

HYDROGEN SULFIDE: UK OCCUPATIONAL EXPOSURE LIMITS

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Hydrogen sulfide (H_2S) is a toxic gas with an offensive odour reminiscent of rotten eggs. There is the potential for widespread occupational exposure to H_2S , including in the oil and water treatment industries. There is a particular concern for exposure in confined spaces such as manholes and sewer pipes; the high concentrations that can build up in such conditions (> 1000 parts per million (ppm)) can lead to the rapid development (within minutes) of unconsciousness and death. There are many reports throughout the literature of fatalities caused by exposure to H_2S . However, there is also a concern for adverse health effects caused by day to day occupational exposures to low concentrations (< 10 ppm); this is because H_2S selectively binds to the enzymes involved in cellular respiration thereby causing a shift towards anaerobic respiration. The recently revised UK occupational exposure limits for H_2S are designed to protect against the development of such effects.

SETTING OCCUPATIONAL EXPOSURE LIMITS FOR H_2S

The purpose of this paper is to outline the evidence and rationale underpinning the recently updated UK occupational exposure limits (OELs) for H_2S . To place this information in context it is helpful to have an understanding of the UK regulatory framework surrounding OELs. A previous paper in this series has already covered this topic.¹ Box 1 and fig 1 summarise the key features involved in OEL setting in the UK. The reason why the OELs for H_2S were recently reviewed in the UK is because in the mid 1990s a series of human volunteer studies were published that suggested exposures as low as 10 ppm might cause a shift to anaerobic metabolism under conditions of physical exertion. This leads to a concern for adverse physiological effects at what were at the time the existing occupational exposure standard (OES) values for H_2S of 10 ppm (8 hour time weighted average (TWA)) and 15 ppm (short term exposure limit (STEL)). Given that there are thousands of workers exposed to H_2S in the UK, this substance was viewed as a priority for review in the OEL programme via the Working Group on the Assessment of Toxic Chemicals/Advisory Committee on Toxic Substances (WATCH/ACTS) system.

Once it has been decided to place a chemical on the UK OEL review programme, a multidisciplinary team from the UK Health and Safety Executive (HSE) assembles a scientific and technical package that will go forward for evaluation at WATCH. The components of the HSE package on H_2S summarised in this paper are the toxicology (including human epidemiology) and the occupational hygiene assessments. The HSE toxicology assessment was based partly on a 1992 Criteria Document² commissioned by the European Directorate responsible for worker health, supplemented by a full literature search to identify studies published after 1992. The occupational hygiene assessment was based on an HSE survey of the industrial uses and exposures to H_2S across UK industry.

The published literature on H_2S goes back over many years. From this, longstanding beliefs and assumptions have been perpetuated regarding the toxic effects of H_2S . For example, the impression is given that H_2S is a very irritant gas, and has also been associated with a phenomenon known as “gas eye”. However, as can be seen from the following critical scientific evidence of the toxicity data, beliefs such as these turn out not to be particularly well supported by hard data.

OVERVIEW OF INDUSTRIAL EXPOSURES TO H_2S

H_2S is produced from the anaerobic decomposition of animal and vegetable waste—for example, in slurry and manure storage pits, in effluent waste and sewage. The gas is a natural component of petroleum and of natural gas where it is known as “sour gas” (table 1).

There is no commercial production of H_2S or any recovery of the gas from natural sources within the UK for distribution and/or use. All of the H_2S utilised in UK industry is imported. H_2S is produced as a byproduct during the manufacture of viscose rayon, synthetic rubber compounds, and phosphorus pentasulfide. The gas is also released during petroleum refining operations.

Large amounts of liquefied H_2S are imported into the UK for use in the production of dyes, chemical intermediates, and pharmaceuticals. There is also some specialised use of the liquefied gas in the treatment of metals and in research and quality control establishments.

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Box 1: Occupational exposure limits (OELs)

- ▶ In the UK, the Control of Substances Hazardous to Health Regulations (COSHH) 1988 provides the legal basis for OELs
- ▶ OELs refer to airborne concentrations of a substance measured over a specified time period, either an 8 hour time weighted average (TWA) and/or a 15 minute reference period. The latter is referred to as a short term exposure limit (STEL)
- ▶ STELs are applied to substances capable of causing immediate health effects following brief peaks of exposure. Typically, such effects would be sensory irritation of the eyes and respiratory tract, or central nervous system (CNS) depression, or acute lethality (for example, as with hydrogen cyanide or phosgene). In contrast, OELs (8 hour TWA) are aimed at controlling against the more slowly developing effects of long term repeated exposures
- ▶ In the UK, OELs are set by the Health and Safety Commission on advice from its Advisory Committee on Toxic Substances (ACTS), which in turn takes advice from its scientific subcommittee known as the Working Group on the Assessment of Toxic Chemicals (WATCH)
- ▶ Under the UK COSHH Regulations there are two types of OEL. These are occupational exposure standards (OESs) and maximum exposure limits (MELs)
- ▶ OESs represent exposures that, according to available scientific knowledge, will not cause any injury to health *and* which are also reasonably practicable for industry to achieve
- ▶ MELs are applied to substances with serious health concerns (typically carcinogens and asthmagens) for which it is not always possible to identify a threshold level of exposure below which there would be no residual risk to health. Alternatively, a threshold may be identifiable but industry is unable to control exposures to below this threshold. For these reasons, the legal duty associated with MELs requires that employers reduce exposure to as low as is reasonably practicable below the value of the MEL

In the UK, around 125 000 workers are potentially exposed to H₂S in work related to the treatment of sewage, effluent waste, and farm slurry. In the offshore oil and gas industries about 3000 workers are potentially exposed.

HSE's survey of occupational exposures revealed that most exposures to H₂S in the offshore oil and gas industry are generally below 5 ppm (8 hour TWA) and 10 ppm (15 minute reference period). In effluent waste and sewage treatment, and work on landfill sites, most exposures are below 5 ppm (8 hour TWA). However, concentrations up to 600 ppm were recorded at the base of a sump tank and concentrations > 300 ppm were measured in a settlement tank. Under normal handling of farm slurry personal exposures to H₂S should be below 5 ppm (8 hour TWA) and 10 ppm (15 minute reference period). However, HSE recorded high concentrations of H₂S of up to 1000 ppm during the mixing of farm slurry. Also, high exposures to H₂S exceeding 2000 ppm can occur when working in manholes, drains, sewers, and other confined spaces.

TOXICOLOGICAL PROFILE OF H₂S**Toxicokinetics**

H₂S is rapidly absorbed from the lungs following inhalation exposure. Absorption of the gas through the skin is minimal.² Following absorption, H₂S is widely distributed around the body, primarily as undissociated H₂S or as HS⁻ ions. H₂S binds

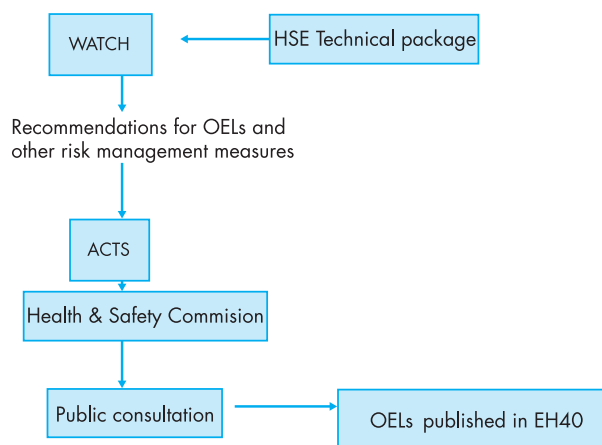


Figure 1 UK occupational exposure limit (OEL) setting process. ACTS, Advisory Committee on Toxic Substances; HSE, Health and Safety Executive; WATCH, Working Group on the Assessment of Toxic Chemicals.

reversibly to metalloenzymes, including those involved in aerobic cellular respiration such as cytochrome oxidase.

The main detoxification pathway for H₂S is oxidation to sulfate, occurring primarily in the liver and to a lesser extent in the blood, followed by excretion in the urine in free or conjugated form. Another minor metabolic route for H₂S, occurring primarily in the intestinal mucosa and liver, is methylation to methanethiol and dimethylsulfide. Metabolism to sulfate is relatively rapid and hence H₂S is unlikely to bioaccumulate.

Effects of single exposure

The literature contains many case reports of fatal poisonings in workers exposed to H₂S; the data clearly indicate that short term single exposures to concentrations of 500 ppm and above may be fatal.³ Studies in animals confirm the human evidence regarding the acute toxicity of H₂S. An LC₅₀ (concentration causing lethality in 50% of animals) of 444 ppm was measured in rats following a four hour exposure period.² Human evidence suggests that exposure to higher concentrations, in the region of 1000 ppm and above, causes death very rapidly (within minutes). Deaths at such high exposure concentrations are caused by inhibition of cytochrome oxidase; this causes a blockage of the mitochondrial electron transport system, and an inhibition of cellular respiration. This leads to inactivation of the respiratory centres in the brain, leading to respiratory arrest, unconsciousness, and death. In addition, more prolonged exposures to somewhat lower concentrations can cause severe pulmonary oedema and congestion which can also lead to death. Hence, there is a duality of the mechanisms leading to death involving both centrally mediated respiratory depression and lung damage. The relative significance of these mechanisms depends on the exposure conditions. Neurological sequelae, such as memory loss, are common in survivors following periods of unconsciousness caused by H₂S exposure.²

A recent series of human volunteer studies involving short term exposures to H₂S demonstrated that exposure during exercise may cause a shift to anaerobic respiration⁴⁻⁸; blood lactate concentrations were found to increase following maximal exercise at 5 ppm and submaximal exercise at 10 ppm, and there was some evidence to suggest that enzymes involved in aerobic metabolism, such as cytochrome oxidase in muscle tissue, were inhibited by H₂S. However, despite these effects,

Table 1 Exposures to hydrogen sulfide

Emissions from natural sources	Industrial byproduct emissions	Industrial uses
Anaerobic decomposition of vegetable/animal matter in slurry and manure storage pits, in effluent waste, sewage and landfill sites	Emitted during manufacture of: –viscose rayon –synthetic rubber compounds –phosphorous pentasulfide –paper and pulp making	Manufacture of sulfuric acid and other sulfur compounds
Volcanoes, stagnant water, swamps and sulfurated spring waters		Liquefied gas used in the manufacture of pharmaceuticals, dyes, chemical intermediates, heavy water, and refining of metals, particularly copper
A component of petroleum and natural gas where it is known as “sour gas”		Used in research and quality control laboratories
Released during the drilling of gas wells, and well testing operations		

the volunteers (fit, healthy young adults) did not report any accompanying adverse symptoms such as fatigue, nausea or headache. Whether or not older less fit adults would have experienced adverse symptoms under equivalent exposure conditions is unknown. Furthermore, the exposures to H₂S typically were of 30 minutes duration only, and the effects of more prolonged exposures are again unknown.

Exposures to high (near lethal) concentrations of H₂S also cause direct damage to the upper respiratory tract epithelium. Inhalation studies in rats showed that a four hour exposure to 400 ppm caused cell death and hair loss of the nasal and respiratory epithelium, with indications that an inflammatory response was occurring.^{9–10} However, below 200 ppm, these effects were only minimal. Exposure of rats to 50 ppm, but not 10 ppm, for four hours caused inhibition of lung cytochrome oxidase.¹¹ It seems possible that the inhibition of lung cytochrome oxidase may possibly account for the pulmonary oedema observed at high exposure concentrations in animals and humans.

It is well documented that following high acute exposures to irritant gases—for example, sulfur dioxide—there can be residual bronchial hypersensitivity. However, HSE is not aware of any work carried out to investigate this phenomenon following exposures to H₂S alone.

“Gas eye”

There are many reports throughout the literature describing eye irritation in both humans and animals exposed to H₂S.^{2–3} Most of these reports are old and the exposure conditions were not always well defined. Several early studies from the viscose-rayon industry suggest that occupational exposures to relatively low concentrations of H₂S can cause a form of eye damage, “keratitis superficialis punctatis”, commonly known as “gas eye” or “spinners eye”. However, work in this industry also involves exposure to other substances such as carbon disulfide and acid gases such as sulfur dioxide as well as acid mists from sulfuric acid. It has been suggested that exposure to other agents may “sensitise” the eyes to the subsequent effects of H₂S.¹²

A cross sectional epidemiological study was conducted in workers from a Belgian viscose-rayon factory has recently been published.¹³ Subjective reports of eye effects such as eye pain, eye burning, seeing coloured halos, photophobia, and hazy sight were assessed by questionnaire. In addition, ophthalmological examinations were conducted on all subjects. Measurements of personal exposures to carbon disulfide and H₂S were carried out. Exposures to carbon disulfide were above 10 ppm in the majority of jobs. Exposures to H₂S ranged

between 0.14–6.4 ppm with the highest exposures being in areas with the highest exposures to carbon disulfide. There were no detectable amounts of sulfuric acid in the air in this factory. The results showed a high correlation between combined exposure to carbon disulfide and H₂S, and the prevalences of eye complaints. No subjects were exposed to H₂S alone, and the statistical analysis was unable to distinguish the separate effects of these gases. However, the study did demonstrate that exposures up to 4 ppm H₂S, even in the presence of 29 ppm carbon disulfide, did not cause any eye effects.

There are studies that do not seem to support the view that H₂S causes “gas eye”. In a study in rats and mice, involving specific ophthalmological tests, no signs of eye irritation were observed following 90 days of repeated exposures (six hours/day) to 80 ppm.¹⁴ Similarly, in a separate study in rats only, no eye damage was observed following exposures up to 100 ppm H₂S for three hours/day for five consecutive days.¹⁵

Clearly, work in viscose-rayon manufacture has been associated with “gas eye”, but a specific causal role for H₂S in the development of this condition is an area of uncertainty. Animal evidence convincingly demonstrates a lack of ability to cause eye irritation following repeated exposures to H₂S alone at concentrations up to 100 ppm. This makes it seem very unlikely that exposures to H₂S at concentrations of current occupational relevance could be a cause of eye irritation. However, eye irritation has been reported in a number of early acute lethality studies in animals with H₂S and has also been reported in humans exposed to concentrations in the region of 500 ppm.³ Overall, the balance of evidence suggests that eye irritation is a phenomenon only associated with high exposures to H₂S, in the hundreds of ppm.

Effects of repeated exposure

Only a limited amount of information is available concerning the effects of repeated exposures to H₂S. A cross sectional study in Finnish pulp mill workers showed no effects on pulmonary function (forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC)) or on bronchial reactivity to histamine challenge with exposures of non-asthmatics to H₂S in the region of 2–7 ppm.¹⁶ A cross sectional study in US sewer workers employed for up to 20 years suggested a reduced pulmonary function in these workers compared to a referent group. However, there were no quantitative measures of H₂S exposure in the sewer workers.¹⁷ A study in Japanese workers from three viscose-rayon plants showed no evidence for effects on pulmonary function or on the reporting of respiratory symptoms; workers were exposed to mean concentrations of H₂S of 3 ppm.¹⁸

A couple of studies of individuals exposed environmentally or occupationally to H₂S suggested a variety of medical and neurophysiological effects.^{19, 20} However, the individuals involved had all received confounding exposures to a range of chemicals, and in one study were all involved in litigation proceedings. Some of the subjects had been previously rendered unconscious by single high exposures to H₂S which may well have led to neurological sequelae. No reliable conclusions concerning the effects of repeated exposure to H₂S could be drawn from these studies.

A recent study in workers from a viscose-rayon factory did not show any link between exposure to H₂S and the development of neuropsychological effects.²¹ In this factory, workers received combined exposures to carbon disulfide (1–37 ppm) and up to 6 ppm H₂S. Another recent study investigated the potential effects of H₂S on olfaction.²² The eight subjects of the study complained of problems related to the sense of smell following exposures to H₂S 2–3 years previously. Four of the subjects had been rendered unconscious for several minutes. Sense of smell was assessed by questionnaire and by a standard battery of smell tests. Although all subjects reported smell dysfunction, the objective tests revealed normal olfactory function in all eight. HSE felt that no firm conclusions could be drawn from this isolated study. Given that high exposures to H₂S have been shown to cause nasal epithelial cell damage in animals, and human survivors of high exposure have shown neurological sequelae, it seems plausible that periods of high exposure would have the potential to cause an impairment in olfaction.

There is some evidence concerning the effects of repeated exposure to H₂S from animal studies. In brief, the most useful data derive from a good quality 90 day inhalation study in rats and mice. This study included detailed neurological and pathological examinations. The results demonstrated overt toxicity including deaths and inflammation in the nasal mucosa in mice, but not rats, following exposure to 80 ppm H₂S for 90 days. No systemic or local signs of toxicity occurred in either species at 30 ppm.¹⁴ Hence, 30 ppm would appear to be a “no observed adverse effect level” (NOAEL) for the effects of repeated exposure to H₂S in animals.

Mutagenicity and carcinogenicity

No studies into the mutagenic or carcinogenic potential of H₂S were located. However, a study in which rats were orally dosed with sodium sulfide for 78 weeks did not present any evidence of carcinogenicity.² This provides some limited reassurance that H₂S is unlikely to be carcinogenic.

Reproductive toxicity

There are no studies in humans concerning the potential reproductive effects of H₂S. In animals, no fertility studies were located. However, a number of developmental toxicity studies were located although the design of these studies did not conform to standard regulatory protocols. The results did not reveal any effects on fetal mortality or incidence of malformations or morphological variations^{23, 24}; the only finding was altered concentrations of the amino acid neurotransmitters glutamate, aspartate, and GABA in the offspring of rats exposed to 75 ppm during gestation and for 21 days post-partum. The interpretation of these findings is unclear but they are not regarded as providing clear evidence of overt developmental toxicity.

BASIS FOR UK OELS

WATCH concluded that the recent series of studies in human volunteers were key studies of relevance to the potential effects

Box 2: Hydrogen sulfide—key points

- ▶ Hydrogen sulfide (H₂S) is a colourless, flammable gas
- ▶ H₂S has a pungent odour reminiscent of rotten eggs. The odour is detectable at very low concentrations; the threshold for perception is between 0.02–0.13 ppm
- ▶ But! Odour perception is unreliable as a warning of high exposures; olfactory fatigue may develop at concentrations of 100 ppm and above
- ▶ H₂S is a metabolic poison; it blocks the electron transport chain in mitochondria, inhibiting cellular utilisation of oxygen
- ▶ Exposures for a few hours to concentrations of 500 ppm and above are likely to be fatal. Exposure for a few minutes to concentrations of 1000 ppm and above are likely to cause rapid unconsciousness and death. At higher concentrations, death is caused by depression of respiratory centres in the brain; at lower concentrations, death is caused by pulmonary oedema and congestion. The relative importance of each mechanism depends on the exposure conditions. Many fatalities have occurred in workers exposed in confined spaces such as manholes. Survivors of periods of unconsciousness may suffer permanent neurological sequelae such as memory loss. High exposures to near lethal concentrations in animals have shown destruction of nasal epithelium
- ▶ During vigorous exercise, low level exposures (5–10 ppm) cause a shift to anaerobic respiration, leading to increased lactic acid formation
- ▶ Evidence on eye irritation is inconsistent. The balance of evidence suggests that eye irritation is only likely to occur at high exposure concentrations, in region of hundreds of ppm
- ▶ In the UK, control of inhalation exposure to H₂S in the workplace must comply with occupational exposure standards (OESs) of 5 ppm (8 hour TWA) and 10 ppm (STEL). These values replace the previous OESs of 10 ppm (8 hour TWA) and 15 ppm (STEL)
- ▶ The treatment of victims of H₂S poisoning is similar to that used for hydrogen cyanide poisoning. It involves parenteral administration of a methaemoglobin inducing agent such as sodium nitrite. Methaemoglobin binds with HS⁻ ions to form sulfamethaemoglobin, and thus restores the activity of the sulfide inhibited cytochrome oxidase enzyme.

of occupational exposure. The findings from these studies demonstrate that brief periods (15–30 minutes) of exposure to 5 and 10 ppm, while undergoing maximal and submaximal exercise, respectively, cause a shift towards anaerobic respiration. No symptoms such as fatigue or muscle pain were reported as a consequence of these exposures. The effects of more prolonged exposures on metabolism are uncertain, although workers would be unlikely to maintain such high levels of physical exertion for substantial periods of time. However, the volunteers were all young fit healthy adults, and the worker population would include older and less fit subjects. It was also noted that a NOAEL of 30 ppm was available from a repeated exposure study in rats and mice; there were no signs of any systemic target organ toxicity or local effects on the eyes or respiratory tract at this concentration.

Taking all of these factors into consideration, together with knowledge of the exposure concentrations that occur in industry, WATCH considered that H₂S met the criteria for the establishment of an OES. WATCH recommended that an OES of 5 ppm (8 hour TWA) would be appropriate; in addition, WATCH felt that in view of the acute toxicity of H₂S, a STEL was necessary to emphasise the need to control short term

peak exposures. Consideration of the human and animal evidence suggested that a STEL OES of 10 ppm would be appropriate. In reaching its decision, WATCH agreed that from the occupational hygiene data available, it would be reasonably practicable for UK industry to achieve control to these levels.

In relation to other possible risk management measures that can accompany OELs, WATCH noted that as there was no evidence for the ability of H₂S to induce occupational asthma, a “sensitising notation” should not be applied. Given that skin absorption of H₂S is considered to be negligible, a “skin notation” is not considered appropriate. Finally, exposure to H₂S can be assessed from measurements of sulfide in blood or thiosulfate in urine. Such measurements tend to have been taken only for acute exposure incidents, and not as a routine in the workplace. However, the fact that H₂S is not absorbed via the skin, and that respiratory protective equipment is not routinely used in workers exposed to H₂S, meant that the UK criteria for establishing a biological monitoring standard were not met. Hence, WATCH did not recommend the setting of a biological monitoring standard for H₂S.

These recommendations from WATCH were subsequently endorsed by ACTS, and are now listed in the HSE publication EH40/2002.²⁵ A summary document giving details of the basis for the UK limits will also be available during 2002 as part of the EH64 series.²⁶

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QUESTIONS (SEE ANSWERS ON P 270)

(1) When humans are exposed to H₂S indicate which of these statements are true or false:

- (a) the odour of H₂S is strong, and provides a good warning of dangerously high exposure situations
- (b) the phenomenon of “gas eye” occurs following exposure to very low concentrations of H₂S (< 10 ppm)
- (c) survivors of high exposures to H₂S, sufficient to cause brief periods of unconsciousness, may suffer from neurological changes such as memory loss
- (d) repeated exposures to H₂S have the potential for cause bioaccumulation of sulfide in the body

(2) In terms of toxicological mechanism, which of these statements are true of H₂S:

- (a) the mechanism of toxicity for H₂S is based on its ability to bind avidly to haemoglobin thereby reducing the oxygen carrying capacity of the blood
- (b) H₂S binds to cytochrome oxidase in mitochondria
- (c) H₂S can cause a shift to anaerobic metabolism leading to an increased blood lactic acid concentration
- (d) there are two mechanisms whereby H₂S causes death—depression of the respiratory centres in the brain, and pulmonary oedema

(3) Studies in workers have shown that H₂S does not appear to cause impairment of pulmonary function when exposures are controlled in the region of:

- (a) 300 ppm
- (b) 30 ppm
- (c) 3 ppm
- (d) 0.3 ppm

(4) The following sets of exposure conditions carry at least a 50% probability of death in either humans or animals:

- (a) 10 ppm for 8 hours
- (b) 400 ppm for 1 hour
- (c) 500 ppm for 4 hours
- (d) 2000 ppm for 5 minutes

(5) Which of the following statements are true and which are false:

- (a) The UK OESs for H₂S are designed primarily to control against non-lethal physiological changes
- (b) A STEL was not thought to be necessary for H₂S as it does not cause immediate sensory irritation
- (c) A “no observed adverse effect level” for H₂S was identified in animals at 75 ppm
- (d) Given that there were human data available, animal data were not used by WATCH in deriving the OESs for H₂S.