceiling level for exposure from methyl mercaptan to protect workers so no worker would be exposed to a higher level for any 15-minute work period. The ITSL is derived to protect all individuals including sensitive subgroups in a population, such as asthmatics, children, and the elderly, from levels of methyl mercaptan that could cause any adverse health effects. A ceiling level applies to 15-minute periods; however, ITSLs such as this one that are based on a ceiling level are applied with a 1-hour averaging time because of dispersion modeling limitations. Rule 232(1)(c) directs that ITSLs may be based on an occupational exposure level (OEL) divided by 100, as was done for methyl mercaptan. The rationale for the 100-fold adjustment is to help ensure protection of the general public, including sensitive

subgroups, from any adverse health effects even with potentially repeated exposures attributable to permitted air emissions.

The commenter suggested that the ITSL may have been based on the odor threshold. The ITSL is not based on an odor threshold, which is listed in the methyl mercaptan screening level justification document as ranging from 0.02 to 2.0 µg/m^3.

The acute toxicity table, provided by the commenter, shows the acute inhalation toxicity in rats (2 rats per dose group) exposed to methyl mercaptan. The table shows a concentration-response relationship for methyl mercaptan (lethality in rats was 0% at 500 ppm exposed for 4 hours and 100% for rats exposed to 750 ppm and higher concentrations for less than 4 hours). This table is also included in the United States Environmental Protection Agency's National Research Council (NRC, 2013) evaluation of Acute Exposure Guideline Levels (AEGLs) for methyl mercaptan. An "AEGL-1 is the airborne concentration (expressed as ppm [parts per million] or mg/m^3 [milligrams per cubic meter]) of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic non-sensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure" (NRC, 2013). The NRC evaluated all available data on methyl mercaptan and determined that no AEGL-1 value could be derived. The data in the table from the comment was evaluated and included in the determination of an AEGL-3 of 130 mg/m^3 (1-hour exposure). An AEGL-3 is "the airborne concentration (expressed as ppm or mg/m^3) of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening adverse health effects or death" (NRC, 2013). The MDEQ does not use AEGL-3 values in developing ITSLs.

NIOSH (1978) evaluated the n-alkane mono thiols, including cyclohexanethiol, together as a class of compounds to determine a recommended exposure limit for most of the aliphatic thiols. Multiple studies were evaluated and led to establishing the NIOSH REL for aliphatic thiols at 0.5 ppm (1 mg/m^3).

NIOSH (1978) noted a subchronic inhalation study on rats by Selyuzhitskii (1972) who exposed rats to methyl mercaptan. White rats (15 per dose group) were exposed to methyl mercaptan at concentrations of 0.51, 0.05, or 0.003 ppm (1.0 mg/m^3, 0.1 mg/m^3, or 0.0005 mg/m^3) 6 hours/day for 6 months. Rats exposed to 1.0 mg/m^3 methyl mercaptan:

> "…exhibited a reduced growth rate, an increase in the ratio of heart weight to body weight and changes in the distribution of corticosteroids in adrenal tissue. Electroencephalographic (EEC) recordings from rats exposed 6 hours/day for 6 months showed that these animals perceived a concentration of methanethiol of 0.5 µg/m^3, but were not distressed by it; a concentration of 5 µg/m^3 (0.005 mg/m^3) reportedly caused desynchroni-zation of the EEG, persistent disturbance of breathing, and irregular heart-beats. A concentration of 0.1 mg/m^3 caused a number of alterations in the

> biochemistry of the rats, including increased concentrations of carbon dioxide, sulfhydryl (-SH) groups, cholesterol, and lactic and pyruvic acids in the blood. A concentration of 1 mg/m^3 decreased the rate of growth of the rats, increased the relative weight of the heart, and altered the distribution of corticosteroids in adrenal tissues" (NIOSH, 1978).

The Selyuzhitskii (1972) study is in Russian and an English translation is not available for our review.

NIOSH found that there was no definitive study that allows a derivation of a dose-effect relationship for thiols in humans or in animals:

> The minimal effects of olfactory fatigue and mucosal irritation observed when individuals were exposed to 4 ppm (10 mg/m^3) ethanethiol ceased when the inhalation exposure was stopped, and no effects were observed at 0.4 ppm (1 mg/m^3) exposure. Because there is no evidence that adherence to the threshold limit value (TLV) of 0.5 ppm has resulted in any cases of toxicity, NIOSH recommends that the concentration of C_1-C_{12}, C_{16}, C_{18} alkane thiols or cyclohexanethiol, or any combination of these thiols, in the workplace air should not exceed 0.5 ppm as a ceiling concentration for any 15-minute period. Since the toxic action of thiols, on short-term exposure, is expressed largely by reversible mucosal irritation, a ceiling concentration limit is deemed more appropriate than a time weighted average (TWA) concentration limit. The use of a ceiling concentration instead of a TWA has the effect of increasing the protection provided to the worker about twofold. NIOSH believes that adherence to the proposed ceiling concentration would prevent both irritative and systemic effects arising from occupational exposure to the aliphatic thiols (NIOSH, 1978).

The commenter argues that a higher ITSL of 200 µg/m^3 (1-hour averaging time) would be more appropriate, and supported this statement with rat subchronic inhalation study (apparently, Tansy et al. 1981). The Tansy et al (1981) study was evaluated in the derivation of the methyl mercaptan ITSL. Tansy et al. (1981) used 31 Sprague-Dawley rats/group were exposed to 0, 2, 17, or 57 ppm (0, 3.9, 33, or 110 mg/m^3) methyl mercaptan for 7 hours/day, 5 days/week for 3 months to determine sub-chronic toxicological effects. An additional 10 animals/group were randomly selected for metabolic performance tests. Tansy et al. (1981) determined that the most significant clinical sign was a decrease in body weight. The average terminal weights for all exposed groups were statistically significantly lower than the control group and showed a dose dependent trend. Other observations included: hyperplastic nodules found in four livers from rats exposed to 3.9 and 110 mg/m^3 dose groups and a hepatic carcinoma was detected in a rat in the 33 mg/m^3 dose group. Hyperplastic nodules were also observed in the control group and therefore were not considered to be associated with methyl mercaptan exposure. There was a change in behavior (crowding together with upturned noses) which was observed during exposure even at the lowest concentration tested (3.9 mg/m^3). This was regarded as a non-specific symptom of

intolerance (possibly due to nasal irritation or offensive taste as exposure was administered whole-body). The lowest concentration tested (3.9 mg/m^3) can be regarded as the study lowest observable adverse effect level (LOAEL) for methyl mercaptan (MAK, 2012). Even though an inhalation reference concentration (RfC) could be developed from Tansy et al, (1981), a sub-chronic rat study may not appropriately account for the acute irritant effects from methyl mercaptan exposure.

The ITSL for methyl mercaptan of 10 µg/m^3 is close to what other agencies have used in their acute values which are listed in the Table 1, below:

Table 1. Methyl mercaptan acute toxicity benchmarks and candidate acute ITSLs.

Available Benchmark Type	Value (µg/m^3)	Candidate Acute ITSL	Candidate ITSL Averaging Time
AEGL-1	No recommended value	-	-
ERPG-1	9.8 µg/m^3	9.8 µg/m^3	1-hour
NIOSH REL (Ceiling)	**1,000 µg/m^3**	**10 µg/m^3**	**1-hour**
ACGIH TLV-TWA	1,000 µg/m^3	10 µg/m^3	8-hour
MAK (Germany)	1,000 µg/m^3	10 µg/m^3	8-hour
OSHA PEL	1,000 µg/m^3	10 µg/m^3	8-hour

Summary and Conclusions:

In summary, an ITSL of 10 µg/m^3 was calculated using Rule 232(1)(c) and continues to be appropriate and defensible to protect public health as an AQD screening level. The available animal toxicity data do not appear to be sufficiently robust to support a more appropriate and defensible ITSL.

The primary AQD reviewer for these comments was Doreen Lehner, AQD Toxicologist. The secondary (peer) reviewer was Robert Sills, AQD Toxics Unit Supervisor.

References:

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