ACUTE TOXICITY SUMMARY

HYDROGEN SULFIDE

(sulfur hydride; sulfuretted hydrogen)

CAS Registry Number: 7783-06-4

I. Acute Toxicity Summary (for a 1-hour exposure)

Inhalation reference exposure level	**42 µg/m³**
Critical effect(s)	Headache, nausea, physiological responses to odor
Hazard Index target(s)	CNS

II. Physical and Chemical Properties (AIHA, 1991 except as noted)

Description	colorless gas
Molecular formula	H_2S
Molecular weight	34.08
Density	1.39 g/L @ 25°C
Boiling point	-60.7°C
Melting point	unknown
Vapor pressure	1 atm @ -60.4°C
Flash point	26°C
Explosive limits	upper = 4.3% by volume in air lower = 46% by volume in air
Solubility	soluble in water, hydrocarbon solvents, ether, and ethanol
Odor threshold	0.0081 ppm (Amoore and Hautala, 1983)
Odor description	resembles rotten eggs
Metabolites	bisulfite (HSO_3), thiosulfate ($S_2O_3^{2-}$) (Baxter and Van Reen, 1958)
Conversion factor	1 ppm = 1.4 mg/m³ @ 25°C

II. Major Uses or Sources

Hydrogen sulfide (H_2S) is used as a reagent and an intermediate in the preparation of other reduced sulfur compounds. It is also a by-product of desulfurization processes in the oil and gas industries and rayon production, sewage treatment, and leather tanning (Ammann, 1986).

IV. Acute Toxicity to Humans

Hydrogen sulfide is an extremely hazardous gas (ACGIH, 1992). Hydrogen sulfide exposure is reported to be the most common cause of sudden death in the workplace (NIOSH, 1977). The mortality in acute hydrogen sulfide intoxications has been reported to be 2.8% (Arnold *et al.*, 1985) to 6% (WHO, 1981). While severe intoxication is especially of concern when exposure

occurs in confined spaces, an accidental release of hydrogen sulfide into the air surrounding industrial facilities can cause very serious effects. For example, at Poza Rica, Mexico 320 people were hospitalized and 22 died (WHO, 1981). An inhalation LC_{Lo} of 600 and 800 ppm (840 and 1,120 mg/m^3) for 30 and 5 minutes, respectively, is reported (Hazardtext, 1994). A lethal exposure was documented for a worker exposed to approximately 600 ppm H_2S for 5-15 minutes (Simson and Simpson, 1971). Inhalation of 1,000 ppm (1,400 mg/m^3) is reported to cause immediate respiratory arrest (ACGIH, 1992). Concentrations greater than 200 ppm (280 mg/m^3) H_2S are reported to cause direct irritant effects on exposed surfaces and can cause pulmonary edema following longer exposures (Spiers and Finnegan, 1986). The mechanism of H_2S toxicity, cellular hypoxia caused by inhibition of cytochrome oxidase, is similar to that for cyanide and can be treated by induction of methemoglobin or with hyperbaric oxygen (Elovaara *et al*., 1978; Hsu *et al*., 1987).

At concentrations exceeding 50 ppm (70 mg/m^3), olfactory fatigue prevents detection of H_2S odor. Exposure to 100-150 ppm (140-210 mg/m^3) for several hours causes local irritation (Haggard, 1925). Exposure to 50 ppm for 1 hour causes conjunctivitis with ocular pain, lacrimation, and photophobia; this can progress to keratoconjunctivitis and vesiculation of the corneal epithelium (ACGIH, 1992). Bhambhani and Singh (1991) showed that 16 healthy subjects exposed to 5 ppm (7 mg/m^3) H_2S under conditions of moderate exercise exhibited impaired lactate and oxygen uptake in the blood. Bhambhani and Singh (1985) reported that exposure of 42 individuals to 2.5 to 5 ppm (3.5 to 7 mg/m^3) H_2S caused coughing and throat irritation after 15 minutes.

In another study, ten asthmatic volunteers were exposed to 2 ppm H_2S for 30 minutes and pulmonary function was tested (Jappinen *et al*., 1990). All subjects reported detecting "very unpleasant" odor but "rapidly became accustomed to it." Three subjects reported headache following exposure. No significant changes in mean FVC or FEV_1 were reported. Although individual values for specific airway resistance (SR_{aw}) were not reported, the difference following exposure ranged from -5.95% to +137.78%. The decrease in specific airway conductance, SG_{aw}, ranged from -57.7% to +28.9%. The increase in mean SR_{aw} and the decrease in mean SG_{aw} were not statistically significant. However, significantly increased airway resistance and decreased airway conductance were noted in two of ten asthmatic subjects which may be biologically significant.

Hydrogen sulfide is noted for its strong and offensive odor. Based on a review of 26 studies, the average odor detection threshold ranged from 0.00007 to 1.4 ppm (Amoore, 1985). The geometric mean of these studies is 0.008 ppm. In general, olfactory sensitivities decrease by a factor of 2 for each 22 years of age above 20 (Venstrom and Amoore, 1968); the above geometric mean is based on the average age of 40.

For hydrogen sulfide, concentrations that substantially exceed the odor threshold result in the annoying and discomforting physiological symptoms of headache or nausea (Amoore, 1985; Reynolds and Kauper 1985). The perceived intensity of the odor of hydrogen sulfide depends on the longevity of the concentration, and the intensity increases 20% for each doubling concentration (Amoore, 1985). Several studies have been conducted to establish the ratio of discomforting annoyance threshold to detection threshold for unpleasant odors (Winneke, 1975;

Winneke and Kastka, 1977; Hellman and Small, 1974; Adams *et al.,* 1968; and NCASI, 1971). The geometric mean for these studies is 5, indicating that when an unpleasant odor reaches an average concentration of 5 times its detection threshold, the odor will result in annoying discomfort. Applying the 5-fold multiplier to the mean detectable level, 0.008 ppm, results in a mean annoyance threshold of 0.04 ppm. At the current California Ambient Air Quality Standard (CAAQS) of 0.03 ppm, the level would be detectable by 83% of the population and would be discomforting to 40% of the population. These estimates have been substantiated by odor complaints and reports of nausea and headache (Reynolds and Kauper 1985) at 0.03 ppm H2S exposures from geyser emissions. The World Health Organization (WHO) reports that in order to avoid substantial complaints about odor annoyance among the exposed population, hydrogen sulfide concentrations should not be allowed to exceed 0.005 ppm (7 $\mu g/m^3$), with a 30-minute averaging time (WHO, 1981; National Research Council, 1979; Lindvall, 1970).

Predisposing Conditions for Hydrogen Sulfide Toxicity

Medical: Unknown

Chemical: Ethanol has been shown to potentiate the effects of H_2S by shortening the mean time-to-unconsciousness in mice exposed to 800 ppm (1,120 mg/m^3) H_2S (Beck *et al*., 1979).

V. Acute Toxicity to Laboratory Animals

A median lethal concentration (LC_{50}) in rats exposed to H_2S for 4 hours was estimated as 440 ppm (616 mg/m^3) (Tansy *et al*., 1981). An inhalation LC_{Lo} of 444 ppm for an unspecified duration is reported in rats, and a lethal concentration of 673 ppm (942 mg/m^3) for 1 hour is reported in mice (RTECS, 1994). In another study, mortality was significantly higher for male rats (30%), compared to females (20%), over a range of exposure times and concentrations (Prior *et al*., 1988). A concentration of 1,000 ppm (1,400 mg/m^3) caused respiratory arrest and death in dogs after 15-20 minutes (Haggard and Henderson, 1922). Inhalation of 100 ppm (140 mg/m^3) for 2 hours resulted in altered leucine incorporation into brain proteins in mice (Elovaara *et al*., 1978). Kosmider *et al*. (1967) reported abnormal electrocardiograms in rabbits exposed to 100 mg/m^3 (71 ppm) H_2S for 1.5 hours.

Khan *et al*. (1990) exposed groups of 12 male Fischer 344 rats to 0, 10, 50, 200, 400, or 500-700 ppm hydrogen sulfide for 4 hours. Four rats from each group were sacrificed at 1, 24, or 48 hours post-exposure. Cytochrome c oxidase activity in lung mitochondria was significantly ($p<0.05$) decreased at 50 ppm (15%), 200 ppm (43%), and 400 ppm (68%) at 1-hour post-exposure compared to controls. A NOAEL of 10 ppm was identified in this study for effects on lung mitochondrial cytochrome c oxidase activity.

VI. Reproductive or Developmental Toxicity

Xu *et al*. (1998) conducted a retrospective epidemiological study in a large petrochemical complex in Beijing, China in order to assess the possible association between petrochemical exposure and spontaneous abortion. The facility consisted of 17 major production plants which

are divided into separate workshops, allowing for the assessment of exposure to specific chemicals. Married women (n = 2853), who were 20-44 years of age, had never smoked, and who reported at least one pregnancy during employment at the plant, participated in the study. According to their employment record, about 57% of these workers reported occupational exposure to petrochemicals during the first trimester of their pregnancy. There was a significantly increased risk of spontaneous abortion for women working in all of the production plants with frequent exposure to petrochemicals compared with those working in nonchemical plants. Also, when a comparison was made between exposed and non-exposed groups within each plant, exposure to petrochemicals was consistently associated with an increased risk of spontaneous abortion (overall odds ratio (OR) = 2.7 (95% confidence interval (95% CI) = 1.8 to 3.9) after adjusting for potential confounders). When the analysis was performed with the exposure information obtained from the women' interview responses for (self reported) exposures, the estimated OR for spontaneous abortions was 2.9 (95% CI = 2.0 to 4.0). The analysis was repeated by excluding those 452 women who provided inconsistent reports between recalled exposure and work history, and a comparable risk of spontaneous abortion (OR 2.9; 95% CI 2.0 to 4.4) was found. In analyses for exposure to specific chemicals, an increased risk of spontaneous abortion was found with exposure to most chemicals. There were 106 women (3.7% of the study population) exposed only to hydrogen sulfide, and the results for hydrogen sulphide (OR 2.3; 95% CI = 1.2 to 4.4) were significant. No hydrogen sulfide exposure concentration was reported.

VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

Reference Exposure Level (protective against mild adverse effects): 42 μg/m³
(California Ambient Air Quality Standard)

Study	California State Department of Public Health, 1969; CARB, 1984; Reynolds and Kamper, 1985; Amoore, 1985
Study population	panel of 16 people; general population
Exposure method	inhalation of increasing concentrations of H_2S
Critical effects	headache, nausea
LOAEL	0.012-0.069 ppm (range of odor threshold)
NOAEL	≤ 0.01 ppm
Exposure duration	not stated (tested until odor detected)
Extrapolated 1 hour concentration	0.012-0.069 ppm (geometric mean = 0.03 ppm) (1 hour = minimum duration for an air standard)
LOAEL uncertainty factor	not used
Interspecies uncertainty factor	1
Intraspecies uncertainty factor	1
Cumulative uncertainty factor	1
Reference Exposure Level	0.03 ppm (0.042 mg/m³; 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 H_2S 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 H_2S. 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 H_2S 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/m^3) 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). Thus this recommended level protective against mild adverse effects may be need to be reexamined as more data become available.

Level Protective Against Severe Adverse Effects

No recommendation can be made due to the limitations of the database.

An ERPG-2 of 30 ppm (AIHA, 1991) was based on experimental data showing that exposure of rats to 45 ppm (63 mg/m^3) H_2S for 4 hours resulted in no deaths (Rogers and Ferin, 1981). In addition, rabbits exposed to 71 ppm (100 mg/m^3) H_2S for 1.5 hours developed cardiac irregularities, measured by electrocardiogram, and decreased myocardial ATP phosphorylase (Kosmider *et al.*, 1967). The rationale for the margin of safety used for the ERPG-2 is not presented.

Level Protective Against Life-threatening Effects

No recommendation can be made due to the limitations of the database.

The AIHA ERPG-3 for hydrogen sulfide of 100 ppm (AIHA, 1991) was based on case reports of conjunctivitis, respiratory irritation, and unconsciousness in humans exposed to estimated concentrations of 200-300 ppm (280-420 mg/m^3) H_2S for 20 minutes to 1 hour (Ahlborg, 1951; Yant, 1930). In addition, a 1-hour LC_{50} of 712 ppm (997 mg/ m^3) in rats is cited (CIIT, 1983). The case reports cited in the ERPG document are inadequate to establish acute exposure levels in humans because the concentrations and durations of exposure are only estimates. In addition, there are no LC_{50} data in the CIIT (1983) report. Rats (5 female and 5 male) exposed to H_2S concentrations ranging from 400-600 ppm (560-840 mg/m^3) for 4 hours showed dose-dependent lethality rates ranging from 30% - 100% (Tansy *et al.*, 1981). On the other hand, two of three rhesus monkeys exposed to a concentration of 500 ppm (700 mg/m^3) for only 35 minutes or less died, which suggests that primates are more sensitive to the lethal effect of H_2S than rats (Lund and Wieland, 1966). The rationale for the margin of safety used for the ERPG-3 was not presented.

NIOSH (1995) reports a (revised) IDLH for hydrogen sulfide of 100 ppm based on acute inhalation toxicity data in humans and animals, but the values from animals appear to be more heavily weighted than the human data in the selection of the IDLH.

VII. References

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