

Committee for Risk Assessment
RAC

Opinion
proposing harmonised classification and labelling
at EU level of

hydrogen sulphide, hydrogen sulfide

EC Number: 231-977-3
CAS Number: 7783-06-4

CLH-O-0000007029-73-01/F

Adopted
16 September 2021

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: hydrogen sulphide, hydrogen sulfide

EC Number: 231-977-3

CAS Number: 7783-06-4

The proposal was submitted by **Germany** and received by RAC on **30 September 2020**.

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

PROCESS FOR ADOPTION OF THE OPINION

Germany has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at <http://echa.europa.eu/harmonised-classification-and-labelling-consultation/> on **19 October 2020**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **18 December 2020**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Michal Martínek**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **16 September 2021** by **consensus**.

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	016-001-00-4	hydrogen sulphide, hydrogen sulfide	231-977-3	7783-06-4	Press. Gas Flam. Gas 1 Acute Tox. 2* Aquatic Acute 1	H220 H330 H400	GHS02 GHS04 GHS06 GHS09 Dgr	H220 H330 H400			Note U
Dossier submitters proposal	016-001-00-4	hydrogen sulphide, hydrogen sulfide	231-977-3	7783-06-4	Retain Press. Gas Modify Flam. Gas 1A Acute Tox. 2	Retain H220 H330	Retain GHS02 GHS06 Dgr Remove GHS04	Retain H220 H330		Add Inhalation: ATE = 100 ppmV (gases)	Retain Note U
RAC opinion	016-001-00-4	hydrogen sulphide, hydrogen sulfide	231-977-3	7783-06-4	Retain Press. Gas Modify Flam. Gas 1A Acute Tox. 2	Retain H220 H330	Retain GHS02 GHS06 Dgr Remove GHS04	Retain H220 H330		Add Inhalation: ATE = 440 ppmV (gases)	Retain Note U
Resulting Annex VI entry if agreed by COM	016-001-00-4	hydrogen sulphide, hydrogen sulfide	231-977-3	7783-06-4	Press. Gas Flam. Gas 1A Acute Tox. 2 Aquatic Acute 1	H220 H330 H400	GHS02 GHS06 GHS09 Dgr	H220 H330 H400		Inhalation: ATE = 440 ppmV (gases)	Note U

FOUNDATIONS FOR ADOPTION OF THE OPINION

RAC general comment

Hydrogen sulfide (H₂S) is registered under REACH and mainly used as an intermediate at industrial sites. Being a gas at room temperature and standard pressure, it is supplied in pressurised vessels. H₂S is slightly (1.2-fold) heavier than air and has a characteristic odour of rotten eggs.

H₂S is a product of anaerobic decomposition of sulphur-containing organic matter. It is highly toxic by inhalation and a large number of fatal accidents have been reported in relation to sewers and manure handling. H₂S is also present in natural gas and petroleum, and occurs as a by-product of several industrial processes (e.g. paper production or petroleum refining processes). Some fatal cases involve liberation of H₂S upon acidification of sulfide-containing materials.

According to the existing Annex VI entry, H₂S is classified as Flam. Gas 1, Pres. Gas 1 (with Note U), Acute Tox. 2* (inhalation) and Aq. Acute 1. The substance was already classified under the DSD system and its classification was included in the CLP Regulation in 2008.

The classification system for 'flammable gases' has changed since then (Reg. 487/2013, Reg. 521/2019), the most important change with regard to H₂S being the division of category 1 into subcategories 1A and 1B. One of the aims of this CLH proposal is to ensure classification of the substance in the correct subcategory.

The second aim of the current CLH proposal is to resolve the minimum classification for acute inhalation toxicity and to set a harmonised ATE value. By proposing a low ATE value the DS expects to increase worker protection through classification of H₂S-containing mixtures.

Lastly, the DS also reassessed the hazard of 'gases under pressure', confirming the current classification but proposing a change in labelling based on the 2nd ATP (Reg. 286/2011).

RAC evaluation of physical hazards

Summary of the Dossier Submitter's proposal

Flammable gases

According to the CLP definition, a flammable gas is a gas having a flammable range with air at 20 °C and a standard pressure of 101.3 kPa. Gases meeting this criterion are classified in an appropriate (sub)category based on their flammability range, chemical stability and pyrophoric properties.

The flammable range of H₂S in air, determined according to EN 1839 (tube method), is 3.9 to 50.2 mol % (equivalent to volume % for an ideal gas) at 20 °C and a standard pressure. The auto-ignition temperature determined according to DIN 51794 is 270 °C at a standard pressure.

Hydrogen sulfide has not been tested for chemical instability with an UN test. Still, it can be considered chemically stable according to the DS due to a positive standard Gibbs energy value (+33.4 kJ/mol) of the decomposition reaction $\text{H}_2\text{S} (\text{g}) \rightarrow \text{H}_2 + \text{S}$.

Based on this information, the DS proposed to classify H₂S with Flam. Gas 1A; H220.

Gases under pressure

According to the CLP definition, gases under pressure are gases which are contained in a receptacle at a pressure of 200 kPa (gauge) or more at 20 °C, or which are liquefied or liquefied

and refrigerated. The definition comprises compressed gases, liquefied gases, dissolved gases and refrigerated liquefied gases.

The distinction between compressed gases and liquefied gases is based on the critical temperature (the temperature above which a pure gas cannot be liquefied) according to the following criteria (CLP Regulation, Annex I, Table 2.5.1):

Group	Criteria
Compressed gas	A gas which when packaged under pressure is entirely gaseous at $-50\text{ }^{\circ}\text{C}$; including all gases with a critical temperature $\leq -50\text{ }^{\circ}\text{C}$.
Liquefied gas	A gas which, when packaged under pressure, is partially liquid at temperatures above $-50\text{ }^{\circ}\text{C}$. A distinction is made between: <ul style="list-style-type: none">i. high pressure liquefied gas: a gas with a critical temperature between $-50\text{ }^{\circ}\text{C}$ and $+65\text{ }^{\circ}\text{C}$; andii. low pressure liquefied gas: a gas with a critical temperature above $+65\text{ }^{\circ}\text{C}$.

With a critical temperature of $100\text{ }^{\circ}\text{C}$, H_2S meets the criteria for classification as low pressure liquefied gas when packaged in a receptacle at a pressure of 200 kPa (gauge) or more at $20\text{ }^{\circ}\text{C}$. This is in line with the classification assigned by the transport regulations (ADR/RID/ADN, entry 1053).

For gases under pressure Note U applies. According to this note, when put on the market, gases have to be classified in one of the groups: compressed gas, liquefied gas, refrigerated liquefied gas or dissolved gas. The group depends on the physical state in which the gas is packaged and therefore has to be assigned case by case. If it is packaged in a receptacle at a pressure of 200 kPa (gauge) or more at $20\text{ }^{\circ}\text{C}$, H_2S has to be classified as Press. Gas (Liq.); H280.

Since the 2nd ATP to the CLP Regulation (Reg. 286/2011), labelling with pictogram GHS04 (gas cylinder) is not required for gases under pressure where pictogram GHS02 (flame) or pictogram GHS06 (skull and crossbones) appears. As GHS02 and GHS06 apply to H_2S (due to classification as Flam. Gas 1A and Acute Tox. 2), the DS proposed to remove GHS04 from the labelling.

Comments received during consultation

A manufacturer supported the DS's proposal.

Assessment and comparison with the classification criteria

Flammable gases

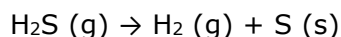
The classification criteria for flammable gases are given in CLP Annex I, Table 2.2.1.

With a flammable range of 3.9 to 50.2 mole % (approximately equal to volume %) and in the absence of data on fundamental burning velocity, H_2S meets the criteria for flammable gas 1A.

With an autoignition temperature of $270\text{ }^{\circ}\text{C}$, H_2S does not meet the criteria for a pyrophoric gas.

Chemical instability means the propensity of a gas to react dangerously even in the absence of any reaction partner (e.g., air or oxygen) by decomposing and thereby causing a temperature and/or pressure increase (UN Manual of tests and criteria, 35.1.2). Expert judgment should be applied to decide whether a flammable gas is a candidate for classification as chemically unstable in order to avoid unnecessary testing (UN-MTC, 35.2.4; Guidance on the application of the CLP criteria, 2.2.4.2).

No test according to the method described in UN-MTC section 35 is available. An inference on the liability of a substance to decompose in a closed system at a given temperature and pressure can be made from the Gibbs energy of the decomposition reaction. In this case, the standard Gibbs energy of the decomposition reaction:



at 25 °C is +33.4 kJ/mol. Generally, a negative Gibbs energy value indicates that the spontaneous direction of a reaction is as written in the equation. If the Gibbs energy is positive, as is the case here, the opposite reaction will occur spontaneously. Thus, the spontaneous reaction is H₂S formation, not decomposition, and H₂S can be considered chemically stable at 25 °C and a standard pressure of 101.3 kPa. Thus, the criteria for classification of H₂S as chemically unstable gas A are not met.

The criteria for chemically unstable gas B refer to 'a temperature greater than 20 °C and/or a pressure greater than 101.3 kPa'. On comparison with the UN test (UN-MTC 35.4.3.2b), these conditions appear to correspond to a temperature of 65 °C and the corresponding initial pressure (defined in UN-MTC 35.1.2). In general, for endothermic reactions (such as H₂S decomposition) the conversion increases with increasing temperature. Spontaneous decomposition of H₂S is reported to begin around 500 °C (Startsev, 2017), which means that H₂S is still stable at 65 °C. An increase in decomposition due to increased pressure will not occur as the amount of substance in gas phase on the right-hand side of the equation is equal to or higher than that on the left-hand side (depending on the physical state of H₂S and elemental sulfur). Consequently, the criteria for classification as chemically unstable gas, subcategory A or B, are not met.

In conclusion, the substance meets the criteria for flammable gas subcategory 1A but is not chemically unstable nor pyrophoric. Therefore, RAC agrees with the DS's proposal of **Flam. Gas 1A; H220**.

Gases under pressure

RAC agrees with the DS's proposal to retain the current classification as **Pres. Gas** with **Note U** and furthermore agrees that the hazard pictogram GHS04 can be omitted from the labelling.

HUMAN HEALTH HAZARD EVALUATION

RAC evaluation of acute inhalation toxicity

Summary of the Dossier Submitter's proposal

The current classification is Acute Tox. 2*. According to the DS, this classification is based on the lowest 4-hour rodent LC₅₀ of 444 ppm (Tansy *et al.*, 1981).

Besides animal data, the DS reviewed a number of reports of H₂S poisoning in humans. The DS proposed classification in Category 2 (100 ppm < ATE ≤ 500 ppm) with a converted ATE of 100 ppm based on human data. The following justification for the selected ATE is provided in the CLH report:

- The available rodent studies forming the basis of the current classification are old and were not conducted according to the current guidelines.
- While the minimum concentration causing lethality in humans is unknown, prolonged exposure to 100 ppm has been suggested to cause severe toxicity or lethality.
- Humans may be more sensitive than rodents.
- The dose-response relationship for lethality is very steep.
- Odour sensation (a warning sign) disappears from approx. 100 ppm.

- First neurological symptoms, i.e., loss of consciousness, disable victims from escaping the danger zone.
- The respiratory system is the main target organ, certain subpopulations (elderly, asthmatics, children) are more vulnerable.
- With the currently used ATE of 444 ppm, mixtures with an H₂S content below 22000 ppm are not classified. If the ATE is lowered 100 ppm, classification as Acute Tox. 4 will apply from 5000 ppm H₂S.

Comments received during consultation

Comments were received from a manufacturer, who made the following points:

- Although most of the animal data are relatively old and not conducted according to current guidelines, this does not negate their validity. The ATEs are rather consistent across studies, which confirms correctness of the studies.
- The available data suggest an ATE of 300-500 ppm (animal data) or 100-500 ppm (human data), which results in a classification as Acute Tox. 2, hence, Acute Tox. 1 would not be justified. Still, the DS proposed an ATE of exactly 100 ppm, which is in the range for Category 1 (ATE ≤ 100 ppm). The ATE should be in the range of > 100 to ≤ 500 ppm to avoid confusion.
- Hydrogen sulfide is mainly used as an intermediate in the EU. When used as an intermediate, technical and organisational measures are in place and low occupational exposure limits (e.g., 5 ppm) are complied with. Hydrogen sulfide is most dangerous as an unwanted (and sometimes unexpected) by-product, e.g., in sewers, biogas plants, manure. It is questionable whether a stricter harmonised classification will lead to a higher level of safety for the workers concerned.

The DS replied that by using the ATE of 100 ppm a mixture containing 5000 ppm would still be labelled as acutely toxic, whereas otherwise a warning sign would not be applied. The DS acknowledged in the reply to comments received during the consultation that an ATE of 100 ppm may lead to confusion but did not change their proposal.

Assessment and comparison with the classification criteria

Animal data

Acute studies using a 4-hour exposure

The available acute studies employing a 4-hour exposure are summarized in the following table. The results of Tansy *et al.* (1981) and Prior *et al.* (1988) are considered sufficiently robust for classification purposes. The lowest LC₅₀ of 444 ppm comes from a study by Tansy *et al.* (1981), this result is very close to the LC₅₀ of 501 ppm reported by Prior *et al.* (1988). The dose-response relationship for lethality was rather steep in both studies: from 30% at 400 ppm to 100% at 600 ppm in Tansy *et al.*, and from 0% at ca. 300 ppm to 100% at ca. 600 ppm in Prior *et al.*

Acute studies using a 4-hour exposure		
Species; reference	Method	LC ₅₀ (ppm)
Rat Strain: Sprague-Dawley Tansy <i>et al.</i> (1981)	Concentrations: 0, 400, 440, 475, 500, 525, 554, 600 ppm 5/sex/concentration 14-day postexposure period	444

Rat Strain: Long Evans, Sprague Dawley, Fischer 344 Prior <i>et al.</i> (1988)	Concentrations: 8 concentration levels, ca. 300-600 ppm (estimated from a graph) 9/sex/concentration (pooled strains) 14-day postexposure period	501
Rat Strain: F344 Khan <i>et al.</i> (1990)	Mechanistic study (no aim to determine an LC ₅₀ value) Males Concentrations: 0, 10, 50, 200, 400, 500-700 ppm; 4-6 animals per concentration, killed immediately after exposure Post-exposure effects monitored at 0, 200 and 400 ppm; 4 animals per concentration and time point killed at 1, 24 or 48 hours post-exposure	LC ₅₀ not determined No mortality up to 400 ppm Mortality during exposure at 500-700 ppm

Acute studies using other exposure durations

Two studies in rats and mice employed a 1-hour exposure. An LC₅₀ from a 1-hour exposure can be converted to a 4-hour ATE by dividing by a factor of 2 for gases (CLP, Annex I, note to Table 3.1.1). The experimentally determined and converted LC₅₀ values are presented in the following table. Nevertheless, robust experimentally determined 4-hour LC₅₀ values, where available, are considered preferable to ATEs extrapolated from a 1-hour exposure.

Acute studies using a 1-hour exposure			
Species; reference	Method	Experimentally determined 1-hour LC₅₀ (ppm)	Converted 4-hour LC₅₀ (ppm)
Rat Strain: Wistar Zwart <i>et al.</i> (1990)	Concentrations: 318, 499, 550, 572, 586, 667, 690 ppm 5/sex/concentration 14-day postexposure period	675	338
Rat Strain: Sprague-Dawley THRU Laboratories (1972)	Concentrations: 400, 504, 635, 800 ppm 10 males/concentration 14-day postexposure period	712	356
Mouse Strain: Swiss Zwart <i>et al.</i> (1990)	Concentrations: 318, 499, 550, 572, 586, 667, 690 ppm 5/sex/concentration 14-day postexposure period	667	334
Mouse Strain: CF-1 THRU Laboratories (1972)	Concentrations: 400, 504, 635, 800 ppm 10 males/concentration 14-day postexposure period	634	317

Some studies investigated mortality after exposures shorter than 1 hour. Zwart *et al.* (1990) reported a 10-min LC₅₀ of 824 ppm in rats and 1143 ppm in mice. In a study by Lopez *et al.* (1989), all rats exposed to ca. 1660 ppm died within 3 minutes. Exposure to 500-1000 ppm for 14-30 minutes was lethal for rabbits (Kage *et al.*, 1992).

Lund and Wieland (1966) exposed 3 rhesus monkeys to a concentration of 500 ppm. The animals became unconscious and stopped breathing after 17 to 35 minutes of exposure.

Human data

Hydrogen sulfide poisoning in humans, with its distinct features, was first described in the 18th century in relation to sewers. H₂S intoxication with a fatal outcome still continue to occur. The typical features of H₂S toxicity are the following (adapted from Guidotti, 2010):

- “Knockdown”
- Pulmonary oedema
- Conjunctivitis
- Odour perception followed by olfactory paralysis

An abrupt loss of consciousness, colloquially called a “knockdown”, occurs due to an acute effect on the central nervous system. Knockdowns can be acutely fatal as a consequence of respiratory paralysis and cellular anoxia. A knockdown may be fatal if exposure at a concentration of ca. 500 to 1000 ppm is prolonged, but if exposure is transient, it may also be reversible. At concentrations in excess of ca. 1000 ppm breathing may stop within 1 or 2 breaths and the collapse is practically immediate, often leading to death.

H₂S is irritating to mucous membranes. This mostly affects the deep lung and the epithelium of the eye. Eye irritation may occur from ca. 50 ppm. The concentration threshold for induction of pulmonary oedema (resulting from cytotoxic alveolar injury) after prolonged exposure is reported to lie around 250 ppm (Guidotti, 2010; OSHA, 2019; Knight and Presnell, 2005).

H₂S has an unpleasant odour of rotten eggs. The odour threshold is in the order of 0.01 to 0.1 ppm. At higher concentrations the odour becomes rather offensive. However, around 100 ppm the odour disappears due to paralysis of olfactory nerves (a neurotoxic effect). Unfortunately, this phenomenon removes the primary warning sign of H₂S exposure.

The CLH report summarizes a number of case reports from poison centres (Table 12) and the open literature (Table 13). Exposure information is often missing or inadequate, and the contribution of other toxicants, mechanical trauma (due to a fall at the moment of knockdown) or liquid aspiration (after a fall into a liquid or slurry) cannot be excluded in some of the cases. The cases from Table 13 of the CLH report for which measured H₂S concentrations are available have been summarized below. In some cases, the H₂S concentration was above the measuring range of the device (e.g. > 100 ppm).

Human cases from the CLH report for which a measured H ₂ S concentration is available				
Reference	Setting	Outcome	Measured H ₂ S concentration; exposure duration (if known)	Remarks
Will (2005)	Biogas plant	4 dead, 11 injured	On the next day: > 100 ppm Exposure duration: 20-30 min	
Christia-Lotter <i>et al.</i> (2007)	Sewer	1 dead	1 h after the accident: > 30 ppm Exposure duration: > 40 min	
Nogue <i>et al.</i> (2011)	Silo with sludge from water treatment plants	3 dead	6 h after accident: 100 ppm	
Knight and Presnell (2005)	Sewer (manhole)	2 dead	Before retrieving the bodies but sometime after the incident: 34 ppm	

Human cases from the CLH report for which a measured H ₂ S concentration is available				
Reference	Setting	Outcome	Measured H ₂ S concentration; exposure duration (if known)	Remarks
Osbern and Crapo (1981)	Liquid manure storage pit	3 dead, 1 injured	8 days after the accident (different conditions): 76 ppm	2 of the dead had massive aspiration of manure
Hsu (1987)	Not specified	5 dead, 5 injured	4 h after the accident: 429 ppm	
Kage <i>et al.</i> (2004)	Dye works, spillage of H ₂ S-containing sludge	4 dead	After the accident: 1 ppm At a reconstruction of the accident 2 months later: 850 ppm	The victims had sludge in airways
Kage <i>et al.</i> (2002)	Industrial waste site, pit for seepage collection	3 dead, 1 injured	6 h after the accident: 1400 ppm	
Kage <i>et al.</i> (1998)	Geothermal power plant, oil separator room	1 dead	At a simulation on the accident site one week later: 3500-5000 ppm	
Kage <i>et al.</i> (1997), case 1	Factory producing regenerated paper	4 injured	3 h after the accident: 114 ppm	
Kage <i>et al.</i> (1997), case 2	Wastewater tank in a hospital	1 dead	1 month after the accident: > 150 ppm	
Kage <i>et al.</i> (1997), case 3	Drainage pump room, spillage of sewage	1 dead	4 h after the accident: 123 ppm	
Gabbay <i>et al.</i> (2001)	Sour gas line in an oil refinery	1 injured	30 min after the accident: 1000 ppm	A pipe fitter fell from a ladder after exposure to sour gas from a pipe, the fall prevented further exposure
Smilkstein <i>et al.</i> (1985)	Wastewater from oil-pumping operation	1 injured	Air above a sample of the tank contents: 717 ppm Exposure duration: 5-10 min	
NIOSH (1991)	Sewer manhole in a hide tanning factory	2 dead	6 days after the accident: 200 ppm	Both victims found in a tank with liquid waste, faces underwater

Human cases from the CLH report for which a measured H ₂ S concentration is available				
Reference	Setting	Outcome	Measured H ₂ S concentration; exposure duration (if known)	Remarks
Gregorakos <i>et al.</i> (1995)	Sewer containing wine outcasts	5 dead, 3 injured	> 800 ppm	
Kilburn (1993)	Offshore oil rig	1 injured	14000 ppm, the worker was wearing a supplied-air respirator	
Tanaka <i>et al.</i> (1999)	Petroleum refinery	3 injured	The affected workers opened a pipe with a gas containing 15000 ppm H ₂ S	Estimated exposure concentrations 250-600 ppm and 500-900 ppm, but no information on how these estimates were obtained

For very few cases in the table does measured data exist that can be considered to reflect the actual exposure of the victims with reasonable certainty (e.g., the simulations by Kage *et al.*, 1998, 2004). These limited data do not contradict the general consensus that even short exposures to H₂S concentrations above 500 ppm can be lethal.

The case described by Kage *et al.* (2004) provides an important piece of information regarding the stability of H₂S concentrations after an accident. A worker suddenly lost consciousness after spillage of H₂S-containing sludge in a pit. Three other workers entered the pit to rescue him but lost consciousness too. They were sent to hospitals but died 1-3 h after the accident. All had black sludge in their airways. Although the H₂S concentration determined in the pit after rescuing the victims was as low as 1 ppm, 850 ppm was measured in the pit during a simulation of the accident 2 months later. Further details of this case can be found in the Background Document.

The DS, in their argumentation for an ATE of 100 ppm, referred to several cases where the concentration measured sometime after the accident was around or below 100 ppm (Knight and Presnell, 2005; Osbern and Crapo, 1981; Nogue *et al.*, 2011; Kage *et al.*, 1997). The details of these cases are provided in the Background Document. However, as demonstrated by Kage *et al.* (2004), the concentration measured sometime after the accident may be orders of magnitude below that present at the moment the victims were losing consciousness. If this is not taken into account, erroneous conclusions may be drawn on the thresholds of H₂S toxicity.

In this context, some doubts arise about the statements in UBA (2006) and OSHA (2019) that concentrations below 100 ppm are dangerous to life within several hours, or that at 100 ppm death may occur after 48 hours. Unfortunately, no evidence allowing verification of this information is provided in those two references nor in the CLH report. Nor do these sources provide an explanation regarding the mode of action leading to death in this concentration range (pulmonary oedema is stated to occur from 200-300 ppm in OSHA, 2019; no mention of pulmonary oedema in UBA, 2006). RAC notes that a number of other sources refer to death or life-threatening symptoms only at higher concentrations (e.g., Guidotti, 2010; Knight and Presnell, 2005; NIOSH 2014; WHO, 2003; for more details see the Background Document). According to these latter references, death may occur from prolonged exposure 250-500 ppm, with the mortality being primarily linked to pulmonary oedema in this concentration range. Higher exposures in excess of ca. 500-700 ppm usually cause death quickly primarily via a neurotoxic effect.

NIOSH (2014) derived an IDLH (Immediately Dangerous to Life or Health value) for H₂S of 100 ppm, cited by the DS in support of an ATE of 100 ppm. IDLH is defined as a maximum airborne concentration level above which only a highly reliable breathing apparatus providing maximum worker protection is permitted (NIOSH, 2013). The IDLH for H₂S has been derived using the estimated animal and human 30-min lowest lethal concentrations as points of departure (ranging from 354 to 1141 ppm), which were then divided by an assessment factor of 10. Other human information was considered in addition, for example a reference stating that 170 to 300 ppm is the maximum concentration that can be endured for 1 hour without serious consequences. Thus, the IDLH for H₂S has been derived from, but is not equal to, ATE values.

Several references listed in the CLH report suggest that the lowest concentration that may cause mortality in humans after prolonged exposure lies around 250 ppm and appears to be related to pulmonary oedema. Two sources suggest mortality at or below 100 ppm. Unfortunately, RAC has not identified in the dossier primary information that would allow verification of lethal effects at either concentration. Sufficiently robust evidence is provided in the dossier for lethality only at concentrations in excess of 700-1000 ppm.

Conclusion

The lowest 4-hour rodent LC₅₀ was derived from a reliable study is 444 ppm (Tansy *et al.*, 1981). The threshold for mortality in rats after a 4-hour exposure lies in the range of 300-350 ppm (Prior *et al.*, 1988).

The primary human information provided in the CLH report documents mortality after a brief exposure to ca. 700-1000 ppm (Kage *et al.*, 2004). Reviews of human data indicate a threshold for mortality after short exposure of about 500-700 ppm, and a potentially lethal pulmonary oedema from prolonged exposure to ca. 250 ppm. It is possible that these thresholds are based on a combination of human and animal information.

RAC acknowledges the difficulty in determination of exposure concentration over a longer period (e.g., hours) in human poisoning cases because of fluctuations and a steep dose-response. For example, a lethal knockdown may be caused by a brief peak of e.g., 2000 ppm, but the toxic atmosphere may be diluted with air shortly thereafter, before rescue personnel arrived and measurements were taken. For this reason, and in the absence of well documented poisoning cases at exposure levels below the 4-hour mortality threshold in rats (i.e., 300-350 ppm), it is not possible to conclude that humans are more sensitive than rats. Consequently, RAC gives preference to the animal ATE of 444 ppm, rounded off to 440 ppm.

In conclusion, RAC proposes a classification with **Acute Tox. 2; H330** and an **ATE of 440 ppm** based on a 4-hour acute toxicity study in rats.

Additional references

NIOSH (2013) Current intelligence bulletin 66: derivation of immediately dangerous to life or health (IDLH) values. NIOSH Publication 2014-100. Online:

<https://www.cdc.gov/niosh/docs/2014-100> (accessed 04/06/2021)

Policastro and Otten (2007) Case files of the University of Cincinnati fellowship in medical toxicology: two patients with acute lethal occupational exposure to hydrogen sulfide. *Journal of Medical Toxicology*, 3:73-81

Startsev (2017) The reaction mechanisms of H₂S decomposition into hydrogen and sulfur: application of classical and biological thermodynamics. *Journal of Thermodynamics & Catalysis* 8:2, doi: 10.4172/2157-7544.1000186

ANNEXES:

- Annex 1 The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in 'RAC boxes'.
- Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).