

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

January 25, 2018

To: File for Hydrogen Sulfide (H₂S) (CAS No. 7783-06-4)

From: Michael Depa, Air Quality Division, Toxics Unit

Subject: Initial Threshold Screening Level Derivation Update

The new H₂S chronic ITSL of 10 µg/m³ with annual averaging time replaces the previous ITSL of 2 µg/m³ with annual averaging time. There is no change to the acute ITSL of 100 µg/m³ with 24-hour averaging time (see attached memo for calculations and derivation of the acute ITSL).

The purpose of this memo is to update the chronic ITSL derived in March of 2012 (Depa, 2012; see attached memorandum) using updated U.S. Environmental Protection Agency (EPA, 2012) methodology for calculation of the dosimetric adjustment factor (DAF) for extrathoracic effects (new DAF = 1, previous DAF = 0.184).

The EPA (2003) derived a chronic reference concentration (RfC) for H₂S of 0.002 mg/m³ (2 µg/m³) based on a 10-week inhalation study (Brenneman et al., 2000). Brenneman et al. (2000) exposed 10-week-old male CD rats (12/exposure group) to 0, 10, 30, or 80 parts per million (ppm) (0, 13.9, 42, or 111 mg/m³) H₂S for 6 hr/day, 7 days/week, for 10 weeks. Nasal lesions of the olfactory mucosa were observed in the 30 and 80 ppm (42 and 111 mg/m³) exposure animals. Lesions consisted of multifocal, bilaterally-symmetrical olfactory neuron loss and basal cell hyperplasia affecting the lining of the dorsal medial meatus and dorsal and medial region of the ethmoid recess. The severity of the observed lesions varied between mild and severe. Nasal lesions were not observed in either the exposure group of 10 ppm (13.9 mg/m³) or in the controls rats; therefore, 13.9 mg/m³ was identified as the no-observed-adverse-effect-level (NOAEL).

To derive the new ITSL, a dosimetric adjustment factor (DAF) of 1 was used to extrapolate from the animal exposure dose to the human equivalent concentration (HEC). The DAF of 1 differs from the previous DAF of 0.184 used by EPA (2003) because EPA (2012) updated their previous RfC dosimetry methodology (EPA, 1994) for extrathoracic (ET) (e.g., nasal) effects of gases. EPA (2012) states that:

[I]nterspecies target tissue doses (human:animal) in the ET region relative to external exposure are close to or greater than 1:1.

EPA concludes that for ET effects of gases there is:

Strong evidence indicating that in the absence of modeling the default DAF = 1.

The same uncertainty factors (UFs) used by EPA (2003) were applied in the present calculation (see below). The ITSL was derived using the following UFs:

- 10 for subchronic to chronic exposure.
- 10 for sensitive populations, and
- 3 ($10^{1/2}$) was applied for interspecies (animal to human) extrapolation rather than 10 because of the dosimetric adjustment from rat to human,

A summary of the key values used to derive the new ITSL is shown in Table 1.

Table 1: Summary of the Derivation of ITSL

Type	Chronic
Source, Year	U.S. EPA RfC, 2003
NOAEL Exposure Dose	13.9 mg/m ³
Adjusted ^a Dose	3.48 mg/m ³
Point of Departure (POD)	NOAEL-HEC ^b = 3.48 mg/m ³
Study Group	Rat Inhalation Study
Study Exposure Duration	Subchronic
Study Critical Effect	Nasal lesions of the olfactory mucosa
Uncertainty Factors (UFs)	
LOAEL ^c to NOAEL	Not applicable
Subchronic to Chronic (UF1)	10
Sensitive Individuals (UF2)	10
Animal to Human (UF3)	3
Database Deficiencies	1
Total Uncertainty Factor	300

^a Adjusted dose = exposure dose x 6hr/24hrs x 7day/7day (for continuous exposure duration)

^b Human Equivalent Concentration (HEC) = Adjusted Dose x Dosimetric Adjustment Factor (DAF), where the DAF = 1 (i.e., animal dose = human dose).

^c LOAEL = lowest-observed-adverse-effect-level

The human equivalent concentration (HEC) was calculated as follows:

$$\text{HEC} = \text{Adjusted dose} \times \text{DAF}$$

Where DAF = 1

$$\text{HEC} = 3.48 \text{ mg/m}^3 \times 1$$

$$\text{HEC} = 3.48 \text{ mg/m}^3$$

The Point of Departure (POD) is equivalent to the HEC.

Pursuant to Rule 229(2)(b), the ITSL was calculated as follows:

$$\text{ITSL} = \text{POD}/(\text{UF1} \times \text{UF2} \times \text{UF3}) \times \text{unit conversion}$$

Where UFs are defined in Table 1 (see above).

$$\text{ITSL} = (3.48 \text{ mg/m}^3) / (10 \times 10 \times 3) \times 1000 \mu\text{g/mg}$$
$$\text{ITSL} = 11.6 \mu\text{g/m}^3$$

Rounding to one significant figure:

$$\text{ITSL} = 10 \mu\text{g/m}^3$$

Pursuant to Rule 232(2)(b) the averaging time is annual.

References

Brenneman, KA; James, RA; Gross, EA; Dorman, DC. (2000) Olfactory loss in adult male CD rats following inhalation exposure to hydrogen sulfide. Toxicologic Pathology 28(2): 326-333.

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EPA. 1994. Methods for derivation of inhalation reference concentrations and application of inhalation dosimetry. U.S. Environmental Protection Agency. Washington, D.C., Office of Research and Development. EPA/600/8-90/066F. October 1994.

EPA. 2003. Chemical Assessment Summary of Hydrogen sulfide; 7783-06-4. Integrated Risk Information System (IRIS). National Center for Environmental Assessment. U.S. Environmental Protection Agency. Accessed 1-23-2018: https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0061_summary.pdf

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MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

MARCH 16, 2012

TO: File for Hydrogen Sulfide (CAS No. 7783-06-4)

FROM: Michael Depa, Toxics Unit, Air Quality Division

SUBJECT: Acute Screening Level Update

The chronic (long-term exposure) ITSL of 2 µg/m³ (annual) was based on the U.S. Environmental Protection Agency (US EPA) Reference Concentration (RfC). The acute (short-term exposure) ITSL was based on the Agency for Toxic Substances and Disease Registry (ATSDR) Minimal Risk Level (MRL). Details of and basis for the ITSLs are shown in Table 1.

Table 1. Screening Levels, Their Basis and Derivation

		ITSLs (averaging time)	
		2 µg/m ³ (annual)	100 µg/m ³ (24-hr)
Type		Chronic	Acute
Source, Year		U.S. EPA RfC, 2003	ATSDR, 2006
Point of Departure		NOAEL* (HEC): 0.64 mg/m ³	LOAEL** 2 ppm
Study Group		Rat Inhalation Study	Human Asthmatics
Study Exposure Duration		Subchronic	30-minutes
Study Critical Effect		Nasal lesions of the olfactory mucosa	Decreased lung function; i.e., increased resistance, decrease air conductance
LOAEL to NOAEL			3
Subchronic to Chronic		10	
Sensitive Individual		10	3
Animal to Human		3	
Database Deficiencies			3
Total Uncertainty Factor		300	30

*No Observable Adverse Effect Level (NOAEL), Human Equivalent Concentration (HEC)

**Lowest Observed Adverse Effect Level (LOAEL)

A chronic ITSL of 2 µg/m³ was previously set in 2003, and was assigned an averaging time of 24-hrs pursuant to Rule 232(2)(b). Because an acute ITSL is now being established, the averaging time for the chronic ITSL is changing from 24-hr to annual. The acute ITSL averaging time will be set at 24-hrs.

Details regarding the derivation of the US EPA's RfC for hydrogen sulfide are found on the EPA IRIS website: <http://www.epa.gov/iris/subst/0061.htm>.

Key Study for Acute ITSL (ATSDR, 2006)

Lung function was evaluated in three male and seven female subjects with bronchial asthma requiring medication for 1–13 years; none of the subjects had severe asthma (Jäppinen et al., 1990). The subjects were exposed to 2 ppm hydrogen sulfide for 30 minutes. Respiratory function in response to a histamine challenge was assessed prior to exposure and after exposure. In two subjects, there were changes of over 30% in both airway resistance (Raw) and specific airway conductance (SGaw); these changes were suggestive of bronchial obstruction. Additionally, 3 of 10 subjects complained of headaches after exposure. The 2 ppm concentration was considered a minimally adverse effect level because the changes in airway resistance and specific airway conductance were only observed in 2 of 10 subjects. Because the study was conducted using asthmatics, who are likely to be a sensitive subpopulation, a partial uncertainty factor of 3 was used to account for human variability. An uncertainty factor of 3 was used for database deficiencies because of lack of studies on children exposed to hydrogen sulfide and concern for short (30 minute) exposure duration in the principal study.

Other Organization's Acute Health Benchmarks for Hydrogen Sulfide

Acute Exposure Guideline Level (AEGL) for Hydrogen Sulfide

Controlled human data were used to derive AEGL-1 values. Three of 10 volunteers with asthma exposed to H₂S at 2 ppm for 30 min complained of headache and 8 of 10 experienced nonsignificant increased airway resistance (Jäppinen et al. 1990). As there were no clinical symptoms of respiratory difficulty and there were no significant changes in forced vital capacity (FVC) or forced expiratory volume in 1 second (FEV₁), the AEGL-1 was based exclusively on increased complaints of headache in the three volunteers (Jäppinen et al. 1990). A modifying factor of 3 was applied to account for the wide variability in complaints associated with the foul odor of H₂S and the shallow concentration response at the relatively low concentrations that are consistent with definition of the AEGL-1. The 30-min experimental value was scaled to the 10-min and 1-, 4-, and 8-h time points by using the concentration-exposure duration relationship, $C^{4.4} \times t = k$, where C is concentration, t is time, and k is a constant. The exponent 4.4 was derived from rat lethality data ranging from 10-min to 6-h exposures.

10 min	30 min	1 hr	4 hr	8 hr
0.75 ppm	0.60 ppm	0.51 ppm	0.36 ppm	0.33 ppm
(1.05 mg/m ³)	(0.84 mg/m ³)	(0.71 mg/m ³)	(0.50 mg/m ³)	(0.46 mg/m ³)

California Acute Reference Exposure Level for Hydrogen Sulfide (1-hr REL = 42 µg/m³)

The 1-hour California Ambient Air Quality Standard (AAQS) for hydrogen sulfide was originally based on an olfactory perception study by the California State Department of Public Health (1969). Sixteen individuals were each exposed to increasing concentrations of H₂S until his or her odor threshold was reached. The range of the odor thresholds was 0.012–0.069 ppm, and the geometric mean was 0.029 ppm (geometric standard deviation = 0.005 ppm). The mean odor threshold (rounded to 0.03 ppm) was selected as the AAQS for H₂S. However, others have reported that the

odor threshold is as low as 0.0081 ppm (Amoore and Hautala, 1983). In 1984 CARB reviewed the AAQS for H₂S and found that the standard was necessary not only to reduce odors, but also to reduce the physiological symptoms of headache and nausea. (CARB, 1984). Furthermore, Amoore (1985) conducted a study that estimated 40% of the population would find 0.03 ppm (0.042 mg/m³) to be an objectionable concentration. In public testimony before the ARB it was stated that some people reported headaches and other symptoms at the standard (Reynolds and Kamper, 1985).

References

ATSDR. 2006. Toxicological Profile for Hydrogen Sulfide. July 2006. Agency for Toxic Substances and Disease Registry (ATSDR). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. <http://www.atsdr.cdc.gov/toxprofiles/tp114.pdf> <March 15, 2012>

Jäppinen P, Vikka V, Marttila O, et al. 1990. Exposure to hydrogen sulphide and respiratory function. *Br J Intern Med* 47:824-828.