CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2

International Chemical Identification:

Hydrogen Sulfide; Hydrogen Sulphide

EC Number: **231-977-3**

CAS Number: **7783-06-4**

Index Number: **016-001-00-4**

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CONTENTS

1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	hydrogen sulfide
Other names (usual name, trade name, abbreviation)	hydrogen sulfide, sulfane
EC number	231-977-3
EC name	hydrogen sulphide
CAS number	7783-06-4
Molecular formula	H_2S
Structural formula	
SMILES notation	S
Molecular weight or molecular weight range	34.0809 g/mol
Degree of purity (%)	not relevant

1.2 Composition of the substance

Table 2: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
See table 6			

Table 3: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The impurity contributes to the classification and labelling
-				

Table 4: Additives (non-confidential information) if relevant for the classification of the substance

Additive (Name and numerical identifier)	Function	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The additive contributes to the classification and labelling
-					

Table 5: Test substances (non-confidential information) (this table is optional)

Identification of test substance	Purity	Impurities and additives (identity, %, classification if available)	Other information	The study(ies) in which the test substance is used
-				

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 6: 1.1 Proposed harmonised classification and labelling according to the CLP criteria

	Index No	International Chemical Identification	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	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		hydrogen sulphide, hydrogen sulfide			**Remove** Acute Tox. 2* **Add** Acute Tox. 2 **Modify** Flam. Gas 1A **Maintain** Press. Gas Aquatic Acute 1	 H330 H330 H220 H400	GHS02 GHS06 GHS09 Dgr	H220 H330 H400		**Add** Inhalation: ATE = 100 ppmV (gases)	Note U
Resulting Annex VI entry if agreed by RAC and COM					Press. Gas Flam. Gas 1A Acute Tox. 2 Aquatic Acute 1	 H220 H330 H400	GHS02 GHS06 GHS09 Dgr	H220 H330 H400		Inhalation: ATE = 100 ppmV (gases)	Note U

Table 7: Reason for not proposing harmonised classification and status under public consultation

Hazard class	Reason for no classification	Within the scope of public consultation
Explosives	hazard class not assessed in this dossier	No
Flammable gases (including chemically unstable gases)	**harmonised classification proposed**	**Yes**
Oxidising gases	hazard class not assessed in this dossier	No
Gases under pressure	**harmonised classification proposed**	**Yes**
Flammable liquids	hazard class not assessed in this dossier	No
Flammable solids		
Self-reactive substances		
Pyrophoric liquids		
Pyrophoric solids		
Self-heating substances		
Substances which in contact with water emit flammable gases		
Oxidising liquids		
Oxidising solids		
Organic peroxides		
Corrosive to metals		
Acute toxicity via oral route		
Acute toxicity via dermal route		
Acute toxicity via inhalation route	**harmonised classification proposed**	**Yes**
Skin corrosion/irritation	hazard class not assessed in this dossier	No
Serious eye damage/eye irritation		
Respiratory sensitisation		
Skin sensitisation		
Germ cell mutagenicity		
Carcinogenicity		
Reproductive toxicity		
Specific target organ toxicity-single exposure		
Specific target organ toxicity-repeated exposure		
Aspiration hazard		
Hazardous to the aquatic environment		
Hazardous to the ozone layer		

3 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

According to Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation), hydrogen sulfide is currently allocated to the hazard category acute inhalation toxicity (H330: fatal if inhaled), category 2. As the hazard category is provided with an asterisk, the classification is considered the minimum classification (lowest possible classification) as a result of the translation from the old DSD legislation. The current harmonised classification for physical hazard classes "Flammable gases" and "Gases under pressure" have been reassessed due to the Adaptation to classification criteria by Regulation (EU) 2019/521 (12th ATP to CLP) and Commission Regulation (EU) No 286/2011 (2nd ATP to the CLP Regulation).

4 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

[B.] Justification that action is needed at Community level is required.

Reason for a need for action at Community level:

- *Change in existing entry due to new interpretation/evaluation of existing data*
- *Differences in self-classification*
- *Requirement for harmonised classification by other legislation or process.*

5 IDENTIFIED USES

Hydrogen sulfide is used by consumers, by professional workers (widespread uses), in formulation or re-packing, at industrial sites and in manufacturing. According to the registration data the application fields for hydrogen sulfide are agriculture, forestry and fishing and municipal supply (e.g. electricity, steam, gas, water) and sewage treatment. Further uses are the manufacture of chemicals, pulp, paper and paper products, food products, textile, leather, wood and wood products.

6 DATA SOURCES

Sources: PUBMED, SCOPUS, WEB OF SCIENCE, ECHA dissemination site, IUCLID (registration data)

7 PHYSICOCHEMICAL PROPERTIES

Table 8: Summary of physicochemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	Gaseous, colourless	(NIOSH, 1994)	
Melting/freezing point	-86 °C	(Nabert and Schoen, 1963)	
Boiling point	-60 °C	(Nabert and Schoen, 1963)	
Relative density	1.19	(BAM, 2010)	
Vapour pressure	20 851 hPa at 25 °C	(Daubert and Danner, 1989)	
Surface tension			Study is scientifically not necessary.
Water solubility	3 980 mg/L at 20 °C	(Kirk-Othmer, 1991)	
Partition coefficient n-octanol/water			Hydrogen sulfide is an inorganic compound. Therefore, partition coefficient determination is not required.
Granulometry			The particle size distribution study does not need to be conducted, as hydrogen sulfide is a gaseous substance.
Stability in organic solvents and identity of relevant degradation products	Avoid mixtures with amines (methylamine, dimethylamine, trimethylamine, ethyl amine), ethylene oxide, ammonia, fluorine, chlorine, sulphur dioxide, nitrogen dioxide.		
Viscosity	0.0128 mPa s at 25 °C	(Braker and Mossmann, 1980)	

8 EVALUATION OF PHYSICAL HAZARDS

The current harmonised classification for physical hazard classes "Flammable gases" and "Gases under pressure" have been reassessed due to the Adaptation to classification criteria by Regulation (EU) 2019/521 (12th ATP to CLP)

8.1 Flammable gases

Table 9: Summary table of studies on flammable gases

Method	Results	Remarks	Reference
DIN EN 1839-T (Tube method) as referred to in CLP Annex I Section 2.2.4.1.	Lower explosion limit: 3.9 mol% Upper explosion limit: 50.2 mol% (for an ideal gas: mol% = vol%)	Temperature/Pressure: at 20 °C / 101.3 kPa	CHEMSAFE (2016)
The lower and upper explosion levels are determined in closed or small vessels.	Lower Explosion Limit (LEL) = 4.3 % (vol) Upper Explosion Limit (UEL) = 45 % (vol)		Coward H.F. and Jones G. W. (1952)
No data	Lower Explosion Limit (LEL) = 4.3 % (vol air) Upper Explosion Limit (UEL) = 45.5 %		Nabert K. and Schoen G. (1963)
No data	Lower Explosion Limit (LEL) = 4.0 % (vol) Upper Explosion Limit (UEL) = 44.0 % (vol)		Zabetakis M. G. (1965)
DIN 51794	Auto ignition temperature: 270 °C	at 1 atm (101.3 kPa)	Nabert K. and Schoen G. (1963)

Expert statement on Hydrogen sulfide as a chemically unstable gas (Schröder, V. (2020):

Hydrogen sulfide is not chemically unstable in the sense of the test method according to the UN Manual of Tests and Criteria, Part III, Section 35 "DETERMINATION OF CHEMICAL INSTABILITY OF GASES AND GAS MIXTURES".
This can be derived from the thermodynamic data for the possible degradation reaction shown in equation (1):

H_2S (g) => H_2 + S Gibbs Free Energy = +33,4 kJ/mol (1)

The free standard reaction enthalpy is +33.4 KJ/mol (Lit.: THE PROPERTIES OF GASES AND LIQUIDS, Bruce E. Poling, John M. Prausnitz and John P. O'Connell, Fifth Edition, McGRAW-HILL, New York 2001). This does not release energy but consumes it. Another decomposition reaction, which possibly releases energy, is not conceivable with the molecular structure of Hydrogen sulfide. Experimental testing can therefore be dispensed with.

8.1.1 Short summary and overall relevance of the provided information on flammable gases

The explosion limits at atmospheric conditions were determined with an apparatus in accordance with EN 1839 "Tube method", which is a so-called "open vessel method". Experimental data on lower and upper explosion limit are 3.9 mol%- 50.2 mol%.

Registration dossier reported data on the upper and lower explosion limits from scientific literature, in which the methods were not provided.

In Europe, the determination of explosion limits at atmospheric conditions is standardized by EN 1839. The used EN 1839:2003 comprises two different methods: the tube method (T) and the bomb method (B). The tube method uses the visual ignition criterion. A mixture which is ignited in a transparent cylindrical test vessel (h = 300 mm, r = 40 mm) is seen as flammable either when a flame detaches from the ignition source and moves upward for more than 100 mm.

Explosion limits are not independent physicochemical parameters. They are influenced by the determination method and by apparatus parameters, as most safety characteristics are. To ensure comparability, the international standardization of determination methods is particularly important. According to the European standard EN 1839 the explosion limit itself is not a part of the explosion range. Instead the lower explosion limit (LEL) is the highest concentration of a flammable gas in a gaseous mixture, in which a flame just fails to propagate after ignition. Therefore, for the purpose of classification, the information on explosion limits determined in accordance with a European standard should be taken into account.

Pyrophoricity shall be determined at 54 °C in accordance with DIN 51794 "Determining the ignition temperature of petroleum products". The auto-ignition temperature has been determined at 270 °C which excludes spontaneous ignition in air at a temperature of 54 °C or below.

Hydrogen sulfide does not need to be considered as a chemically unstable gas, based on the free standard reaction enthalpy.

8.1.2 Comparison with the CLP criteria

Flammable gas means a gas or gas mixture having a flammable range with air at 20 °C and a standard pressure of 101,3 kPa. The flammability range of a flammable gas is defined between the ''lower explosion limit'' (LEL) in air and the ''upper explosion limit'' (UEL) in air.

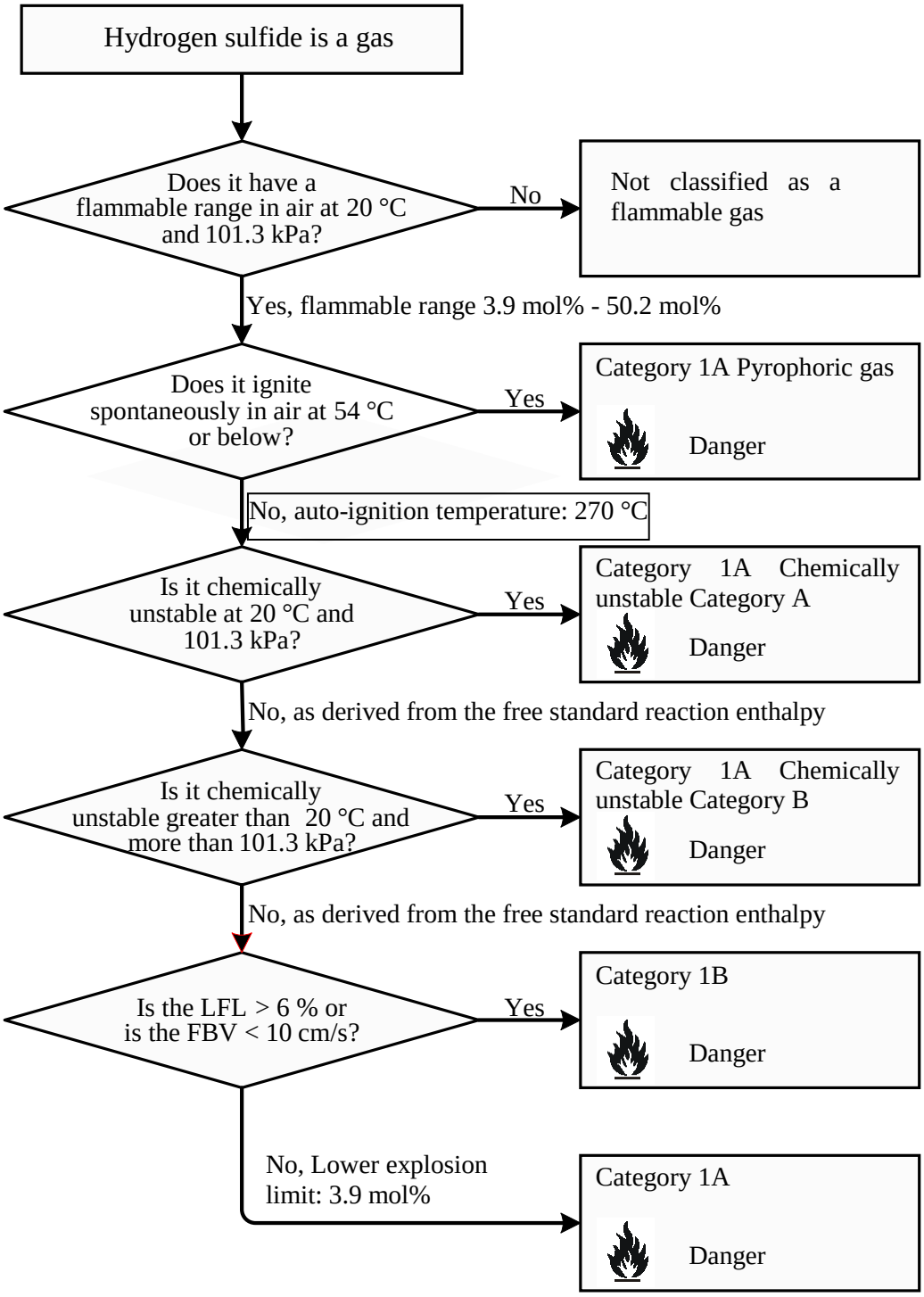
The criteria for category 1 have been amended by Regulation (EU) 2019/521 (12th ATP to CLP) as a new sub-classification in categories 1A and 1B of the hazard class "flammable gases. The CLP Regulation considers for flammable gases three categories 1A, 1B and 2. Category 1A is divided in four sub-categories: Flammable gas, Pyrophoric gas, Chemically unstable gas A and Chemically unstable gas B.

Criteria for categorization of flammable gases which have been amended by Regulation (EU) 2019/521 (12th ATP to CLP):

Category			Criteria
1A	Flammable gas		Gases, which at 20 °C and a standard pressure of 101,3 kPa are: (a) ignitable when in a mixture of 13 % or less by volume in air; or (b) have a flammable range with air of at least 12 percentage points regardless of the lower flammability limit unless data show they meet the criteria for Category 1B
	Pyrophoric gas		Flammable gases that ignite spontaneously in air at a temperature of 54 °C or below
	Chemically unstable gas	A	Flammable gases which are chemically unstable at 20 °C and a standard pressure of 101,3 kPa
		B	Flammable gases which are chemically unstable at a temperature greater than 20 °C and/or a pressure greater than 101,3 kPa
1B	Flammable gas		Gases which meet the flammability criteria for Category 1A, but which are not pyrophoric, nor chemically unstable, and which have at least either: (a) a lower flammability limit of more than 6 % by volume in air; or (b) a fundamental burning velocity of less than 10 cm/s;
2	Flammable gas		Gases, other than those of Category 1A or 1B, which, at 20 °C and a standard pressure of 101,3 kPa, have a flammable range while mixed in air.

Due to the flammable range at 20 °C and a standard pressure of 101,3 kPa between 3.9 mol% and 50.2 mol%, hydrogen sulfide fulfills the criteria for Category 1A as the lower explosion limit of more than 6 % by volume in air for Category 1B is not meet. Within Category 1A, hydrogen sulfide does not meet the criteria for classification as a pyrophoric and chemically unstable gas.

The classification procedure, in slightly modified form of the decision logic in section 2.3.3 in Figure 2.2.1



8.1.3 Conclusion on classification and labelling for flammable gases

Due to the lower explosion limit of 3.9 mol% and the given criteria hydrogen sulfide has to be classified as “Flam. Gas 1A, H220”. H220: Extremely flammable gas.

8.2 Gases under pressure

Table 10: Summary table of studies on gases under pressure

Properties of gases under pressure	Results	Remarks	Reference
Vapour pressure at 50 °C	3650.0 kPa		Molnarne, M., Schendler, Th., Schröder, V., (2008)
Vapour pressure at 20 °C	1810.0 kPa		
Critical temperature	100.1 °C		
Critical pressure	8937 kPa		
Critical density	0.346 g/cm^3		

8.2.1 Short summary and overall relevance of the provided information on gases under pressure

The Registration dossier provides the classification as "Liquefied gas H280: Contains gas under pressure; may explode if heated" without further information. The hazard class 'Gases under pressure' corresponds to Class 2 'Gases' in the UN RTDG Model Regulations and hydrogen sulfide is mentioned by name in the Dangerous Goods List in Chapter 3.2.and is assigned to UN No 1053.

8.2.2 Comparison with the CLP criteria

According to Section 2.5.1.1 of Annex I of CLP, Gases under pressure are gases which are contained in a receptacle at a pressure of 200 kPa (gauge) or more, or which are liquefied or liquefied and refrigerated. They comprise compressed gases, liquefied gases, dissolved gases and refrigerated liquefied gases.
For this group of gases, the following information is required to be known:
— the vapour pressure at 50 °C;
— the physical state at 20 °C at standard ambient pressure;
— the critical temperature.
In addition, pure gases are already classified in the UN Recommendations on the Transport of Dangerous Goods, Model Regulations.

Gases under pressure shall be classified, according to their physical state when packaged, in one of four groups in accordance with Table 2.5.1 in Annex I of CLP:

Group	Criteria
Compressed gas	A gas which when packaged under pressure is entirely gaseous at - 50 °C; including all gases with a critical temperature ≤ - 50 °C.
Liquefied gas	A gas which, when packaged under pressure, is partially liquid at temperatures above - 50 °C. A distinction is made between: i) high pressure liquefied gas: a gas with a critical temperature between - 50 °C and + 65 °C; and ii) low pressure liquefied gas: a gas with a critical temperature above + 65 °C.
Refrigerated liquefied gas	A gas which when packaged is made partially liquid because of its low temperature.
Dissolved gas	A gas which when packaged under pressure is dissolved in a liquid phase solvent.

Compressed and liquefied gases are distinguished based on the critical temperature .
Due to the critical temperature of 100.1 °C, hydrogen sulfide fulfills the criteria for a low pressure liquefied gas.

The dangerous goods of Class 2 in ADR/RID/ADN indicate with a number in the 'classification code' the 'groups' of 'gases under pressure'.

Classification code in ADR/RID/ADN	Corresponding groups according to CLP
1	Compressed gases
2	Liquefied gases
3	Refrigerated liquefied gases
4	Dissolved gases

Hydrogen sulfide is assigned to UN No 1053 and classification code in ADR is “2TF”, which means “Liquefied, toxic, flammable gas”.

8.2.3 Conclusion on classification and labelling for gases under pressure

For gases under pressure “Note U” applies:

When put on the market gases have to be classified as ‘Gases under pressure’, 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. The following codes are assigned:

Press. Gas (Comp.)

Press. Gas (Liq.)

Press. Gas (Ref. Liq.)

Press. Gas (Diss.)

In case when packaged in a receptacle at a pressure of 200 kPa (gauge) or more at 20 °C, hydrogen sulfide has to be classified as “Press. Gas (Liq.), H280”. H280: Contains gas under pressure; may explode if heated.

Labelling with pictogram GHS04 (gas cylinder) is not required for gases under pressure where pictogram GHS02 (flame) or pictogram GHS06 (skull and crossbones) appears. This precedence rule was introduced by the Regulation (EU) No 286/2011 (2nd ATP to the CLP Regulation).

9 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

Not addressed in this dossier.

10 EVALUATION OF HEALTH HAZARDS

Acute toxicity

10.1 Acute toxicity - oral route

Not addressed in this dossier.

10.2 Acute toxicity - dermal route

Not addressed in this dossier.

10.3 Acute toxicity - inhalation route

Table 11: Summary table of animal studies on acute inhalation toxicity

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, form and particle size (MMAD)	Dose levels, duration of exposure	Value LC_{50}	Reference
Acute inhalation toxicity study (published journal article) No guideline specified No GLP Deviations: no individual observation records, purity not specified	**Rat** Sprague-Dawley Male/female n = 5 (sex/conc.)	hydrogen sulfide (purity: not specified) 231-977-3	Concentration: Control, 400, 440, 475, 500, 525, 554, and 600 ppm Duration: **4 h** inhalation of H_2S gas + 14 days observation	*LC50 (4 h):* **444 ppm** (95 % CL: 416 – 473)	(Tansy et al., 1981)
Acute inhalation toxicity study (published journal article) No guideline specified No GLP Deviations: test concentrations not specified, no response data and concentration level for each animal, no individual observation records (clinical	**Rat** Long Evans, Sprague Dawley, and Fischer 344 Male/female n = 9-12 (sex/conc.)	hydrogen sulfide (purity: 99.5 %) 231-977-3	Concentration: Control + various concentrations (not specified) Duration: **2 h, 4 h** and **6 h** inhalation of H_2S gas + 14 days observation	*LC50 (2, 4, 6 h):* 587 ppm (2 h), **501 ppm** (4 h), 335 ppm (6 h) Mortality and weight loss was higher in males as compared to females (details not specified)	(Prior et al., 1988)

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, form and particle size (MMAD)	Dose levels, duration of exposure	Value LC_{50}	Reference
signs, histological examination)					
Acute inhalation toxicity study (published journal article) No guideline specified No GLP Deviations: no individual observation records, purity not specified, younger animals, shorter exposure duration, weight changes, clinical signs, and necropsy findings not reported	**Rat** Wistar Male/female **Mouse** Swiss Male/female n = 5 (species/sex/conc.)	hydrogen sulfide (purity: not specified) 231-977-3	Concentration (in mg/m^3): *5 min:* 931, 1196, 1831 *10 min:* 931, 1199, 1821 *30 min:* 449, 706, 813, 833, 881, 935, 972, 1032 60 min: 448, 703, 774, 806, 826, 939, 972 No control Duration: **5, 10, 30** and **60 min** inhalation of H_2S gas + 14 days observation	*LC50 (10, 30, 60 min):* *Rat (mg/m^3;ppm*):* 1160;824 (10 min) 1010;717 (30 min) 950;675 (60 min) *Mouse (mg/m^3;ppm):* 1610;1143 (10 min) 1110;788 (30 min) 940;667 (60 min) *****calculated according to: 1 mg/m3 = 0.71 ppm (WHO (CICAD) (2003))	(Zwart et al., 1990)
Acute inhalation toxicity study (study report, publicly available) No guideline specified No GLP Deviations: one sex only, no individual observation records, purity not specified, shorter exposure duration, age not specified	**Rat** Sprague-Dawley Male **Mouse** CF-1 Male n = 10 (species/conc.)	hydrogen sulfide (purity: not specified) 231-977-3	Concentration: 400, 504, 635, and 800 ppm No control Duration: **1 h** inhalation of H_2S gas + 14 days observation	*LC50 (1 h):* *Rat:* 712 ppm *Mouse:* 634 ppm	(THRU Laboratories, 1972)
Acute inhalation toxicity study (published journal article) No guideline specified No GLP Deviations: one concentration only, only mean concentration	**Rat** Sprague-Dawley Male n = 5 (conc.)	hydrogen sulfide (purity: not specified) 231-977-3	Concentration: Control and 1655.4 +/- 390.9 ppm (mean) Duration: **5 min** inhalation of H_2S gas	*LC100 (3 min):* 1655.4 +/- 390.9 ppm	(Lopez et al., 1989)

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, form and particle size (MMAD)	Dose levels, duration of exposure	Value LC_{50}	Reference
reported, one sex only, no individual observation records, purity not specified, older animals (twice as old as recommended)					
Acute inhalation toxicity study (published journal article) No guideline specified No GLP Deviations: number of animals per group only as range, one sex only, no individual observation records, purity not specified, shorter observation period, concentration only as range	**Rat** Fischer 344 Male n = 4-6 (conc.)	hydrogen sulfide (purity: not specified) 231-977-3	Concentration: Control, 10, 50, 200, 400, and 500-700 ppm Duration: **4 h** inhalation of H_2S gas + 1, 24 and 48 h observation (only for 0-400 ppm)	No deaths observed in animals exposed to 0-400 ppm All animals died at 500-700 ppm	(Khan et al., 1990)
Acute inhalation toxicity study (published journal article) No guideline specified No GLP Deviations: one animal/group only, sex not specified, purity not specified, shorter observation period, age and weight not specified	**Monkey** Rhesus Sex not specified n = 1 per treatment (3 animals in total)	hydrogen sulfide (purity: not specified) 231-977-3	Concentration: 500 ppm No control Duration: *Animal 1:* 35 min *Animal 2:* 25 min and 17 min (3 days later) + 5 days observation *Animal 3:* 22 min + 10 days observation	*Animal 1:* acute respiratory and cardiac arrest with lethality *Animal 2:* survived exposure with necrotic alterations of the cerebral cortex and basal ganglia *Animal 3:* survived exposure with necrotic alterations of the cerebral cortex	(Lund and Wieland, 1966)
Acute inhalation toxicity study (published journal article) No guideline	**Rabbit** Japanese White Sex not specified	hydrogen sulfide (purity: not specified)	Concentration: 100-200 ppm 500-1000 ppm Duration:	All animals (5/5) died at 500-1000 ppm	(Kage et al., 1992)

Method, guideline, deviations if any	Species, strain, sex, no/group	Test substance, form and particle size (MMAD)	Dose levels, duration of exposure	Value LC_{50}	Reference
specified No GLP Deviations: sex not specified, no individual observation records, purity not specified, shorter duration, concentration only as range, shorter observation period	n = 5 (conc.)	231-977-3	14-30 min. + 2 h and 24 h observation		

Table 12: Summary table of case reports from national poison centres and adverse event notification schemes

Type of data/ year/toxicant/ route of exposure	Relevant information (case description)	Observations (symptoms, outcome, latency[1])
Case report (BfR) 1999 H_2S inhalation	Domestic case Involving one adult (♂)	Fatal outcome
Case report (NPC) 2001 H_2S inhalation	Domestic case Involving three victims	Pulmonary oedema , respiratory insufficiency, epileptic seizure
Case report (BfR) 2004 H_2S inhalation	Occupational case (sewage collection) Involving one adult (♂)	Cyanosis, unconsciousness, aspiration, pulmonary oedema , respiratory insufficiency, anisocoria, epileptic seizure Partial recovery
Case report (BfR) 2004 H_2S inhalation	Occupational case (sewage collection) Involving one adult (♂)	Unconsciousness Fatal outcome
Case report (BfR) 2004 H_2S inhalation	Occupational case (sewage collection) Involving one adult (♂)	Unconsciousness Fatal outcome
Case report (NPC) 2005 H_2S inhalation	Occupational case Involving one adult (♂)	Latency: 1 h Seizure, respiratory insufficiency, increased methaemoglobin (following 4-dimethylaminophenol administration)
Case report (NPC) 2005	Occupational case (biogas plant) Involving one adult (♂)	Latency: > 1 h Comatose, respiratory insufficiency

[1] time between exposure and the emergency call at the poison centre

Type of data/ year/toxicant/ route of exposure	Relevant information (case description)	Observations (symptoms, outcome, latency[1])
H_2S inhalation		
Case report (NPC) 2005 H_2S inhalation	Occupational case (biogas plant) Involving one adult (♀)	Latency: > 1 h Cardiac arrest, cardiac arrhythmias, respiratory insufficiency, suspected hypoxic–ischemic encephalopathy
Case report (NPC) 2005 H_2S inhalation	Occupational case (biogas plant) Involving one victim (♂)	Latency: ~ 30 h Respiratory insufficiency, reflux, increased leucocytes, increased bilirubin
Case report (BfR) 2006 H_2S inhalation	Occupational case Involving one victim (♂)	Coma, respiratory insufficiency, aspiration, hypoxia, pleural effusion, creatine kinase increased, C-reactive protein increased, leukocytosis, electroencephalographical alterations, disorientation, thought disorder, corneal erosion, superficial punctate keratitis, eye irritation, miosis, discoloration of skin Sequelae possible
Case report (BfR) 2008 H_2S inhalation	Occupational case Involving one victim (♂)	Asystole, reduced oxygen partial pressure Fully recovered
Case report (BfR) 2008 H_2S inhalation	Occupational case Involving one victim (♂)	Coma, brain damage, respiratory insufficiency, coughing, pleural effusion, pulmonary oedema , hypotension, tachycardia, right bundle branch block, LDH increased, C-reactive protein increased, liver enzymes increased Sequelae possible
Case report (NPC) 2009 H_2S inhalation	Occupational case (container) Involving one adult (♂)	Latency: ~ 3 h Cardiac arrest, respiratory insufficiency, hypertension, dilated pupils, increased methaemoglobin (following 4-dimethylaminophenol administration)
Case report (NPC) 2010 H_2S inhalation	Occupational case Involving one adult (♂)	Latency: 1 h Transient unconsciousness, enuresis
Case report (NPC) 2012 H_2S inhalation	Occupational case (pit) Involving two adults (♂)	Latency: 1 h Symptoms not given
Case report (NPC) 2012 H_2S inhalation	Occupational case (pit) Involving one adult (♂)	Latency: few minutes Cardiac arrest
Case report (NPC) 2012 H_2S inhalation	Occupational case (pit) Involving one adult (♂)	Latency: 3 d Traumatic brain injury, pulmonary oedema, respiratory insufficiency, bradycardia, atrioventricular dissociation, ST-segment elevation
Case report (NPC) 2012 H_2S inhalation	Occupational case (pit) Involving one adult (♂)	Latency: 6 d Brief reactive psychosis

Type of data/ year/toxicant/ route of exposure	Relevant information (case description)	Observations (symptoms, outcome, latency[1])
Case report (NPC) 2012 H_2S inhalation	Occupational case (pumping of liquid manure) Involving one adult (♂)	Latency: > 30 min Vertigo, swollen anatomical airways, dyspnoea, bronchospasm, mild tachycardia, presyncope
Case report (BfR) 2014 H_2S inhalation	Occupational case (liquid manure gas) Involving one adult	Immobility, crackling sound on the lungs, tachycardia
Case report (BfR) 2014 H_2S inhalation	Occupational case (liquid manure gas) Involving one adult (♂)	Bradycardia, breathing difficulties, reduced consciousness
Case report (BfR) 2015 H_2S inhalation	Occupational case Involving one adult (♂)	Vertigo, weakness, nausea, gait abnormality, narrow visual field, hearing impairment, circulatory collapse, coma, seizure, pulmonary oedema, insomnia
Case report (NPC) 2015 H_2S inhalation	Domestic case (liquid manure) Involving one child (♀)	Latency: 3 ½ h Respiratory insufficiency
Case report (NPC) 2015 H_2S inhalation	Occupational case Involving one adult	Latency: > 5 h Epileptic seizure, wheezing, collapse, respiratory insufficiency
Case report (NPC) 2015	Occupational case (Container cleaning) Involving one adult (♂)	Latency: 2 h Epileptic seizure, heat sensation, cardiac arrest, unconsciousness
Case report (NPC) 2015 H_2S inhalation	Domestic case (blocked drain) Involving one adult (♂)	Latency: 20 min Collapse, multiple emesis
Case report (BfR) 2018 H_2S inhalation	Occupational case Involving one adult (♂)	Fatal outcome
Case report (BfR) 2018 H_2S inhalation	Occupational case Involving one adult (♂)	Brain damage, hypoxia Fatal outcome

Table 13: Summary table of case reports published in the open literature

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
1) Journal article 2) Report (fire department, educational material)	Occupational exposure in a **biogas plant**, Germany *Concentration:* 1000 ppm (estimated by operational forces) *Duration of exposure:* 20-30 min *Toxicant:* H_2S	4 fatalities 11 injured Workers were exposed after transferring slaughterhouse waste into a biogas tank already containing dung (acidic), lid of tank was opened H_2S formation occurred due to chemical reaction and spontaneous release of H2S within a biogas plant Deceased victims: foaming at the mouth Survivors: nausea, headache, fatigue, collapse, lung injury	(Hedlund and Madsen, 2018) (Will, 2005) (Oesterhelweg et al., 2006)
Journal article / Case report	Occupational exposure in a silage pit in a **biogas station**, Czech Republic *Concentration:* no data *Duration of exposure:* 20-30 min *Toxicant:* uncertain (possibly H_2S)	2 fatalities Employees entered the silage pit to repair a pump where they lost consciousness Safety procedures were not respected (pit was not emptied and ventilated before, no breathing equipment used) Deceased victims: foamy pinkish fluid in airways and lung tissue, intra alveolar oedema, dilation of alveolar spaces, severe brain-swelling, concluded cause of death: asphyxia	(Handlos et al., 2018)
Journal article / Case report	Occupational exposure in a **biogas plant**, Denmark *Concentration:* no data *Duration of exposure:* 30-50 min *Toxicant:* uncertain (presumably high concentrations of H_2S)	4 injured (one of them severely) Four workers were exposed to gas next to a feedstock pit containing pork abattoir waste (mainly intestines) and discarded wine gums (candy) when new organic material (food waste) was delivered and the lid was kept open while the pit stirrer was switched on Survivors: Difficulty in breathing, urge to urinate, illness, unconsciousness	(Hedlund and Madsen, 2018)
Online-newspaper article	Occupational exposure in a **biogas plant**, Germany *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S + methane (H_2S leak confirmed via measurement on site)	1 injured Leaky lid/pusher: release of 5-10m3 of substrate + biogas containing H_2S and methane	(Gonzalez-Tepper, 2017)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case report	Occupational exposure, Italy *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S confirmed via measurements of thiosulfate concentrations in blood and urine (values not available)	3 fatalities 3 injured All victims were sailors, no further information available	(Ventura Spagnolo et al., 2019)
Journal article / Case report	Occupational exposure at a sludge recycling tank in a **wastewater treatment** system, Italy *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S	6 fatalities Workers were exposed to sudden of H_2S gas emission at a valve of a sludge recycling tank in a wastewater treatment system, 5 workers died due to H_2S intoxication, the sixth worker lost consciousness and drowned Deceased victims : Blue-greenish skin + internal organs, pulmonary edema, congestion of brain, lungs, spleen and liver, extensive erosion and submucosal hemorrhage in respiratory tract (main findings) H_2S concentrations in blood were analysed, however the obtained levels in H_2S victims were indistinguishable from those generated during normal putrefaction	(Barbera et al., 2017)
Journal article / Case report	Occupational exposure at a **sewer**, France *Concentration:* > 30 ppm (above the upper detection threshold, 1 h after the accident following partial ventilation) *Duration of exposure:* > 40 min *Toxicant:* H_2S	1 fatality A sewer worker (22-year-old male) fell into a manhole and lost consciousness (no protective equipment), he was rescued 30 min later and died later in the hospital < 24 h after exposure Deceased victim: Coma, severe dyspnea, massive myocardial necrosis, ischemic and anoxic brain lesions, inhalation pneumonia	(Christia-Lotter et al., 2007)
Journal article / Case report	Occupational exposure at a **sewer**, U.S.A. *Concentration:* no data *Duration of exposure:* no data, (last contact 5-7 min before found unconscious) *Toxicant:* H_2S (assumed based on odour)	1 severely injured /survival unclear A worker was exposed to H_2S in a sewer, no use of appropriate safety equipment Survivor: unconsciousness, pink frothy sputum in airway, sonorous respiration bilaterally (rales), clenched jaw	(Yalamanchili and Smith, 2008)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case report	Occupational exposure at a large **pelt processing** factory, Austria *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S	6 fatalities 4 injured Gas leakage from tanks containing chromium sludge and sulfuric acid, no use of appropriate safety equipment Survivors (severely injured): shock, unconsciousness, respiratory failure, hypoxaemia, hypotension, pulmonary oedema, elevated cardiac biomarkers, cerebral oedema, cerebral ischemia Survivors (mildly injured): headache, dizziness, nausea, emesis, dyspnoea, mucosal irritation, coughing, sore throat, eye strain Deceased victims: ventricular fibrillation, cerebral ischaemia and oedema, pulmonary oedema, malignant hyperthermia, cardio-respiratory arrest, atrial fibrillation, cerebral ischemia and oedema, pulmonary oedema, respiratory distress syndrome, two worker died after 2 and 8 days, respectively	(Lindenmann et al., 2010)
Journal article	Systematic overview: accidental H_2S exposure within manure tanks or barns in the Netherlands from 1980-2013 (35 accidents) Additional information on one case: *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S	35 incidents involving 56 victims 29 fatalities 24 injured 3 with unknown fate <u>Case:</u> 1 injured Survivor: unconsciousness, respiratory and cardiac arrest, involuntary movements, left-sided hemiparesis; 4 months after accident: linguistic disorder	(Mooyaart et al., 2016)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article	3 cases of occupational exposure in an **animal rendering plant** / in a **chicken rendering plant** / at a **biodigester**, UK *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S (suspected)	*Case 1:* 2 injured Two workers lost consciousness in an waste intake area in an animal rendering plant Injured: unconsciousness, urine-thiosulphate levels: 326 mmol/l (worker 1) and 10 mmol/l (worker 2) *Case 2:* 3 injured Three workers lost consciousness next to a storage vessel in a chicken rendering plant Survivors: unconsciousness, blood-samples taken from two workers: thiosulfate not detectable, no urine samples taken *Case 3:* 1 fatality Exposure in a biodigester Deceased victims: urine and blood samples: blood-thiosulphate level: 22 mmol/l, no thiosulfate detected in urine	(Jones, 2014)
Journal article / case report	Occupational exposure at a **petroleum refinery**, Sri Lanka *Concentration:* no data *Duration of exposure:* 10 min *Toxicant:* H_2S (confirmed via measurement at accidental site)	2 fatalities 4 injured (two of them severely) Workers were exposed to H_2S during repair works on a leak at a pipeline Survivors: unconsciousness, cyanosis, bronchospasms, muscle-spasms, hypotension, neurotoxicity (delayed) respiratory failure, dyspnoea, sonorous respiration (wheezes), pneumonitis, hypoxic cardiac ischemia, mild perioral numbness	(Shivanthan et al., 2013)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / case report	**Domestic exposure**, Marseille, France *Concentration:* unknown *Duration of exposure:* unknown *Toxicant:* H_2S (confirmed in lung tissue samples)	2 fatalities (mother + 9 month old child) H_2S exposure from a plunger (wastewater-pocket containing H_2S, incorrect installation of household-wastewater pipes) Deceased victims: asphyxia, cyanosis, congestion of the brain, lungs, liver, adrenal glands, and kidneys. hemorrhagic infiltration of the head of the pancreas, lung and brain edema, H_2S-levels in lung tissues of both victims: 1.46 and 1.92 mg/kg respectively	(Sastre et al., 2013)
Journal article / Case report	Occupational exposure, **sour gas industry**, near Perugia, Italy *Concentration:* no data *Duration of exposure:* no data, max. 10 min *Toxicant:* H_2S	1 fatality A worker died during the transfer of hydrochloric acid in a tank containing residues of sodium sulfide without using appropriate protective equipment Deceased victims: congestion of the brain, lungs, liver spleen and kidney, haemorrhagic pulmonary oedema in the lung and brain, dark-red fluid blood on the mucosal tissue of the bronchia, thiosulfate-levels: blood: 1.020 mM/L; liver: 0.266 mM/L); lungs 1.013 mM/L; brain: 1.111 mM/L	(Lancia et al., 2013)
Journal article / Case report	Occupational exposure, 2 cases, **silo containing sludge / wastewater treatment plant**, Spain *Concentration:* Case 1: 100 ppm (6 h after accident) Case 2: no data *Duration of exposure:* Case 1: no data Case 2: max 15 min *Toxicant:* H_2S (assumption based on situation at accidental sites and blackening of metal objects)	*Case 1:* 3 fatalities Three workers lost consciousness next to a silo containing sludge *Case 2:* 1 fatality A worker lost consciousness next to a wastewater pumping substation and died 8 hours later in the hospital.	(Nogue et al., 2011)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case report	Occupational exposure, **sewer** (manhole), U.S.A. *Concentration:* 34 ppm (measured before retrieving the bodies) *Duration of exposure:* no data *Toxicant:* H_2S (suspected, smell of rotten eggs, 34 ppm H_2S at accidental site)	2 fatalities Two workers lost consciousness over a sewer manhole and fell in Deceased victims: no drowning, congestion of head, neck, shoulders, lung oedema, white froth in respiratory tract, fingernail beds cyanotic, blood thiosulfate levels: 0.09 mg/L (both workers), liver-tissue: negative for thiosulfate	(Knight and Presnell, 2005)
Journal article / Case report and Guideline	Occupational exposure, underground **liquid manure storage** pit, U.S.A. *Concentration:* 76 ppm (air samples taken a week after the accident) *Duration of exposure :* no data *Toxicant:* H_2S	3 fatalities 1 injured Four workers exposed to H_2S in a liquid manure storage pit Survivor: hemodynamic instability, respiratory distress syndrome, pulmonary infection Deceased victims: liquid pulmonary aspiration (1^{st} / 2^{nd} victim); pulmonary oedema, increased sulfide-levels in blood (3^{rd} victim)	(Osbern and Crapo, 1981) (National Research Council, 2010)
Journal article and Guideline	1987, location + circumstances not specified *Concentration:* 429 ppm (4 h after the accident) *Duration of exposure:* no data *Toxicant:* H_2S	5 fatalities 5 severely injured Survivors: loss of consciousness (within 2 to 20 min following the accident), deep coma, cardiac T- and P-wave changes	(Hsu, 1987) (National Research Council, 2010)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case report / Brief Communication	Occupational exposure, pit for wastewater treatment in a **dye works**, Japan *Concentration:* 850 ppm (estimation) *Duration of exposure:* no data *Toxicant:* H_2S (reconstruction of accident-circumstances 2 month later: H_2S in pit-atmosphere = 850 ppm)	4 fatalities Four workers lost consciousness in a wastewater-pit containing sodium hydrogen sulfide-, sodium sulfide- and hydrogen sulfide-sludge. Deceased victims: black sludge in airway and stomach of all 4 victims, Sulfide-levels in cardiac blood samples taken at hospital shortly after death: 0.26, 0.58, 0.32, 1.48 mg/L respectively Sulfide in blood-samples at autopsy: 0.86, 0.32, 9.36, 2.56 mg/L respectively *(normal sulfide-levels below 0.05 mg/L)* Thiosulfate-levels in blood-samples taken at hospital shortly after death: 0.0.13, 0.09, 1.22, 0.13 mmol/L Thiosulfate-levels in blood-samples at autopsy: 0.20, 0.11, 0.20, 0.23 mmol/L *(normal thiosulfate-levels below 0.003 mg/L)* Thiosulfate-levels in urine: not detected	(Kage et al., 2004)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case report	Occupational exposure, pit for seepage collection in an **industrial waste site**, Japan *Concentration:* 1400 ppm (measurement 6 h after accident) *Duration of exposure:* no data *Toxicant:* H_2S	3 fatalities 1 injured Four workers lost consciousness in a pit for seepage collection in an industrial waste site used to dump industrial waste Toxicological analysis: increased blood sulfide levels and blood thiosulfate levels in the two victims who died immediately after the accident, increase urine thiosulfate levels in the victims who died 22 days after and the surviving person 1st victim (died shortly after accident): whole blood sulfide-level: 0.13 mg/L, whole blood thiosulfate-level: 10.53 mg/L, urine-thiosulfate-level: 0.90 mg/L 2nd victim (died shortly after accident): whole blood sulfide-level: 0.11 mg/L, whole blood thiosulfate-level: 4.59 mg/L, urine-thiosulfate-level: not detected 3rd victim (died 22 days after accident): plasma sulfide-level: not detected, plasma thiosulfate-level: 4.14 mg/L, urine-thiosulfate-level: 137.20 mg/L 4th victim (survived): plasma sulfide-level: not detected, plasma thiosulfate-level: not detected, urine-thiosulfate-level: 29.34 mg/L	(Kage et al., 2002)
Journal article / Case report	Occupational exposure, oil separator room in a **geothermal power plant**, Japan *Concentration:* 3500 – 5000 ppm (simulation one week later on accident site) *Duration of exposure:* no data *Toxicant:* H_2S	1 fatality A worker lost consciousness in an oil separator room, room contained exhaust gas with high levels of hydrogen sulfide Deceased victims: odour of rotten eggs, greenish discoloration of brain-surface, unspecific congestion of organs, increased thiosulfate levels in blood (0.45µg/mL), brain tissue (2.72 µg/g), lung tissue (0.42 µg/g) and femoral muscle 0.16 µg/g)	(Kage et al., 1998)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case reports	*Case 1:* Occupational exposure, tank containing a liquid mixture of used paper and sodium sulphite in a **factory producing regenerated paper**, Japan *Concentration:* 114 ppm (3h after accident) *Duration of exposure:* no data *Case 2:* Occupational exposure, **waste water tank in a hospital**, Japan *Concentration:* 150 ppm (1 month after accident) *Duration of exposure:* no data *Case 3:* Occupational exposure, **underground drainage pump room in a fish market**, Japan *Concentration:* 123 ppm (4h after accident) *Duration of exposure:* no data *Toxicant in all cases:* H_2S	*Case 1:* 4 injured Four workers lost consciousness in a tank containing sodium sulphite and paper in a liquid Blood sulfide-level and blood thiosulfate-level: not detectable in all workers (samples taken 6h-15h after accident) Worker A: urine sulfide level: not detectable, urine thiosulfate level: 0.43 µmol/mL Worker B: urine sulfide level: not detectable, urine thiosulfate level: 0.39 µmol/mL Worker C: urine sulfide level: not detectable, urine thiosulfate level: 0.12 µmol/mL Worker D: urine sulfide level: not detectable, urine thiosulfate level: not detectable *Case 2:* 1 fatality A worker lost consciousness in a drained hospital wastewater tank containing residual sludge Blood sulfide level (22 h postmortem): 0.007 µmol/mL, blood thiosulfate level: 0.025 µmol/mL *Case 3:* A workers lost consciousness in an underground drainage pump room in a fish market Blood sulfide level (24 h postmortem): 0.95 µmol/mL, blood thiosulfate level: 0.12 µmol/mL Blood sulfide level (4 h postmortem): 0.03 µmol/mL, blood thiosulfate level: 0.12 µmol/mL	(Kage et al., 1997)
Journal article / Case reports	Occupational exposure at a sour gas line in an **oil refinery**, USA *Concentration:* 1000 ppm on accident site 30 min after *Duration of exposure:* no data *Toxicant:* H_2S	1 injured A worker lost consciousness while repairing a sour gas line at an oil refinery, falling down a ladder Injuries on head and thoracic spine (from fall), bronchospasms	(Gabbay et al., 2001)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case reports	Occupational exposure at a **cobalt and nickel mine** site, rural Western Australia *Concentration:* no data *Duration of exposure:* max. 30 s *Toxicant:* H_2S	2 persons severely injured Five men were exposed to H_2S in a mixed sulfide tank, when a pressure release valve failed, the five men left the tank within 30 s, two of them lost consciousness thereafter Survivors: unconsciousness, dyspnoea, incontinence, haemorrhagic mucosal irritation, headache dizziness, conjunctival inflammation, coughing, haemoptysis, mid zone consolidation in lungs	(Gunn and Wong, 2001)
Journal article / Case reports	Occupational exposure at an **oil pumping plant**, USA Concentration: 717 ppm Duration of exposure: max. 5-10 min *Toxicant:* H_2S	1 injured A worker lost consciousness in waste water tank in an oil-pumping operation. Survivor: unconsciousness (with Babinski's reflexes), agitation, tremor, apnoea, sonorous respiration (rhonchi, rales), signs of neurological damage (several days later: Babinski's reflexes + slight difficulties with complex tasks)	(Smilkstein et al., 1985)
Report	Occupational exposure in a **sewer manhole in an animal hide tanning company**, USA *Concentration:* 200 ppm (measurement 6 days after incident) *Duration of exposure:* no data (workers retrieved > 1h later, both face underwater / completely under water) *Toxicant:* H_2S	2 fatalities 1injured Two workers lost consciousness in a sewer manhole in a hide tanning company (no ventilation of the manhole before entering, no appropriate protective equipment worn) Survivor: unconsciousness, dizziness Deceased victims: anoxia due to hydrogen sulfide inhalation (county coroner)	(NIOSH, 1991)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal Article / Case report	Occupational exposure in a **sewer pit**, New Jersey, USA *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S	1 fatality 2 injured Two workers and a police officer lost consciousness in a sewer pit. Survivors: unconsciousness (in at least 1 case resulting in a fall, here no signs of head trauma), apnoea, sinus tachycardia, seizures, pulmonary oedema, neurological medium-term damages (agitation, restlessness, impaired language, memory and attention), long-term damages (impaired language, visual memory, slowing, slowing of central information processing and motor, executive function/planning deficits, suspected damage in dopamine production/excretion)	(Schneider et al., 1998)
Journal Article / Case report	Occupational exposure in a **gas cylinder disposal area**, USA *Concentration:* 2000 ppm (author's estimation based on symptoms of injured persons) *Duration of exposure:* no data *Toxicant:* H_2S	4 injured (2 severely, 2 mildly) Two workers became unconscious after opening a gas cylinder containing liquid H_2S Survivors: unconsciousness, dizziness, convulsions, generalized hyperreflexia, incontinence, headache, chest tightness (no pulmonary oedema), sore tongue	(Milby, 1962)
Journal Article / 5 year retrospective study	Systematic overview on occupational exposures from 1979-1983 in Alberta, Canada (250 cases notified to the provincial compensation board) <u>Sites:</u> **86 %: oil and gas industry** (34 % gas plants, 20 % well sites, 12 & oil rigs, 4 % pumping stations) **14 %: other sites** (university laboratories, food processing facilities, pulp and paper operations) *Toxicant:* H_2S	7 fatalities 243 injured Survivors: unconsciousness, headache, nausea, dyspnoea, disequilibrium, conjunctivitis, sore throat/cough, illness, neuropsychological, extremity weakness, chest pain, pulmonary oedema, bradycardia, convulsion, cyanosis, haemoptysis, in 31 cases fall resulting in traumatic lesions (in 2 cases spinal fraction leading to long-term morbidity) Deceased victims: damages on central nervous and respiratory system, hepatic congestion, cardiac petechiae, trauma injuries due to fall	(Arnold et al., 1985)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case report	Occupational exposure at a **tank containing H_2SO_4 and $FeSO_4$**, USA *Concentration:* no data *Duration of exposure:* several minutes *Toxicant:* H_2S	1 fatality A truck driver lost consciousness after having transferred NaHS into a tank containing H2SO4 and FeSO4 by mistake, this led to release of H_2S Deceased victim: pulmonary oedema, congestion in lung, kidney, microscopic congestion in lungs, spleen, kidney and adrenal glands, 34 fold-elevated blood levels of S2- (1.68 µg/mL, vs. 0.03µg/mL in blood samples from persons without exposure to H_2S)	(Chaturvedi et al., 2001)
Journal article / Case report	Non-occupational exposure at a **thermal spring**, Pamukkale, Turkey *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S	1 fatality 1 injured Exposure in a hotel room with a bathroom (taps open) connected to a thermal spring via an illegal well Survivor: unconsciousness, sinus tachycardia, pulmonary edema, mildly elevated liver enzymes Deceased victim: odor of rotten eggs, petechiae on serous membranes, subpleural bleeding on left lung, pulmonary edema and congestion, elevated blood levels of sulfide and thiosulfate, sulfide blood-level (3h postmortem): 0.68 mg/L; thiosulfate blood level: 0.21 mmol/L	(Daldal et al., 2010)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case report	2 cases of occupational exposure in **thermal springs**, Taiwan 1st case: *Concentration:* no data *Duration of exposure:* approximately 15-20 min *Toxicant:* H_2S (odour of rotten eggs on accidental site) 2nd case: *Concentration:* no data *Duration of exposure:* approximately 2:20 h *Toxicant:* H_2S	1st case: 1 fatality 4 injured Five workers lost consciousness in a hot spring reservoir during cleaning (safety measurements disregarded by workers) Survivors: unconsciousness, agitation, vomiting, tachypnoea, cyanosis, clammy skin, grey-greenish sputum, aspiration pneumonia, keratoconjunctivitis 2nd case: 2 fatalities Two workers lost consciousness in a hot spring reservoir during cleaning and died 5 and 12 hours later, respectively Before death: tachypnoea, sonorous respiration (rhonchi, rales, wheezing), pulmonary oedema, respiratory failure	(Deng and Chang, 1987)
Journal article / Case report	Occupational exposure in an **oil refinery**, Saudi Arabia *Concentration:* no data *Duration of exposure:* > 1h *Toxicant:* H_2S	1 injured A worker was welding in a tank formerly containing sulphur compounds Survivor: dizziness, rhinorrhoea, teary eyes, nausea, shortness of breath, chest tightness, haemoptysis, hypotension, tachypnoea, sonorous respiration (rhonchi), short-term neuropsychological abnormalities (aggression + confusion, later lethargy and bad mood), respiratory failure, pleural effusion and consolidation, ischemic cardiac injury, renal insufficiency 40 days later: mixed restrictive and obstructive pulmonary disease, greyish nail bed discoloration, peripheral neuropathy	(Doujaiji and Al-Tawfiq, 2010)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal Article / Review of incidents	Review of fatal occupational incidents involving H_2S in the USA from 1984 to 1994 via US Occupational Safety and Health Administration (OSHA) investigation records (non-exhausting list of cases reporting fatalities due to H_2S) *Toxicant:* H_2S	57 incidents 80 fatalities 37 victims injured	(Fuller and Suruda, 2000)
Journal article / Case report	Occupational **exposure in a cobalt sulfide manufacturing unit**, India *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S	1 fatality 1 injured Two workers lost consciousness after adding sodium sulfide solution in an open plastic cask containing cobalt oxide in sulphuric acid, which one of them stirred with a bamboo pole Survivor: unconsciousness, respiratory insufficiency	(Gangopadhyay and Das, 2007)
Journal article / Case report	Occupational exposure at a **dairy farm**, western Washington state, USA *Concentration:* no data *Duration of exposure:* 5 min *Toxicant:* H_2S (odour of rotten eggs)	1 injured A worker lost consciousness in a tank containing rotten eggs Survivor: unconsciousness, apnoea, hypertonia, sinus tachycardia, anoxic brain injury, elevated blood thiosulfate levels: 3.1 µg/mL (authors state that 2.0 µg/mL is highest limit for non-exposure)	(Gerasimon et al., 2007)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case report	Occupational exposure in a **sewer**, Greece *Concentration:* > 800 ppm *Duration of exposure:* no data *Toxicant:* H_2S	5 fatalities (4 on site, 1 of cardiac arrest 36 h later) 3 injured (1 of them died 2 month later, myocardial infarction) Eight workers lost consciousness in a sewer containing wine outcasts Survivors: unconsciousness, central cyanosis, restlessness, sonorous respiration (rales, wheezing), aspiration pneumonia, irritability and anxiety, visual disturbances, two cases of cardiac arrest (one worker died 36 h after accident), (1 of the 3 surviving workers died 1 month later of myocardial infarction, he had no history/elevated risk factors for myocardial infarction before) Deceased victims: pulmonary oedema, myocarditis, odour of rotten eggs, hemorrhagic gastric mucosae, greenish color of upper regions of intestine and brain	(Gregorakos et al., 1995)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Report	Report of fatal occupation-related hydrogen sulfide cases in the United States from 1993 through 1999: review of United States Bureau of Labor Statistics (USBLS) database entitled Census of Fatal Occupational Injuries (CFOI) (containing death certificates, workers compensation reports, Occupation Safety and Health Administration (OSHA) reports and medical examiner's reports) *Incident sites:* **waste management (24 %), petroleum and natural gas industries (18 %), food processing, asphalt industry, fishing, dye industries.** *Sources for H_2S:* petroleum manufacturing (23 %), sewage (33 %), fishing, asphalt, food processing, dyes, no data sources *Suggested reasons for accidents:* very often lack of knowledge/experience with dangers concerning H_2S-release/exposure	42 incidents 52 fatalities	(Hendrickson et al., 2004)
Journal article / Case report	Occupational exposure at an **offshore oil rig**, USA *Concentration:* 14.000 ppm (detected by H_2S sensor) *Duration of exposure:* unknown *Toxicant:* H_2S	1 injured Although wearing an air supply respirator, a worker who was climbing on the top of a crude oil take was overcome and lost partially consciousness Survivor: partial unconsciousness, nausea, vomiting, diarrhoea, incontinence, leg shaking, sleeping disorders, long-term neurological damages (impaired memory, decreased visual reaction time, slowed blink reflex latency, confusion, anxiety, depression, fatigue, decreased vigour)	(Kilburn, 1993)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Case report	Occupational exposure at an **aquaculture lake**, Japan *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S	4 fatalities (3 victims died immediately, the 4th died 7 days later) Four workers lost consciousness at an artificial aquaculture lake newly connected to a seawater pipe (unused for several years) Deceased victims (3 victims who died soon after accident): slight signs of physical trauma due to fall into the lake, petechial haemorrhage under mucosa, congestion of organs, dark red blood without any clots in the heart, plankton in lung tissues (suffocation due to aspiration of seawater), proof of bis(pentafluorobenzyl)sulfide (BPFBS, sulfide derivative) in blood/tissue samples via GC/MS Sulfide concentrations (in µg/g): 1st Victim: blood (2-3 h postmortem): 0.10; blood: (24 h postmortem): 0.50; brain: 0.20; lung: 0.68; liver: 1.56; kidney: 0.90; spleen: 0.32 2nd Victim: blood (2-3 h postmortem): 0.20; blood: (24 h postmortem): 0.23; brain: 1.06; lung: 0.21; liver: 1.39; kidney: 1.50; spleen: 0.64 3rd Victim: blood (2-3 h postmortem): 0.08; blood: (24 h postmortem): not detected; brain: 0.40; lung: 0.23; liver: 1.30; kidney: 0.47; spleen: 0.45 H_2S concentration was estimated based on sulfide concentration in brains and lungs of workers compared to results of animal experiments in rats (~550-650 ppm)	(Kimura et al., 1994)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Overview	5 cases of occupational exposures in **agricultural sector / biogas plant,** Germany *Concentration:* no data in any of the cases *Duration of exposure:* no data in any of the cases *Toxicant:* H_2S	Case 1 and 2 not related to H_2S <u>Case 3:</u> 1 fatality On a farm next to a pool containing slurry, a child lost consciousness and died shortly after <u>Case 4:</u> 4 fatalities On a farm, four victims lost consciousness in a manure pit (one who was cleaning the pit and 3 who try to rescue the first victim) and died <u>Case 5:</u> Occupational exposure in a Biogas plant in Rhadereistedt, (see 1st entry in this Table)	(Oesterhelweg et al., 2006)
Journal article / Report / Survey	Occupational exposures at manure storage facilities of swine livestock farms from 1998 to 2013, **agricultural sector**, Korea (data incomplete, many cases not reported to authorities or in press / internet) *Toxicant:* H_2S	17 incidents 30 fatalities (18 during work at/in/next to manure storage units, 12 during rescue attempts, asphyxia due to H_2S) 8 injured Nearly all incident during warm season due to faster decomposition of manure	(Park et al., 2016)
Journal article / Case report	Exposure in a **toilet room** in a steel foundry, Spain *Concentration:* no data *Duration of exposure:* no data *Toxicant:* H_2S (odour of rotten eggs)	1 fatality 3 injured 10 mildly injured Four workers were exposed to H_2S in the toilet room at their workplace, no siphons, connected to a manure pit which before was out of order for a few month Survivors: nausea, vomiting, eye, nose and throat irritation, dizziness, dyspnoea, long-term injury in one worker (smoker): pneumonitis with mild bilateral interstitial fibrosis, reddish mucosa in bronchial tract + white blood cell infiltration and mild restrictive disease Deceased victims: cause of death: asphyxia	(Parra et al., 1991)

Type of data/report	Relevant information	Observations: no of victims/ circumstances of the accident/ clinical signs/medical findings/ autopsy findings	Reference
Journal article / Correspondence / Case report	Occupational exposure in a **petroleum refinery, oil industry**, Japan Concentration: tank contained H_2S 1 % = 15,000 ppm Authors estimated exposure levels: Patient 1: 500-900 ppm Patient 2: 500-900 ppm Patient 3: 250-600 ppm Duration of exposure: no data *Toxicant:* H_2S	3 injured Three workers unconscious after opening a valve on a tank containing H_2S Survivors: unconsciousness, convulsions, (mid-)dilated pupils, respiratory and cardiac arrest (successful reanimation), cyanosis, pulmonary oedema, injured erythematous lesion on the bronchi, no long-term sequelae	(Tanaka et al., 1999)

10.3.1 Short summary and overall relevance of the provided information on acute inhalation toxicity

Hydrogen sulfide (H_2S) is a colourless gas. Inhalation is the most relevant route of human exposure. Important targets comprise the neurological, cardiovascular, and respiratory system with the latter being the most sensitive (WHO (CICAD), 2003).

Animal data

Rodents

The effects of H_2S inhalation have been studied in a number of experimental acute inhalation toxicity studies in rodents. With the exception of one study report, the available data consist of older (> 25 years) journal articles extracted from the open literature. These sources provide mostly information on lethality and are not considered equivalent to current guideline studies such as OECD TG 403. Relevant studies are listed in Table 11. Derived rodent LC50 values are summarised in Table 14. Overall, similar toxicity in the same concentration range had been reported. LC50 values based on 4- and 1-hour exposure (the latter converted to 4 h) all consistently give rise to an acute toxicity estimate (ATE) value between approximately 100 and 500 ppm in rats and mice (Table 14). For the current existing classification (acute inhalation toxicity, category 2), the LC50 established by Tansy, *et al.* (1981) in rats was utilised.

Non-rodents

Acute inhalation toxicity was also tested in non-rodent animals. Lund and Wieland (1966) reported the lethality of a single Rhesus monkey following 35 min of inhalational exposure to 500 ppm H_2S and necrotic brain damages in a second and third animal subjected to the same concentration at shorter exposure durations (Lund and Wieland, 1966). A study using Japanese White rabbits reported 100 % lethality at 500-1000 ppm (Kage et al., 1992).

Table 14: LC50 (ppm) values reported in experimental rodent studies

Exposure time	LC50 (ppm) Rat	LC50 (ppm) Mouse	Reference
10 min	824	1143	**(Zwart et al., 1990)**
30 min	717	788	**(Zwart et al., 1990)**
60 min	675 (**342** for 4 h*)	667 (338 for 4 h*)	**(Zwart et al., 1990)**
1 h	712 (**356** for 4 h*)	634 (317 for 4 h*)	**(THRU Laboratories, 1972)**
2 h	587	n.a.	**(Prior et al., 1988)**
4 h	**501**	n.a.	**(Prior et al., 1988)**
4 h	**444**	n.a.	**(Tansy et al., 1981)**
6 h	335	n.a.	**(Prior et al., 1988)**

*Converted according to the CLP regulation (No 1272/2008), table 3.1.1, note (c)

Human data

Source of data and specific aspects related to H_2S exposure

Human data regarding H_2S-related acute inhalation toxicity are available from different sources and have been extensively reviewed (ATSDR, 2016; Beauchamp et al., 1984; Burnett et al., 1977; Guidotti, 1996; Guidotti, 2010; Guidotti, 2015; Milby, 1962; Reiffenstein et al., 1992; US EPA, 2003; WHO (CICAD), 2003). H_2S is generated in the process of organic decomposition. The gas occurs naturally (e.g. natural gas wells, sulphur springs, endogenously in mammalian tissue) and is produced following anthropogenic processes (WHO (CICAD), 2003). Exposure of the general population is uncommon. Communities residing close to industrial areas or drilling operations may be chronically exposed to low-dose H_2S not associated with acute toxicity symptoms (WHO (CICAD), 2003). Very few cases have been reported where lethal human exposure accidentally happened in a non-occupational setting (e.g. domestic cases). In contrast, intentional intoxication originated from homemade H_2S has led to high mortality rates. H_2S-related suicides had taken on a dimension of an "outbreak" with hundreds of casualties in Japan and the United States (Morii et al., 2010; Reedy et al., 2011).

The most relevant and extensive information regarding acute inhalation toxicity in humans, though, is provided by documented cases related to occupational accidents. As a by-product of many industrial processes, H_2S has always been a critical human health issue at the worksite (Ballerino-Regan and Longmire, 2010). Numerous episodes of acute poisoning, i.e. severe toxicity and lethality, following occupational exposure have been reported. H_2S intoxication ranks second among the gases that cause fatal accidents (Guidotti, 2015). Affected industrial sectors include but are not limited to renewable energy (biogas plants), agriculture (manure handling operations, animal rendering plants), sewage management, or oil/gas production/refinery. Accidents related to H_2S are sporadic and often occur as a consequence of the unexpected formation of high H_2S concentrations. Being heavier than air, H_2S tends to accumulate in poorly-ventilated working sites near the ground. Poisoning usually happens in confined spaces such as buildings/barns, manure/sludge pits and tanks, manholes, and sewer lines. Exposed individuals often lose consciousness within seconds of inhalation. Imprudent attempts (e.g. without personal protective equipment) to rescue unconscious H_2S-victims frequently increase the number of casualties as rescuers are likewise intoxicated when entering the danger zone. Survivors of acute H_2S poisoning may not fully recover (Tvedt et al., 1991). Reported exposure durations rank from minutes to hours (ATSDR, 2016).

Table 12 compiles a non-exhausting collection of case reports extracted from a national poison information centre (NPC) and poisonings reported under the obligation of § 16e of German Chemicals Act to the German Federal Institute for Risk Assessment (BfR). Table 13 contains case reports from the open literature. Information on the circumstances of the accident and clinical information describing typical symptoms attributed to H_2S intoxication can be derived and used for a qualitative assessment of acute inhalation toxicity pertaining to H_2S exposure in humans. However, accurate quantitative lethal dose data cannot be derived as retrospective reporting of uncontrolled acute human toxicity cases inherently lack reliable information on the concentration and the duration of H_2S exposure. Occasionally, H_2S concentration had been measured subsequently to the accident which, however, may not represent the levels at the time when the incident actually happened. In addition, pre-existing conditions of exposed individuals are unknown and co-exposure with other toxic chemicals may confound the reporting. The minimum concentration causing mortality in humans is, hence, unknown.

Upon absorption by the lungs, H_2S undergoes metabolisation. The main detoxifying pathway is hepatic oxidation whereas thiosulfate is produced. Thiosulfate levels in the blood and the urine have been utilized as an indicator of H_2S exposure depending on the severity of intoxication (Kage et al., 1997; Kangas and Savolainen, 1987).

Mode of action and clinical signs of acute exposure

On a cellular level, it is thought that H_2S toxicity is conferred by its ability to disrupt the oxidative metabolism within the mitochondria and thus decreasing ATP production (WHO (CICAD), 2003). Yet, other toxicological mechanisms have been described and it is a matter of debate whether the inhibition of the respiratory chain is the predominant mode of action (Guidotti, 2010).

A variety of hazard health effects, both local and systemic, have been associated with H_2S exposure affecting primarily the ocular, respiratory tract and nervous system (Beauchamp et al., 1984; Public Health England, 2016; WHO (CICAD), 2003). Thereby, H_2S induces toxicity directly at the site of contact tissues such as the eyes and the respiratory tract, causing irritation and inflammation of mucous membranes. Systemic effects are predominantly related to the central nervous system. Typical ocular effects, documented upon human exposure, include keratoconjunctivitis, punctate corneal erosion, blepharospasm, lacrimation, and photophobia (ATSDR, 2016; WHO (CICAD), 2003). Respiratory symptoms comprise respiratory irritation, impaired lung function, noncardiogenic pulmonary oedema, and respiratory distress. Severe respiratory symptoms are considered the primary causes of H_2S-related deaths (ATSDR, 2016). Being capable of penetrating deeply into the lung, H_2S can induce alveolar injury leading to noncardiogenic pulmonary oedema and ultimately acute respiratory distress (Deng and Chang, 1987; Guidotti, 2010). Impaired oxidative metabolism in the brain may cause respiratory arrest. Exposure to > 500 ppm is expected to cause rapid respiratory failure and death due to asphyxia (Beauchamp et al., 1984; Milby, 1962). Immediate unconsciousness ("knockdown") is the most apparent neurological effect and critical for survival as it disables victims from escaping the danger zone- thus, prolonging exposure. Other reported neurological symptoms include disturbed equilibrium, nausea, headache, poor memory, insomnia, irritability, delirium, severe vertigo, unusual sweating, neuropsychological symptoms, convulsions, and tremors (ATSDR, 2016). The severity of adverse health effects depends on the intensity of exposure (concentration), the duration, and the individual susceptibility.

The dose-response relationship curve in terms of lethality is remarkably steep- presumably indicative of overloaded detoxification mechanisms (Prior et al., 1988; US EPA, 2003). Consequently, the margin at which non-lethal exposure can be endured is small (Guidotti, 2010). Although individual sensitivity varies, humans have the ability to smell H_2S at extremely low concentrations (odour threshold: 0.003-0.02 ppm) (Reiffenstein et al., 1992). The odour of "rotten eggs" is perceived as unpleasant and may serve as a warning sign. However, as the concentration increases, the odour perception wanes as a consequence of olfactory fatigue and paralysis (WHO (CICAD), 2003). At 100 ppm, the sense of smell disappears after 2 to 15 minutes (Malone Rubright et al., 2017). Exposed individuals may, hence, misinterpret this as non-existing or ceasing exposure while H_2S levels are actually high or rising, insidiously sabotaging the odour warning sign (Jones, 2014; Knight and Presnell, 2005). Thus, the unpleasant odour gives little warning of dangerously high concentrations.

Based on these human experiences, estimated concentration thresholds have been published for a wide range of typical hazardous health effects including mortality (Beauchamp et al., 1984; Guidotti, 2010; OSHA, 2019; WHO (CICAD), 2003). An example of current concentration estimates as published by the U.S. Occupational Safety and Health Administration is given in Table 15 (OSHA, 2019).

Table 15: Symptoms and health effects at estimated H2S concentrations as reported by the U.S. Occupational Safety and Health Administration (OSHA, 2019)

Concentration (ppm)	Symptoms/Effects
0.00011-0.00033	Typical background concentrations
0.01-1.5	Odour threshold (when rotten egg smell is first noticeable to some). Odour becomes more offensive at 3-5 ppm. Above 30 ppm, odour described as sweet or sickeningly sweet.
2-5	Prolonged exposure may cause nausea, tearing of the eyes, headaches or loss of sleep. Airway problems (bronchial constriction) in some asthma patients.
20	Possible fatigue, loss of appetite, headache, irritability, poor memory, dizziness.
50-100	Slight conjunctivitis ("gas eye") and respiratory tract irritation after 1 hour. May cause digestive upset and loss of appetite.
100	Coughing, eye irritation, loss of smell after 2-15 minutes (olfactory fatigue). Altered breathing, drowsiness after 15-30 minutes. Throat irritation after 1 hour. Gradual increase in severity of symptoms over several hours. **Death may occur after 48 hours.**
100-150	Loss of smell (olfactory fatigue or paralysis).
200-300	Marked conjunctivitis and respiratory tract irritation after 1 hour. Pulmonary oedema may occur from prolonged exposure.
500-700	Staggering, collapse in 5 minutes. Serious damage to the eyes in 30 minutes. Death after 30-60 minutes.
700-1000	Rapid unconsciousness, "knockdown" or immediate collapse within 1 to 2 breaths, breathing stops, death within minutes.
1000-2000	Nearly instant death

High concentrations ≥ 500 ppm

As aforementioned, the exact minimum concentration that causes lethality in humans is unknown and may depend on the duration of exposure and the susceptibility of the exposed individuals. Increased sensitivity has been described for individuals with limited respiratory performance such as young children, elderly people, and individuals with predisposing conditions (e.g. asthmatics) (WHO (CICAD), 2003). There is general consensus that instant severe acute toxicity can be expected at ≥ 500 ppm H_2S (ATSDR, 2016; Ballerino-Regan and Longmire, 2010; Beauchamp et al., 1984; Guidotti, 2010; Guidotti, 2015; OSHA, 2019; Reiffenstein et al., 1992; US EPA, 2003). Individuals exposed to such high concentrations may immediately collapse and die at the location of the accident.

Moderate concentrations 100 - 500 ppm

Although the evidence is limited, concentrations between 100 and 500 ppm may also cause mortality after prolonged exposure. Rescued and hospitalized individuals that had been exposed to moderate levels of H_2S over a longer time period may exhibit symptoms such as noncardiogenic pulmonary oedema and cyanosis eventually leading to delayed mortality (Malone Rubright et al., 2017). For instance, two individuals who cleaned a hot-spring reservoir for approximately 2 hours died after being treated in the hospital. The cause of death was acute respiratory distress as a consequence of pulmonary oedema. Given that one of the two victims collapsed only after two hours of exposure while the other man was still able to call for help, the lethal incidence happened as a result of prolonged exposure at presumable moderate H_2S concentrations (Deng and Chang, 1987). Pulmonary oedema may occur at 250 ppm (Beauchamp et al., 1984; OSHA, 2019). In a case report documenting an accident in a petroleum refining company, one of the victims was exposed to

an estimated concentration of ≥ 250 ppm H_2S. Following contact with the gas, he immediately collapsed and was later, upon arrival at the hospital, diagnosed with pulmonary oedema and cyanosis, deteriorating to respiratory and cardiac arrest (Tanaka et al., 1999).

Lower concentration ≤ 100 ppm

It has been suggested by the German Federal Environment Agency (UBA) that less than 100 ppm may cause lethality after several hours of exposure ((UBA), 2006). The National Institute for Occupational Safety and Health (NIOSH), a United States federal agency, has declared 100 ppm as the "Immediately Dangerous to Life or Health Concentrations" (IDLH) and the Occupational Safety and Health Administration (OSHA) of the United States Department of Labor has claimed 100 ppm as a lethal concentration after 48 hours of exposure (Table 15) (NIOSH, 2014; OSHA, 2019). As aforementioned, reports of accidental poisonings usually do not provide reliable data on the quantity of H_2S exposure, both in terms of concentration and duration. Occasionally, though, H_2S concentrations were measured following the incidence. In a case report of a fatal incidence involving two sewer workers, an air concentration of 34 ppm was measured before retrieving the bodies (Knight and Presnell, 2005). In this specific case, the two workers accidentally fell into a manhole. According to the authors of the study, the measured concentration was unlikely to reflect the lethal concentration as the manhole cover was open for a while. However, H_2S is heavier than air and tends to accumulate near the bottom of confined space (WHO (CICAD), 2003). Concentrations around 100 ppm and below are also reported in three other studies including fatalities (Kage et al., 1997; Nogue et al., 2011; Osbern and Crapo, 1981). These values may or may not represent the actual exposure level at the time of the accident.

Taken together, the available evidence from human data indicates that the minimum concentration where mortality can be expected is in the range of 100 and 500 ppm. However, it cannot be excluded that in certain cases, e.g. when susceptible sub-populations (elderly, asthmatics, children) are involved, the minimum lethal concentration may be below 100 ppm.

10.3.2 Comparison with the CLP criteria / weight of evidence

Animal data

As stipulated in the CLP Regulation (EC) No 1272/2008, acute toxicity estimate (ATE) values, usually derived from calculated LD50/LC50 values obtained in animal studies, are utilized to determine an acute toxicity hazard category. According to ECHAs Guidance on the Application of the CLP Criteria (3.1.2.3.2.), classification is based on the lowest available ATE value (ECHA, 2017). Currently, H_2S is assigned to category 2, acute inhalation toxicity (H330: fatal if inhaled; Annex VI of the CLP Regulation (EC) No 1272/2008), based on experimental data in rats showing an LC50 of 444 ppm upon 4 h exposure via inhalation (Tansy et al., 1981). The classification under CLP is considered a minimum classification as it was translated from the DSD legislation (Directive 67/548/EEC). Other experimental animal studies listed in Table 11 have established similar LC50 values, consistently in the range of > 100 ppm and ≤ 501 ppm for both, rats and mice. However, none of the tests listed in Table 11 can be considered equivalent to a current guideline such as the OECD TG 403.

Human data

Numerous case reports have documented severe acute inhalation toxicity and mortality in humans predominantly within the occupational environment. Documented cases are largely consistent and distinctive, comprising unique features attributed to H_2S-related poisoning. Limitations associated with these reports, especially the lack of accurate exposure data (i.e. concentration and duration), preclude their utilisation for a quantitative risk assessment. While the relevance of each individual human study is limited and insufficient for classification, the available human data considered in its entirety may justify the modification of the acute hazard category. A weight of evidence approach including the amply evidence for human mortality/morbidity pertaining to H_2S inhalation is, hence, suggested.

Comparison of animal and human data

According to a WHO assessment document, humans may be more sensitive to H_2S *("Based on limited information, rodents appear to be less sensitive to hydrogen sulfide than humans."* page 5). In non-human

primates, lethality was observed following H_2S exposure for 35 minutes at 500 ppm. In addition, adverse effects with the potential to cause mortality (i.e. severe brain damage) were also noted after H_2S exposure for 22 min and 25 min (+ a second exposure) at the same concentration (Lund and Wieland, 1966). In the study by Zwart et al. (1990), a similar exposure duration (30 min.) did not cause mortality in mice exposed to 319-577 ppm and rats exposed to 319-591 ppm (Zwart et al., 1990). This is consistent with another study where all rats (n = 20) survived a 1-hour exposure to 400/504 ppm H_2S. In the same study, only 2 out of 20 mice died while subjected to the same experimental setting (THRU Laboratories, 1972). In conclusion, based on these limited data, effects attributed to H_2S exposure may be more severe in primates as opposed to rodents.

Arguments in favour of a modification of the acute toxicity hazard category (weight of evidence)

- The current classification is based on information (animal data reported in old journal articles and one study report) not equivalent to current guideline studies such as OECD TG 403
- Extensive human evidence from case reports demonstrating severe toxicity and lethality following inhalation of H_2S exist
- While the minimum concentration causing lethality in humans is unknown, exposure to 100 ppm for prolonged duration has been suggested to cause severe toxicity/lethality (NIOSH, 2014; OSHA, 2019)
- There is uncertainty as to whether the available animal data reflect the lethal potential of H_2S in humans (humans may be more sensitive)
- The dose-response relationship curve in terms of lethality is remarkably steep
- The margin at which non-lethal exposure can be endured is small
- Loss of odour sensation at approximately 100 ppm- the warning sign (unpleasant smell) disappears
- First neurological symptoms, i.e. loss of consciousness, disable victims from escaping the danger zone
- The respiratory system as the main target organ- susceptible sub-populations (elderly, asthmatics, children) are more vulnerable

Classification of mixtures containing H_2S

Based on *"evidence from human exposure that indicates toxic effects but does not provide lethal dose data"* (CLP Regulation (EC) No 1272/2008, section 3.1.3.6.2.1. [b]), a conversion value for the use of the additivity formula (CLP Regulation (EC) No 1272/2008, section 3.1.3.6.1) shall be used to calculate the classification of any mixture containing H_2S. Considering the proposed hazard category, i.e. category 2, the converted Acute Toxicity point Estimate (cATpEs) value of 100 ppm shall be applied within the additivity formula as laid out in Table 3.1.2 of the CLP Regulation (EC) No 1272/2008.

Classification of H_2S within hazard category 2, based on evidence in humans, will result in relevant changes in the classification of mixtures (Table 16). Using the LC50 of 444 ppm (rat) for calculation of mixture classification according to the respective criteria, a mixture with an H_2S content below 2.2 % is not classified. However, an air concentration of 2.2 % H_2S (22.000 ppm) if inhaled will be clearly fatal within seconds. The result of the calculation is therefore difficult to understand for the laymen and has already led to confusion in practice. Applying a cATpEs value of 100 ppm, though, a mixture containing 0.5 % H_2S will be classified as harmful if inhaled according to the CLP criteria. Starting from a concentration of 4 %, the hazard pictogram GHS06 (skull and crossbones) would be required. Given that lethality is likely to occur upon human exposure to 500 ppm (0.05 %) H_2S, the resulting classification and labelling of a mixture would, hence, be considerably more appropriate.

Table 16: Comparison of concentration limits for gaseous mixtures with H_2S using the actual hazard category 2* (based on animal data) and the modified category 2 (based on human data)

Hazard category	**Acute toxicity 2***	**Acute toxicity 2**	**Pictogram**
Mixtures / **H_2S**	**LC_{50} = 444 ppm (rat)**	**cATpEs = 100 ppm**	
Acute toxicity 4	2.2 %	0.5 %	
Acute toxicity 3	17.8 %	4 %	
Acute toxicity 2	88.8 %	20 %	
Acute toxicity 1	–		

10.3.3 Conclusion on classification and labelling for acute inhalation toxicity

As the large body of evidence from human exposure is considered more relevant than the available data from studies using experimental animals, classification shall be based on human data. Hence, classification into category 2 based on an extensive body of evidence describing lethality/severe toxicity in humans following exposure to H_2S, is proposed. The modification of the classification is expected to impinge on the ATE value used to classify H_2S-containing mixtures from currently 444 ppm to 100 ppm.

10.4 Skin corrosion/irritation

Not addressed in this dossier

10.5 Serious eye damage/eye irritation

Not addressed in this dossier

10.6 Respiratory sensitisation

Not addressed in this dossier

10.7 Skin sensitisation

Not addressed in this dossier

10.8 Germ cell mutagenicity

Not addressed in this dossier

10.9 Carcinogenicity

Not addressed in this dossier

10.10 Reproductive toxicity

Not addressed in this dossier

10.11 Specific target organ toxicity-single exposure

Not addressed in this dossier

10.12 Specific target organ toxicity-repeated exposure

Not addressed in this dossier

10.13 Aspiration hazard

Not addressed in this dossier

11 EVALUATION OF ENVIRONMENTAL HAZARDS

Not addressed in this dossier

12 ADDITIONAL LABELLING

Not addressed in this dossier

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