Committee for Risk Assessment

RAC

Annex 1
Background document
to the 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

The background document is a compilation of information considered relevant by the dossier submitter or by RAC for the proposed classification. It includes the proposal of the dossier submitter and the conclusion of RAC. It is based on the official CLH report submitted to consultation. RAC has not changed the text of this CLH report but inserted text which is specifically marked as 'RAC evaluation'. Only the RAC text reflects the view of RAC.

Adopted

16 September 2021

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**

Contact details for dossier submitter:

BAuA

Federal Institute for Occupational Safety and Health
Federal Office for Chemicals
Friedrich-Henkel-Weg 1-25
44149 Dortmund, Germany

Version number: **1.0**

Date: **September 2020**

ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON HYDROGEN SULPHIDE, HYDROGEN SULFIDE

CONTENTS

ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON HYDROGEN SULPHIDE, HYDROGEN SULFIDE

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).

RAC general comment

Hydrogen sulfide (H_2S) 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. H_2S is slightly (1.2-fold) heavier than air and has a characteristic odour of rotten eggs.

H_2S 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. H_2S 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 H_2S upon acidification of sulfide-containing materials.

According to the existing Annex VI entry, H_2S 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 H_2S 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 H_2S-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).

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.

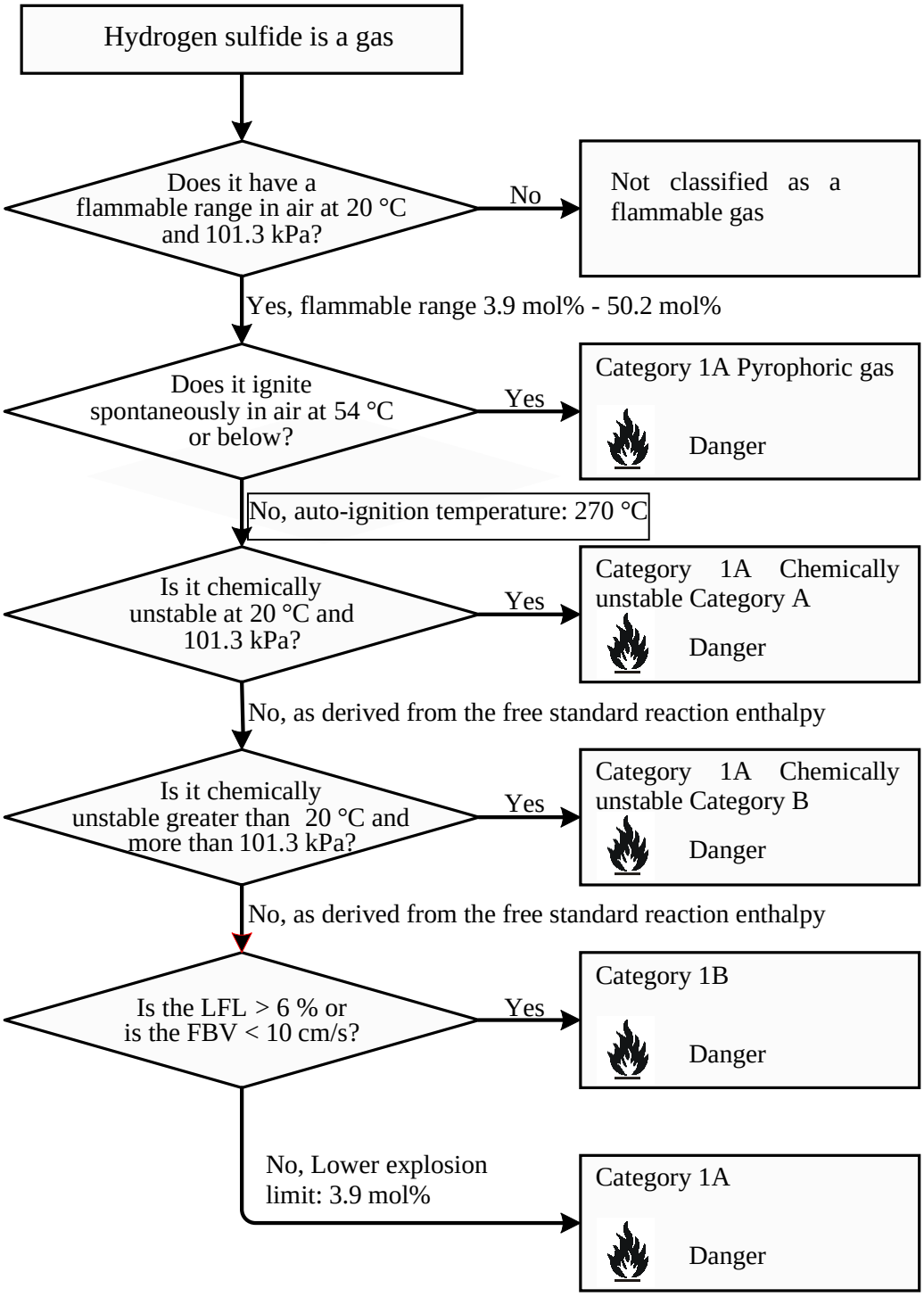
The criteria for category 1 have been amended by Regulation (EU) 2019/521 (12th ATP to CLP) as a new sub-classification in categories 1A and 1B of the hazard class "flammable gases. The CLP Regulation considers for flammable gases three categories 1A, 1B and 2. Category 1A is divided in four sub-categories: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

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 H_2S 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 H_2S (g) → H_2 + S.

Based on this information, the DS proposed to classify H_2S 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 °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.

With a critical temperature of 100 °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 °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 °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 °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:

$$H_2S\ (g) \rightarrow H_2\ (g) + S\ (s)$$

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 H_2S formation, not decomposition, and H_2S can be considered chemically stable at 25 °C and a standard pressure of 101.3 kPa. Thus, the criteria for classification of H_2S 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 H_2S decomposition) the conversion increases with increasing temperature. Spontaneous decomposition of H_2S is reported to begin around 500 °C (Startsev, 2017), which means that H_2S 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 H_2S 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.

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 signs, histological examination)	**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
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 reported, one sex only, no individual	**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
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 specified No GLP	**Rabbit** Japanese White Sex not specified n = 5 (conc.)	hydrogen sulfide (purity: not specified) 231-977-3	Concentration: 100-200 ppm 500-1000 ppm Duration: 14-30 min. + 2 h and 24 h observation	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
Deviations: sex not specified, no individual observation records, purity not specified, shorter duration, concentration only as range, shorter observation period					

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 H_2S inhalation	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])
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
Case report (NPC)	Occupational case (pumping	Latency: > 30 min

Type of data/ year/toxicant/ route of exposure	**Relevant information (case description)**	**Observations (symptoms, outcome, latency[1])**
2012 H_2S inhalation	of liquid manure) Involving one adult (♂)	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)

ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON HYDROGEN SULPHIDE, HYDROGEN SULFIDE

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)

ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON HYDROGEN SULPHIDE, HYDROGEN SULFIDE

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)

ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON HYDROGEN SULPHIDE, HYDROGEN SULFIDE

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 Case 3: 1 fatality On a farm next to a pool containing slurry, a child lost consciousness and died shortly after Case 4: 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 Case 5: 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.

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 LC_{50} of 444 ppm (Tansy *et al.*, 1981).

Besides animal data, the DS reviewed a number of reports of H_2S 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 H_2S content below 22000 ppm are not classified. If the ATE is lowered 100 ppm, classification as Acute Tox. 4 will apply from 5000 ppm H_2S.

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 LC_{50} of 444 ppm comes from a study by Tansy *et al.* (1981), this result is very close to the LC_{50} 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 *et al.* (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 *et al.* (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 *et al.* (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 LC_{50} 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 LC_{50} values are presented in the following table. Nevertheless, robust experimentally determined 4-hour LC_{50} 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 LC_{50} (ppm)**	**Converted 4-hour LC_{50} (ppm)**
Rat Strain: Wistar Zwart *et al.* (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 *et al.* (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 LC_{50} 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. H_2S intoxication with a fatal outcome still continue to occur. The typical features of H_2S 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.

$H_2S$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).

H_2Shas 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 H_2S 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 H_2S concentrations are available have been summarized below. In some cases, the H_2S concentration was above the measuring range of the device (e.g. > 100 ppm).

Human cases from the CLH report for which a measured H_2S concentration is available				
Reference	**Setting**	**Outcome**	**Measured H_2S 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 *et al.* (2007)	Sewer	1 dead	1 h after the accident: > 30 ppm Exposure duration: > 40 min	
Nogue *et al.* (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	
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 *et al.* (2004)	Dye works, spillage of H_2S-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 *et al.* (2002)	Industrial waste site, pit for seepage collection	3 dead, 1 injured	6 h after the accident: 1400 ppm	
Kage *et al.* (1998)	Geothermal power plant, oil separator room	1 dead	At a simulation on the accident site one week later: 3500-5000 ppm	
Kage *et al.* (1997), case 1	Factory producing regenerated paper	4 injured	3 h after the accident: 114 ppm	
Kage *et al.* (1997), case 2	Wastewater tank in a hospital	1 dead	1 month after the accident: > 150 ppm	
Kage *et al.* (1997), case 3	Drainage pump room, spillage of sewage	1 dead	4 h after the accident: 123 ppm	
Gabbay *et al.* (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 *et al.* (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

Gregorakos *et al.* (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 *et al.* (1999)	Petroleum refinery	3 injured	The affected workers opened a pipe with a gas containing 15000 ppm H_2S	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 H_2S 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 H_2S concentrations after an accident. A worker suddenly lost consciousness after spillage of H_2S-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 H_2S 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 H_2S 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 H_2S 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 H_2S 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 H_2S 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 LC_{50} 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.

Supplemental information - In depth analyses by RAC

Details of selected human cases of H_2S poisoning

The DS, to support their case for an ATE of 100 ppm, mentioned several reports where the measured concentration was around or below 100 ppm. The details of these cases as described in the original publications are provided below. Further, the case reported by Kage *et al.* (2004) is described here as well because it provides an interesting piece of

information regarding stability of H_2S concentrations after an accident.

Knight and Presnell (2005)

A worker opened a sewer manhole cover to enter it and suddenly yelled and fell in. Another worker then ran to the manhole to provide assistance and also suddenly fell in. Bystanders called emergency services, and rescue personnel equipped with self-contained breathing apparatuses retrieved the victims, whose faces were reportedly not submerged in water. Both men were pronounced dead at the scene; no resuscitation was performed.

County Water and Sanitation Authority employees reported an air concentration of H_2S of 34 ppm, measured before the bodies were retrieved, but sometime after the incident. Bystanders reported a strong smell of "rotten eggs," which dissipated over time. According to the authors, "in this case, it is likely that much of the H_2S gas had dissipated once Water and Sanitation employees arrived on the scene to test the air, as the manhole had been open for some time."

The autopsy of the two decedents showed congestion of the head, neck and shoulders; cyanotic lips and fingernail beds; red sclerae and conjunctivae; water-immersion change of the hands; mild contusions and abrasions related to the fall; lungs with oedema and congestion; trachea and bronchi containing white oedematous froth and large amounts of oedema fluid exuded from the parenchyma on sectioning.

Osbern and Crapo (1981)

The case occurred in an agricultural setting on a dairy farm. The lid to a large underground liquid manure storage tank was kicked into the tank by a cow. Having entered the tank previously without consequence, the farmer drained the liquid manure to a height of 45 cm and descended into the pit to retrieve the lid. Shortly after entering the tank, he fell unconscious. The farmer's two sons entered the pit to rescue him. When one collapsed, the other escaped to find help.

The county sheriff and town barber responded to the call. The barber entered, took one breath that caused a severe burning sensation in his chest, then lifted the still-gasping boy over his shoulder. Seconds later, the barber lost consciousness and fell, with the boy, back into the manure. The sheriff entered to save the barber and was quickly overcome. When the town ambulance arrived, the barber was fished out of the tank and resuscitation started. The farmer, his son, and the sheriff were pronounced dead at the scene. The autopsies showed that the farmer and the sheriff had massive aspiration of liquid manure. The farmer's son had fulminant pulmonary oedema but had not aspirated manure.

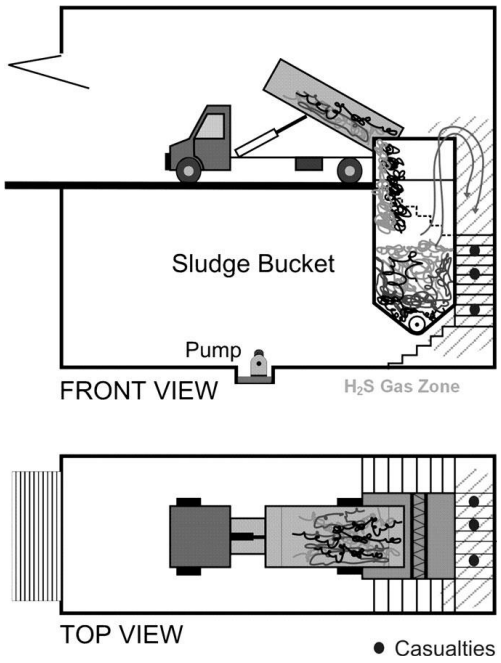
The barber survived. Although he vomited large amounts of manure, endotracheal suctioning after intubation revealed only abundant frothy pink secretions. Mechanical ventilation and oxygen were applied. The clinical course was complicated by hemodynamic instability, respiratory distress syndrome and infection. As the carboxyhaemoglobin level was normal upon arrival to hospital, carbon monoxide is unlikely to have played a significant role in the poisoning.

Eight days after the accident, under conditions different from those at the day of the accident (warmer weather, less concentrated manure), air from the manure storage tank was analysed. Hydrogen sulfide concentration was 76 ppm. Other gases detected were

methane, carbon monoxide (400 ppm), ammonia (1.5 ppm), carbon dioxide (2%), and oxygen (18%). According to the authors, the gas concentrations probably were different on the day of the accident.

Nogue *et al.* (2011)

A truck unloaded several tons of sludge from water purification stations into a silo that was between 33 and 50% full. Unloading lasted only a few minutes, the mud from the truck was dropped from a height of 2 m. At the same time, one worker was checking a pump mechanism in the unconfined space surrounding the silo. As he was climbing the stairs to leave this area, he lost consciousness. Two fellow workers went to his aid but also lost consciousness (see the figure below). When firefighters evacuated the area, the three workers were already dead. The authors explained that H_2S that had accumulated inside the silo had spilled out into the interior of the room due to a 'splashing effect' caused by the impact of the dumped sludge.



An environmental study was carried out 6 h after the accident in the area where the first worker had been working and detected 100 ppm of H_2S. The space was described by the authors as unconfined with natural ventilation.

Kage *et al.* (1997), case 1

Four workers lost consciousness in an underground tank (length 2.9 m, width 3.3 m, height 2.0 m) in a factory producing regenerated paper. The tank contained a liquid mixture of used paper and sodium sulphite to a depth of 50 cm. Two workers (A and B) entered the tank to remove plastic rope and plastic film which had twisted around the blades of the mixer set at the side of the tank. As A lost consciousness, B rushed out to call for help. He and other workers (C and D) entered the tank to rescue A, however, all of them lost consciousness inside the tank. The four men were sent to hospitals and all survived.

The concentrations of H_2S and oxygen within the tank were 114 ppm and 20.7% respectively 3 h after the accident.

Kage *et al.* (1997), case 3

One worker died in an underground drainage pump room (length 4.0 m, width 5.0 m, height 2.5 m) in a fish market. Two workers (A and B) entered the pump room to repair the pump. When A loosened a check valve, sewage within the pipe gushed out. Because B smelled the odour of H_2S, he rushed out to fetch a ventilator. When he returned, A was lying beneath a pool of sewage and died soon after.

The concentrations of H_2S and oxygen in the pump room were 123 ppm and 21.0% respectively 4 h after the accident.

Kage *et al.* (2004)

Gas poisoning occurred at a pit for wastewater treatment in a dye works. The wastewater containing sodium H_2S and sodium sulfide was neutralized with sulfuric acid, and then transferred to a precipitator set underground. A black sludge formed at the bottom of the precipitator and this sludge was carried up to a centrifugal pump on the second floor through a drainage pipe in a pit (width 2.3 m, length 2.4 m, depth 3.8 m). As the drainage pipe was blocked with sludge, an adult man (A) entered the pit to remove it. When he took off a joint of the pipe, the sludge in the pipe flowed into the pit. As he suddenly lost consciousness, three colleagues (B, C, D) entered the pit to rescue him. All of these men (A, B, C, D) lost consciousness in the pit. They were sent to hospitals and died 1-3 h after the accident. The level of the sludge rose to a depth of 1.1 m in the pit. A diagram of the pit is shown below.

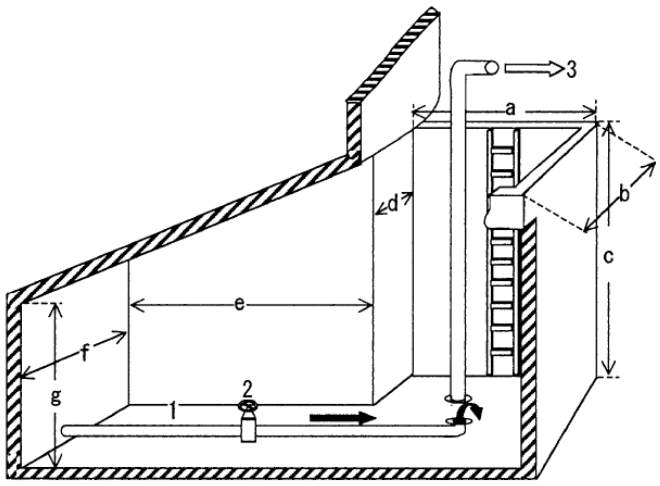


Fig. 1. Diagram of the pit for wastewater treatment where the gas poisoning accident occurred: 1, drainage pipe; 2, valve; 3, centrifugal pump a(width) = 2.3 m, b(length) = 2.4 m, c(depth) = 3.8 m d = 0.5 m, e = 3.5 m, f = 1.0 m, g = 1.1 m.

The sludge in the pit was put into a 100 mL Erlenmeyer flask with a sealed cap and the flask was stirred vigorously. Hydrogen sulfide gas was detected over 4000 ppm from the head space of the flask using a gas detector tube (detection range 10-4000 ppm). Gas poisoning was suspected, however, as the air in the pit had escaped at the time of rescuing the victims, the concentrations of H_2S and oxygen in the pit were 1 ppm and 21% using a gas analyser respectively.

The concentration of H_2S and oxygen in the pit was measured 2 months after the

accident using the same conditions as those on the day of the accident. Hydrogen sulfide and oxygen concentrations were 850 ppm and 21% respectively.

Black sludge was found in the airway and the stomach of each cadaver on autopsy. Serious damage or disease were not evident in any victim.

Thresholds for toxic effects from inhalation of H_2S in humans according to various sources

OSHA (2019)

This table from the website of the US Occupational Safety and Health Administration is included in the CLH report (Table 15). No references are attached to this table on the web page.

Concentration (ppm)	**Symptoms/Effects**
0.00011-0.00033	Typical background concentrations
0.01-1.5	Odor threshold (when rotten egg smell is first noticeable to some). Odor becomes more offensive at 3-5 ppm. Above 30 ppm, odor 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 edema 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 or 2 breaths, breathing stops, death within minutes.
1000-2000	Nearly instant death.

Consistently with some other sources, the threshold for pulmonary oedema from prolonged exposure is stated to lie around 200-300 ppm. Then it is not clear by which mechanism death occurs after exposure to 100 ppm. The text below the table explains that "people who have asthma may be more sensitive to H_2S exposure. That is, they may have difficulty breathing at levels lower than people without asthma." However, no explicit link is made between asthma and possible mortality around 100 ppm.

UBA (2006)

The table below comes from a German document titled 'Zur Sicherheit bei Biogasanlagen' (The safety of biogas plants) issued by the German Environment Agency. The table has been translated into English by RAC. No references are attached to the table in the publication.

< 100 ppm	dangerous to life after several hours
> 100 ppm	dangerous to life < one hour
100 to 150 ppm	irritation of the eyes and airways
200 to 300 ppm	severe local irritation of the mucosa with general signs of toxicity after 30 minutes, effect on the central nervous system (olfactory paralysis)
ca. 500 ppm	dangerous to life in 30 minutes
ca. 1000 ppm	dangerous to life in a few minutes
> 1000 ppm	loss of consciousness, breathing disorders, convulsions that may lead to death in a few minutes
ca. 5000 ppm	lethal in a few seconds

NIOSH (2014)

This web page presents information forming a basis of the current IDLH. Besides animal data, it refers to two human case reports where exposure to concentrations of 600 ppm and 800 ppm resulted in death; "time" (presumably exposure duration) was 30 min and 5 min respectively.

Further, the following human data taken into account in IDLH derivation is presented together with references: "It has been reported that 170 to 300 ppm is the maximum concentration that can be endured for 1 hour without serious consequences and that olfactory fatigue occurs at 100 ppm. It has also been reported that 50 to 100 ppm causes mild conjunctivitis and respiratory irritation after 1 hour; 500 to 700 ppm may be dangerous in 0.5 to 1 hour; 700 to 1000 ppm results in rapid unconsciousness, cessation of respiration, and death; and 1000 to 2000 ppm results in unconsciousness, cessation of respiration, and death in a few minutes."

Guidotti (2010, 1996)

The table below comes from two review articles on H_2S toxicity to humans. Occupational exposure limits have been omitted from the table. The effects in the table are discussed in more detail in the articles and a number of references are given.

Concentration (ppm)	**Effects**
0.01-0.3	Odor threshold (highly variable)
1-5	Moderate offensive odor, may be associated with nausea, tearing of the eyes, headaches, or loss of sleep with prolonged exposure; healthy male participants experience no decline in maximal physical work capacity
10	Anaerobic metabolism threshold during exercise

20	Odor very strong; conjunctivitis may occur
20-50	Conjunctivitis (eye irritation) and lung irritation. Possible eye damage after several days of exposure; may cause digestive upset and loss of appetite
100	Eye and lung irritation; olfactory paralysis, odor disappears
150-200	Sense of smell paralyzed; severe eye and lung irritation
250-500	Pulmonary edema may occur, especially if prolonged
500	Serious damage to eyes within 30 minutes; severe lung irritation; "knockdown" (sudden unconsciousness) and death within 4- to 8-hours; amnesia for period of exposure
1000	Breathing may stop within 1 or 2 breaths; immediate collapse

WHO (CICAD) (2003)

The table below comes from a WHO assessment. The values in mg/m^3 have been converted to ppm by RAC using a conversion factor of 0.71. References are provided for each row in the publication.

Exposure (mg/m^3)	**Exposure (ppm)**	**Effect / observation**
0.011	0.008	Odor threshold
2.8	2.0	Bronchial constriction in asthmatic individuals
5.0	3.6	Increased eye complaints
7 or 14	5 or 10	Increased blood lactate concentration, decreased skeletal muscle citrate synthase activity, decreased oxygen uptake
5-29	4-21	Eye irritation
28	20	Fatigue, loss of appetite, headache, irritability, poor memory, dizziness
>140	>100	Olfactory paralysis
>560	>400	Respiratory distress
≥700	≥500	Death

Knight and Presnell (2005)

This review article and case report contains a table reportedly adapted from another source.

Concentration (ppm)	**Effects**
0.02	Odor threshold
10	Unpleasant odor
30	Intense odor
50	Conjunctival and upper-respiratory irritation over time

100	Olfactory fatigue in minutes
150	Olfactory nerve paralysis
200	Intense immediate stinging, eyes and throat; smell disappears rapidly
300-500	Pulmonary edema, apnea in minutes
700-900	Rapid loss of consciousness, apnea (central respiratory paralysis)
>1000	Near-instant respiratory paralysis and coma

Policastro and Otten (2007)

This case report and review article on H_2S poisoning has been identified by RAC. It contains the following table, which is based on several sources listed in the publication.

Concentration (ppm)	**Clinical effects**
0.025	Detectable odor
0.15	Offensive odor
10	Sore eyes
20-30	Strong intense odor
50	Conjunctival irritation
100	Olfactory fatigue
250	Prolonged exposure may cause death
300-500	Pulmonary edema, immediate threat to life
500	Dizziness, respiratory arrest imminent
1000	Unconscious immediately, imminent death

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

13 REFERENCES

Arnold I.M.F., Dufresne R.M., Alleyne B.C., and Stuart P.J.W. (1985): Health implication of occupational exposures to hydrogen sulfide. Journal of Occupational Medicine 27 (5), 373-376. https://www.scopus.com/inward/record.uri?eid=2-s2.0-0021872033&partnerID=40&md5=1aba8f9c2d2616b5d12b5d2f480ce024

ATSDR (2016): Toxicological Profile for Hydrogen Sulfide / Carbonyl Sulfide. U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, Public Health Service, Agency for Toxic Substances and Disease Registry

Ballerino-Regan D. and Longmire A.W. (2010): Hydrogen Sulfide Exposure as a Cause of Sudden Occupational Death. Archives of Pathology & Laboratory Medicine 134 (8), 1105-1105. DOI: 10.1043/2010-0123-le.1

BAM (2010): Recommended safety characteristics and classifications of flammable gases and gas mixtures. (2007) Datenbank BAM-Projekt CHEMSAFE.

Barbera N., Montana A., Indorato F., Arbouche N., and Romano G. (2017): Evaluation of the Role of Toxicological Data in Discriminating Between H2S Femoral Blood Concentration Secondary to Lethal poisoning and Endogenous H2S Putrefactive Production. Journal of Forensic Sciences 62 (2), 392-394. DOI: 10.1111/1556-4029.13291

Beauchamp R.O., Bus J.S., Popp J.A., Boreiko C.J., Andjelkovich D.A., and Leber P. (1984): A critical review of the literature on hydrogen sulfide toxicity. Critical Reviews in Toxicology 13 (1), 25-97. DOI: 10.3109/10408448409029321

Braker W. and Mossmann A.L. (1980): Matheson Gas Products

Burnett W.W., King E.G., Grace M., and Hall W.F. (1977): Hydrogen sulfide poisoning: review of 5 years' experience. Canadian Medical Association Journal 117 (3), 1277-1280. https://www.scopus.com/inward/record.uri?eid=2-s2.0-0017652080&partnerID=40&md5=e598448a3d7c34b0be5e2972cdd5abda

Chaturvedi A.K., Smith D.R., and Canfield D.V. (2001): A fatality caused by accidental production of hydrogen sulfide. Forensic Sci Int 123 (2-3), 211-214. DOI: 10.1016/s0379-0738(01)00552-7

CHEMSAFE (2016): Database that contains safety characteristic data for fire and explosion prevention, evaluated and recommended by experts at BAM and PTB. CHEMSAFE is a joint project between BAM (Federal Institute for Materials Research and Testing, Berlin), PTB (Physikalisch-Technische Bundesanstalt, Braunschweig) and DECHEMA (Gesellschaft für Chemische Technik und Biotechnologie e.V., Frankfurt am Main).

Christia-Lotter A., Bartoli C., Piercecchi-Marti M.D., Demory D., Pelissier-Alicot A.L., Sanvoisin A., and Leonetti G. (2007): Fatal occupational inhalation of hydrogen sulfide. Forensic Science International 169 (2-3), 206-209. DOI: 10.1016/j.forsciint.2006.02.043

Coward H.F. and Jones G. W., (1952) Limits of flammability of gases and vapors, Bulletin 503, Bureau of mines, United States Government Printing Office, Washington (Pub.).

Daldal H., Beder B., Serin S., and Sungurtekin H. (2010): Hydrogen sulfide toxicity in a thermal spring: A fatal outcome. Clinical Toxicology 48 (7), 755-756. DOI: 10.3109/15563650.2010.508044

Daubert T.E. and Danner R.P. (1989): Physical and themodynamic properties of pure chemicals : data compilation. Design institute for physical property data, american institute of chemical engineers. corp. h.p., New York, NY.

Deng J.F. and Chang S.C. (1987): Hydrogen sulfide poisonings in hot-spring reservoir cleaning: two case reports. Am J Ind Med 11 (4), 447-451. DOI: 10.1002/ajim.4700110407

Doujaiji B. and Al-Tawfiq J.A. (2010): Hydrogen sulfide exposure in an adult male. Annals of Saudi Medicine 30 (1), 76-80. DOI: 10.4103/0256-4947.59379

Fuller D.C. and Suruda A.J. (2000): Occupationally related hydrogen sulfide deaths in the United States from 1984 to 1994. J Occup Environ Med 42 (9), 939-942. https://www.ncbi.nlm.nih.gov/pubmed/10998771

Gabbay D.S., De Roos F., and Perrone J. (2001): Twenty-foot fall averts fatality from massive hydrogen sulfide exposure. Journal of Emergency Medicine 20 (2), 141-144. DOI: 10.1016/S0736-4679(00)00301-2

Gangopadhyay R.K. and Das S.K. (2007): Accident due to release of hydrogen sulphide in a manufacturing process of cobalt sulphide - Case study. Environmental Monitoring and Assessment 129 (1-3), 133-135. DOI: 10.1007/s10661-006-9347-x

Gerasimon G., Bennett S., Musser J., and Rinard J. (2007): Acute hydrogen sulfide poisoning in a dairy farmer. Clin Toxicol (Phila) 45 (4), 420-423. DOI: 10.1080/15563650601118010

Gonzalez-Tepper D. (2017): Gewerbeaufsichtsamt informiert - Ursache für Unfall in Biogasanlage in Klostermoor ermittelt In: Osnabrücker Zeitung. Prof. Dr. Dres. h.c. Werner F. Ebke und Verleger Jan Dirk Elstermann Osnabrück, Germany. https://www.noz.de/lokales/ostfriesland/artikel/969912/ursache-fuer-unfall-in-biogasanlage-in-klostermoor-ermittelt

Gregorakos L., Dimopoulos G., Liberi S., and Antipas G. (1995): Hydrogen sulfide poisoning: management and complications. Angiology 46 (12), 1123-1131. DOI: 10.1177/000331979504601208

Guidotti T.L. (1996): Hydrogen sulphide. Occupational Medicine 46 (5), 367-371. DOI: 10.1093/occmed/46.5.367

Guidotti T.L. (2010): Hydrogen sulfide: Advances in understanding human toxicity. International Journal of Toxicology 29 (6), 569-581. DOI: 10.1177/1091581810384882

Guidotti T.L. (2015): Hydrogen sulfide intoxication. In: Handbook of Clinical Neurology, pp. 111-133. DOI: 10.1016/B978-0-444-62627-1.00008-1

Gunn B. and Wong R. (2001): Noxious gas exposure in the outback: Two cases of hydrogen sulfide toxicity. Emergency Medicine 13 (2), 240-246. DOI: 10.1046/j.1442-2026.2001.00220.x

Handlos P., Gebauerova V., Tomkova J., Zielinski P., and Marecova K. (2018): A fatal case of gas intoxication in silage pit. Journal of Forensic Sciences 63 (6), 1904-1907. DOI: 10.1111/1556-4029.13791

Hedlund F. and Madsen M. (2018): Incomplete understanding of biogas chemical hazards - Serious gas poisoning accident while unloading food waste at biogas plant. Journal of Chemical Health and Safety 25 (6), 13-21. DOI: 10.1016/j.jchas.2018.05.004

Hendrickson R.G., Chang A., and Hamilton R.J. (2004): Co-Worker Fatalities from Hydrogen Sulfide. American Journal of Industrial Medicine 45 (4), 346-350. DOI: 10.1002/ajim.10355

Hsu P. (1987): Acute hydrogen sulfide poisoning treated with hyperbaric oxygen. J. Hyperbaric Med. 2 (2), 215-221

Jones K. (2014): Case studies of hydrogen sulphide occupational exposure incidents in the UK. Toxicol Lett 231 (3), 374-377. DOI: 10.1016/j.toxlet.2014.08.005

Kage S., Ikeda H., Ikeda N., Tsujita A., and Kudo K. (2004): Fatal hydrogen sulfide poisoning at a dye works. Leg Med (Tokyo) 6 (3), 182-186. DOI: 10.1016/j.legalmed.2004.04.004

Kage S., Ito S., Kishida T., Kudo K., and Ikeda N. (1998): A fatal case of hydrogen sulfide poisoning in a geothermal power plant. J Forensic Sci 43 (4), 908-910. https://www.ncbi.nlm.nih.gov/pubmed/9670519

Kage S., Kashimura S., Ikeda H., Kudo K., and Ikeda N. (2002): Fatal and nonfatal poisoning by hydrogen sulfide at an industrial waste site. J Forensic Sci 47 (3), 652-655. https://www.ncbi.nlm.nih.gov/pubmed/12051356

Kage S., Nagata T., Kimura K., Kudo K., and Imamura T. (1992): Usefulness of thiosulfate as an indicator of hydrogen sulfide poisoning in forensic toxicological examination - a study with animal experiments. Japanese Journal of Forensic Toxicology 10, 223-227. https://hero.epa.gov/hero/index.cfm/reference/details/reference_id/12026

Kage S., Takekawa K., Kurosaki K., Imamura T., and Kudo K. (1997): The usefulness of thiosulfate as an indicator of hydrogen sulfide poisoning: three cases. Int J Legal Med 110 (4), 220-222. DOI: 10.1007/s004140050071

Kangas J. and Savolainen H. (1987): Urinary thiosulphate as an indicator of exposure to hydrogen sulphide vapour. Clinica Chimica Acta 164 (1), 7-10. DOI: https://doi.org/10.1016/0009-8981(87)90101-X

Khan A.A., Schuler M.M., Prior M.G., Yong S., Coppock R.W., Florence L.Z., and Lillie L.E. (1990): Effects of hydrogen sulfide exposure on lung mitochondrial respiratory chain enzymes in rats. Toxicol Appl Pharmacol 103 (3), 482-490. https://www.ncbi.nlm.nih.gov/pubmed/2160136

Kilburn K.H. (1993): Case report: profound neurobehavioral deficits in an oil field worker overcome by hydrogen sulfide. Am J Med Sci 306 (5), 301-305. https://www.ncbi.nlm.nih.gov/pubmed/8238084

Kimura K., Hasegawa M., Matsubara K., Maseda C., Kagawa M., Takahashi S., and Tanabe K.-i. (1994): A fatal disaster case based on exposure to hydrogen sulfide — an estimation of the hydrogen sulfide concentration at the scene. Forensic Science International 66 (2), 111-116. DOI: https://doi.org/10.1016/0379-0738(94)90335-2

Kirk-Othmer (1991): Kirk-Othmer Encyclopedia of Chemical Technology. Sons J.W.a., New York, NY

Knight L.D. and Presnell S.E. (2005): Death by sewer gas: case report of a double fatality and review of the literature. Am J Forensic Med Pathol 26 (2), 181-185. https://www.ncbi.nlm.nih.gov/pubmed/15894856

Lancia M., Panata L., Tondi V., Carlini L., Bacci M., and Rossi R. (2013): A fatal work-related poisoning by hydrogen sulfide: Report on a case. American Journal of Forensic Medicine and Pathology 34 (4), 315-317. DOI: 10.1097/PAF.0000000000000055

Lindenmann J., Matzi V., Neuboeck N., Ratzenhofer-Komenda B., Maier A., and Smolle-Juettner F.M. (2010): Severe hydrogen sulphide poisoning treated with 4-dimethylaminophenol and hyperbaric oxygen. Diving and Hyperbaric Medicine 40 (4), 213-217. <Go to ISI>://WOS:000285704700010

Lopez A., Prior M.G., Reiffenstein R.J., and Goodwin L.R. (1989): Peracute toxic effects of inhaled hydrogen sulfide and injected sodium hydrosulfide on the lungs of rats. Fundamental and Applied Toxicology 12 (2), 367-373. DOI: 10.1016/0272-0590(89)90053-5

Lund O.E. and Wieland H. (1966): [Pathologic-anatomic findings in experimental hydrogen sulfide poisoning (H2S). A study on rhesus monkeys]. Int Arch Arbeitsmed 22 (1), 46-54. https://www.ncbi.nlm.nih.gov/pubmed/5957909

Malone Rubright S.L., Pearce L.L., and Peterson J. (2017): Environmental toxicology of hydrogen sulfide. Nitric Oxide - Biology and Chemistry 71, 1-13. DOI: 10.1016/j.niox.2017.09.011

Milby T.H. (1962): Hydrogen sulfide intoxication. Review of the literature and report of unusual accident resulting in two cases of nonfatal poisoning. J Occup Med 4, 431-437. https://www.ncbi.nlm.nih.gov/pubmed/14473818

Molnarne, M., Schendler, Th., Schröder, V., (2008), Safety characteristic data, volume 2: Explosion regions of gas mixtures, NW-Verlag, Bremerhaven.

Mooyaart E.A.Q., Gelderman E.L.G., Nijsten M.W., de Vos R., Hirner J.M., de Lange D.W., Leuvenink H.D.G., and van den Bergh W.M. (2016): Outcome after hydrogen sulphide intoxication. Resuscitation 103, 1-6. DOI: https://doi.org/10.1016/j.resuscitation.2016.03.012

Morii D., Miyagatani Y., Nakamae N., Murao M., and Taniyama K. (2010): Japanese experience of hydrogen sulfide: the suicide craze in 2008. J Occup Med Toxicol 5, 28. DOI: 10.1186/1745-6673-5-28

Nabert K. and Schoen G. (1963): Sicherheitstechnische Kennzahlen brennbarer gase und daempfe. Eichverlag D., Braunschweig (Pub.), 1963-1990, 2 ED

National Research Council (2010): NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health. National Research Council (US) Committee on Acute Exposure Guideline Levels. Acute Exposure Guideline Levels for Selected Airborne Chemicals. Washington (DC): National Academies Press (US)

NIOSH (1991): NIOSH FACE Reports - Two Maintenance Workers Die After Inhaling Hydrogen Sulfide in Manhole. FACE 8928. CDC. https://www.cdc.gov/niosh/face/in-house/full8928.html

NIOSH (1994): NIOSH pocket guide to chemicals hazards. Office U.G.P., Washington, D.C.

NIOSH (2014): Hydrogen sulfide. The National Institute for Occupational Safety and Health (NIOSH). https://www.cdc.gov/niosh/idlh/7783064.html (last accessed 27.11.2019)

Nogue S., Pou R., Fernandez J., and Sanz-Gallen P. (2011): Fatal hydrogen sulphide poisoning in unconfined spaces. Occup Med (Lond) 61 (3), 212-214. DOI: 10.1093/occmed/kqr021

Oesterhelweg L., Kaufmann R., Hornborstel G., Bostelmann J., Schulz F., and Püschel K. (2006): [Fatalities related to biogas] in German. Kriminalistik 60, 594-598

Osbern L.N. and Crapo R.O. (1981): Dung lung: a report of toxic exposure to liquid manure. Ann Intern Med 95 (3), 312-314. https://www.ncbi.nlm.nih.gov/pubmed/7271092

https://annals.org/aim/article-abstract/695050/dung-lung-report-toxic-exposure-liquid-manure?volume=95&issue=3&page=312

OSHA (2019): Hydrogen Sulfide. U.S. Department of Labor, Occupational Safety & Health Administration (OSHA). https://www.osha.gov/SLTC/hydrogensulfide/hazards.html (last accessed 27.11.2019)

Park J., Kang T., Jin S., Heo Y., Kim K., Lee K., Tsai P., and Yoon C. (2016): Asphyxiation Incidents by Hydrogen Sulfide at Manure Storage Facilities of Swine Livestock Farms in Korea. Journal of Agromedicine 21 (2), 144-148. DOI: 10.1080/1059924X.2016.1141735

Parra O., Monso E., Gallego M., and Morera J. (1991): Inhalation of hydrogen sulphide: A case of subacute manifestations and long term sequelae. British Journal of Industrial Medicine 48 (4), 286-287. https://www.scopus.com/inward/record.uri?eid=2-s2.0-0026032638&partnerID=40&md5=e2e489924358ba793f999d572a0e23f6

https://oem.bmj.com/content/oemed/48/4/286.full.pdf

Prior M.G., Sharma A.K., Yong S., and Lopez A. (1988): Concentration-Time Interactions in Hydrogen-Sulfide Toxicity in Rats. Canadian Journal of Veterinary Research-Revue Canadienne De Recherche Veterinaire 52 (3), 375-379. <Go to ISI>://WOS:A1988P236800016

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1255467/pdf/cjvetres00055-0085.pdf

Public Health England (2016): Compendium of Chemical Hazards: Hydrogen Sulphide
Reedy S.J., Schwartz M.D., and Morgan B.W. (2011): Suicide fads: frequency and characteristics of hydrogen sulfide suicides in the United States. West J Emerg Med 12 (3), 300-304. https://www.ncbi.nlm.nih.gov/pubmed/21731786

https://escholarship.org/content/qt3zh3449s/qt3zh3449s.pdf?t=mpb1a3

Reiffenstein R.J., Hulbert W.C., and Roth S.H. (1992): Toxicology of hydrogen sulfide. Annual Review of Pharmacology and Toxicology 32, 109-134. https://www.scopus.com/inward/record.uri?eid=2-s2.0-0026642309&partnerID=40&md5=d0a2c57e42417cb2673ac71cb2892455

https://www.annualreviews.org/doi/pdf/10.1146/annurev.pa.32.040192.000545

Sastre C., Baillif-Couniou V., Kintz P., Cirimele V., Bartoli C., Christia-Lotter M.A., Piercecchi-Marti M.D., Leonetti G., and Pelissier-Alicot A.L. (2013): Fatal accidental hydrogen sulfide poisoning: a domestic case. J Forensic Sci 58 Suppl 1, S280-284. DOI: 10.1111/1556-4029.12015

Schneider J.S., Tobe E.H., Mozley Jr P.D., Barniskis L., and Lidsky T.I. (1998): Persistent cognitive and motor deficits following acute hydrogen sulphide poisoning. Occupational Medicine 48 (4), 255-260. DOI: 10.1093/occmed/48.4.255

Schröder, V. (2020): Volkmar Schröder is Head of Division 2.1 Explosion Protection Gases and Dusts at the Bundesanstalt für Materialforschung und -prüfung (BAM), Department 2 “Chemical Safety Engineering”, Unter den Eichen 87, 12205 Berlin, Germany.

Shivanthan M.C., Perera H., Jayasinghe S., Karunanayake P., Chang T., Ruwanpathirana S., Jayasinghe N., De Silva Y., and Jayaweerabandara D. (2013): Hydrogen sulphide inhalational toxicity at a petroleum refinery in Sri Lanka: A case series of seven survivors following an industrial accident and a brief review of medical literature. Journal of Occupational Medicine and Toxicology 8 (1). DOI: 10.1186/1745-6673-8-9

Smilkstein M.J., Bronstein A.C., Manning Pickett H., and Rumack B.H. (1985): Hyperbaric oxygen therapy for severe hydrogen sulfide poisoning. Journal of Emergency Medicine 3 (1), 27-30. DOI: 10.1016/0736-4679(85)90216-1

Tanaka S., Fujimoto S., Tamagaki Y., Wakayama K., Shimada K., and Yoshikawa J. (1999): Bronchial injury and pulmonary edema caused by hydrogen sulfide poisoning. Am J Emerg Med 17 (4), 427-429. DOI: 10.1016/s0735-6757(99)90102-x

Tansy M.F., Kendall F.M., Fantasia J., Landin W.E., Oberly R., and Sherman W. (1981): Acute and subchronic toxicity studies of rats exposed to vapors of methyl mercaptan and other reduced-sulfur compounds. J Toxicol Environ Health 8 (1-2), 71-88. DOI: 10.1080/15287398109530051

THRU Laboratories (1972): Toxic hazards research unit annual technical report: 1972. Report No. AMRL TR. Aerospace Medical Research Laboratory, Air Force Systems Command. Transportation U.D.o., Wright Patterson Air Force Base, Ohio, study report

Tvedt B., Skyberg K., Aaserud O., Hobbesland A., and Mathiesen T. (1991): Brain damage caused by hydrogen sulfide: A follow-up study of six patients. American Journal of Industrial Medicine 20 (1), 91-101. DOI: 10.1002/ajim.4700200109

UBA (2006): [The safety of biogas plants] in German. https://www.umweltbundesamt.de/sites/default/files/medien/publikation/long/3097.pdf (last accessed 17.01.2020)

US EPA (2003): TOXICOLOGICAL REVIEW OF HYDROGEN SULFIDE. U.S. Environmental Protection Agency

Ventura Spagnolo E., Romano G., Zuccarello P., Laudani A., Mondello C., Argo A., Zerbo S., and Barbera N. (2019): Toxicological investigations in a fatal and non-fatal accident due to hydrogen sulphide (H2S) poisoning. Forensic Science International 300, e4-e8. DOI: 10.1016/j.forsciint.2019.04.026

WHO (CICAD) (2003): HYDROGEN SULFIDE: HUMAN HEALTH ASPECTS

Will M. (2005): Unfall in der Betriebshalle der Biogasanlage in Rhadereistedt Vier Tote ein Schwerverletzter zehn verletzte Feuerwehrleute. Fachausschuss "Brandschutzerziehung Und Brand. Im Landesfeuerwehrverband Nord. e.V. (2005). Unfall_in_der_Biogasanlage2005.pdf.

https://docplayer.org/33745712-Unfall-in-der-betriebshalle-der-biogasanlage-in-rhadereistedt-vier-tote-ein-schwerverletzter-zehn-verletzte-feuerwehrleute.html

Yalamanchili C. and Smith M.D. (2008): Acute hydrogen sulfide toxicity due to sewer gas exposure. American Journal of Emergency Medicine 26 (4), 518.e515-518.e517. DOI: 10.1016/j.ajem.2007.08.025

Zabetakis M. G., (1965) Flammability characteristics of combustible gases and vapors, Bulletin 627, Bureau of mines, United States Government Printing Office, Washington (Pub.).

Zwart A., Arts J.H.E., Klokman-houweling J.M., and Schoen E.D. (1990): Determination of Concentration-Time-Mortality Relationships to Replace LC50 Values. Inhalation Toxicology 2 (2), 105-117. DOI: 10.3109/08958379009145248

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 H_2S decomposition into hydrogen and sulfur: application of classical and biological thermodynamics. Journal of Thermodynamics & Catalysis 8:2, doi: 10.4172/2157-7544.1000186

Annex I to the 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

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

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

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

Contact details for dossier submitter:

BAuA

Federal Institute for Occupational Safety and Health
Federal Office for Chemicals
Friedrich-Henkel-Weg 1-25
44149 Dortmund, Germany

Version number: 2.0 **Date: September 2020**

CONTENTS

ANNEX TO ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON HYDROGEN SULPHIDE, HYDROGEN SULFIDE

1 PHYSICAL HAZARDS

Not provided.

2 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

Not provided

3 HEALTH HAZARDS

Acute toxicity

3.1 Acute toxicity - oral route

3.2 Acute toxicity - dermal route

3.3 Acute toxicity - inhalation route

3.3.1 Animal data

3.3.1.1 Tansy et al. (1981)

Study reference:

Tansy M.F., Kendall F.M., Fantasia J., Landin W.E., Oberly R., and Sherman W. (1981): Acute and subchronic toxicity studies of rats exposed to vapors of methyl mercaptan and other reduced-sulfur compounds. Journal of Toxicology and Environmental Health 8 (1-2), 71-88.

Detailed study summary and results:

Test type

- Acute inhalation toxicity study, no guideline followed, no GLP

Test substance

- *Test substance:* hydrogen sulphide (EC: 231-977-3)
- *Degree of purity:* not specified
- *Impurities:* not specified
- *Batch number:* not specified

Test animals

- *Species/strain/sex:* rat / Sprague-Dawley / male and female (sexes were combined for treatment)
- *No. of animals per sex per dose:* 5
- *Age and weight at the study initiation:* age not specified, 90-100g (weight) at the study initiation

Administration/exposure

- *Type of inhalation exposure and test conditions:* gas inhalation (simultaneous whole body exposure in a glass chamber)
- *Duration of test/exposure period:* **4 h**
- *Doses/concentration levels*: 400, 440, 475, 500, 525, 554, and 600 ppm

- *Analytical verification of test atmosphere concentrations:* not specified
- *Post exposure observation period:* 14 days
- *Control group and treatment:* yes (sham-exposure to air)
- *Statistical methods:* LC50 values + 95 % confidence estimated according to Litchfield and Wilcoxon (1949)

Results and reliability

- *LC50:* 444 ppm, 95 % CL: 416 - 473
- *Number of deaths at each dose level:* following 4 h exposure

Concentration (ppm)	**Mortality**
Control	0/10
400	3/10
440	3/10
475	7/10
500	8/10
525	8/10
554	9/10
600	10/10

Additional information that may be needed to adequately assess data for reliability:

- *Time of death:* all animals that survived 24 h post-exposure, survived till the end of the 14-day post-exposure observation period
- *Clinical signs:* not specified
- *Necropsy findings, including doses affected, severity and number of animals affected:* not specified
- *Potential target organs (if identified in the report):* not specified
- *Other findings:* altered behaviour (exploring, huddling, preening, and obvious distress)
- *If both sexes tested, results should be compared:* not specified

3.3.1.2 Prior et al. (1988)

Study reference:

Prior M.G., Sharma A.K., Yong S., and Lopez A. (1988): Concentration-time interactions in hydrogen sulphide toxicity in rats. Canadian Journal of Veterinary Research 52 (3), 375-379.

Detailed study summary and results:

Test type

- Acute inhalation toxicity study, no guideline followed, no GLP

Test substance

- *Test substance:* hydrogen sulphide (EC: 231-977-3)
- *Degree of purity:* 99.5 %
- *Impurities:* not specified
- *Batch number:* not specified

Test animals

- *Species/strain/sex:* Rat / Long Evans, Sprague Dawley and Fischer 344 / male and female
- *No. of animals per sex per dose:* 9-12
- *Age and weight at the study initiation*: age: 7-8 weeks + 10 days acclimatization, weight: not specified

Administration/exposure

- *Type of inhalation exposure and test conditions:* gas inhalation (whole body exposure in a gas exposure chamber)
- *Duration of test/exposure period:* **2 h, 4 h and 6 h**
- *Doses/concentration levels:* various concentrations (details not given)
- *Analytical verification of test atmosphere concentrations:* yes (H_2S concentration was determined four times / h using gas chromatography)
- *Post exposure observation period:* 14 days
- *Control group and treatment:* yes
- *Statistical methods:*
    - Estimation of the effects of hydrogen sulphide concentration, sex, hours of exposure and strain on the weight loss: standard regression and analysis of covariance techniques
    - Estimation of lethal concentration (LC10 and LC50) values: probit analysis using a maximum likelihood iteration technique
    - Additional statistics: standard deviation, 95% confidence intervals, and chi-square goodness of fit

Results and reliability

- *LC50 and LC10:*

Duration of exposure	**LC50**	**LC10**	**Number of animals (n)**
2 h	587 ppm	549 ppm	156
4 h	501 ppm	422 ppm	144
6 h	335 ppm	299 ppm	156

- *Number of deaths at each dose level:* not specified

Additional information that may be needed to adequately assess data for reliability:

- *Time of death:* not specified

- *Clinical signs:* weight loss due to toxic gas
- *Necropsy findings:* mouth, nose, trachea, and bronchi contained foamy fluid; severe pulmonary edema (most likely cause for death); histology: proteinaceous fluids in conductive airways, alveoli and in perivascular space of major blood vessels
- *Potential target organs (if identified in the report):* whole respiratory tract
- *If both sexes tested, results should be compared:*
    - weight loss due to toxic gas: higher in males vs. females
    - mortality: 30 % in males vs. 20 % in females

3.3.1.3 Zwart et al. (1990)

Study reference:

Zwart A., Arts J.H.E., Klokman-Houweling J.M., and Schoen E.D. (1990): Determination of concentration-time-mortality relationships to replace LC50 values. Inhalation Toxicology 2 (2), 105-117.

Detailed study summary and results:

Test type

- Acute inhalation toxicity study, no guideline followed, no GLP

Test substance

- *Test substance:* hydrogen sulphide (EC: 231-977-3)
- *Degree of purity:* not specified
- *Impurities:* not specified
- *Batch number:* not specified

Test animals

- *Species/strain/sex:*
    - *rat:* Wistar / male and female
    - *mouse:* Swiss / male and female
- *No. of animals per sex per dose:* 5
- *Age and weight at the study initiation:*
    - *rats:* 5-6 weeks + 5 days acclimatization (age); 150-170 g (weight males), 130-140 g (weight females)
    - *mice:* 7-8 weeks + 5 days acclimatization (age); 23-34 g (weight males), 23-27 g (weight females)

Administration/exposure

- *Type of inhalation exposure and test conditions:* gas inhalation (whole body exposure in a gas exposure chamber)
- *Duration of test/exposure period:* **5, 10, 30 and 60 min**
- *Doses/concentration levels:* concentrations are given in mg/m3

- 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

- *Analytical verification of test atmosphere concentrations:* yes
- *Post exposure observation period:* 14 days
- *Control group and treatment:* not specified
- *Statistical methods:* stepwise forward selection procedure based on maximum likelihood regression methods

Results and reliability

- *LC50:*

	Rats (♀/♂)		**Mice (♀/♂)**	
	mg/m³ air	**ppm[1]**	**mg/m³ air**	**ppm[1]**
LC50 (10 min)	1160	~ 824	1610	~ 1143
LC50 (30 min)	1010	~ 717	1110	~ 788
LC50 (60 min)	950	~ 675	940	~ 667

- *Number of deaths at each dose level:*

Exposure Concentration		**Duration (min)**	**Number of animals/sex**	**Mortality rats**		**Mortality mice**	
(mg/m3)	**ppm[1]**			**Males**	**Females**	**Males**	**Females**
931	661	5	5	0	0	0	0
1196	849	5	5	2	0	0	0
1831	1300	5	5	5	5	1	2
931	661	10	5	0	0	0	0
1199	851	10	5	3	5	0	0
1821	1293	10	5	5	5	4	5
449	319	30	5	0	0	0	0
706	501	30	5	0	0	0	0
813	577	30	5	0	0	0	0
833	591	30	5	0	0	-	-
881	626	30	5	4	5	1	1
935	664	30	5	0	1	0	1
972	690	30	5	2	0	1	2
1032	733	30	5	2	1	0	0
448	318	60	5	0	0	0	0
703	499	60	5	0	0	0	3

[1] Calculated according to: 1 mg/m3 = 0.71 ppm (WHO (CICAD) (2003))

774	550	60	5	0	0	0	2
806	572	60	5	0	0	2	1
826	586	60	5	0	0	-	-
939	667	60	5	3	4	3	4
972	690	60	5	3	4	4	2

Additional information that may be needed to adequately assess data for reliability:

- *Time of death:* not specified
- *Clinical signs:* not specified
- *Necropsy findings:* not specified
- *Potential target organs:* not specified
- *If both sexes tested, results should be compared:* not specified

3.3.1.4 THRU Laboratories (1972)

Study reference:

THRU Laboratories (1972): Toxic hazards research unit annual technical report: 1972. Report No. AMRL TR. Aerospace Medical Research Laboratory, Air Force Systems Command. Transportation U.D.o., Wright Patterson Air Force Base, Ohio, study report

Detailed study summary and results:

Test type

- Acute inhalation toxicity study, guideline not specified, no GLP

Test substance

- *Test substance:* hydrogen sulphide (EC: 231-977-3)
- *Degree of purity:* not specified
- *Impurities:* not specified
- *Batch number:* not specified

Test animals

- *Species/strain/sex:*
    - *rat:* Sprague-Dawley / male
    - *mouse:* CF-1 / male
- *No. of animals per sex per dose:* 10
- *Age and weight at the study initiation:*
    - *rats:* age not specified; 200-300 g (weight)
    - *mice:* age not specified; 20-30 g (weight)

Administration/exposure

- *Type of inhalation exposure and test conditions:* gas inhalation (whole body exposure)

- *Duration of test/exposure period:* **1 h**
- *Doses/concentration levels:* 400, 504, 635, or 800 ppm
- *Analytical verification of test atmosphere concentrations:* yes (using an ion specific sulphide electrode)
- *Post exposure observation period:* 14 days
- *Control group and treatment:* no
- *Statistical methods:* not specified

Results and reliability

- *LC50:*
  - *rat:* 712 ppm (1 h)
  - *mouse:* 634 ppm (1 h)
- *Number of deaths at each dose level:*

Concentration (ppm)	Mortality	
	Rat	Mouse
400	0/10	2/10
504	0/10	0/10
635	1/10	5/10
800	9/10	8/10

Additional information that may be needed to adequately assess data for reliability:

- *Time of death:* not specified
- *Clinical signs:*
  - *rat:* gasping
  - *mouse:* gasping + convulsions during exposure
- *Necropsy findings:*
  - *rat:* congestion and mottling of kidney and liver with moderate to severe fatty changes in the liver observed in animals that survived the exposure
  - *mouse:* one mouse in the 635 ppm-group and one mouse in the 800 ppm-group had a blocked urethral opening due to encrustation of the external orifice, and a distended bladder, but both survived until end of the 14-day-obervation period
- *Potential target organs:* not specified
- *Other findings:* normal weight gain (surviving rats/mice during post-exposure period)
- *If both sexes tested, results should be compared:* not specified

3.3.1.5 Lopez et al. (1989)

Study reference:

Lopez A., Prior M.G., Reiffenstein R.J., and Goodwin L.R. (1989): Peracute toxic effects of inhaled hydrogen sulfide and injected sodium hydrosulfide on the lungs of rats. Fundamental and Applied Toxicology : Official Journal of the Society of Toxicology. 12 (2), 367-373.

Detailed study summary and results:

Test type

- Acute inhalation toxicity study, no guideline followed, no GLP

Test substance

- *Test substance:* hydrogen sulphide (EC: 231-977-3)
- *Degree of purity:* not indicated
- *Impurities:* not indicated
- *Batch number:* not indicated

Test animals

- *Species/strain/sex:* rat / Sprague-Dawley / male
- *No. of animals per sex per dose:* 5
- *Age and weight at the study initiation:* appr. 6 month (age), 485.7 +/- 50.1 g (weight)

Administration/exposure

- *Type of inhalation exposure and test conditions:* gas inhalation (whole body exposure in a glass)
- *Duration of test/exposure period:* 5 min
- *Doses/concentration levels:* mean concentration 1655.4 +/- 390.9 ppm (2317.6 +/- 547 mg/m3)
- *Analytical verification of test atmosphere concentrations:* yes (using gas chromatography)
- *Post exposure observation period:* all exposed animals died within 3 min, control animals all survived
- *Control group and treatment:* yes
- *Statistical methods:* not specified

Results and reliability

- *LC100*: 1655 +/- 390.9 ppm (2317 mg/m³ +/- 547 mg/m^3); all exposed animals died within 3 min, all control animals survived

Additional information that may be needed to adequately assess data for reliability:

- *Time of death:* 3 min
- *Clinical signs:* dyspnea, exaggerated abnormal audible respiration, frothy fluid from the nose and mouth
- *Necropsy findings:* pulmonary edema
- *Potential target organs:* not specified
- *Other findings:* not specified
- *If both sexes tested, results should be compared:* not specified

3.3.1.6 Khan et al. (1990)

Study reference:

Khan A.A., Schuler M.M., Prior M.G., Yong S., Coppock R.W., Florence L.Z., and Lillie L.E. (1990): Effects of hydrogen sulfide exposure on lung mitochondrial respiratory chain enzymes in rats. Toxicology and Applied Pharmacology 103 (3), 482-490.

Detailed study summary and results:

Test type

- Acute inhalation toxicity study, no guideline followed, no GLP

Test substance

- *Test substance:* hydrogen sulphide (EC: 231-977-3)
- *Degree of purity:* not specified
- *Impurities:* not specified
- *Batch number:* not specified

Test animals

- *Species/strain/sex:* rat / Fischer 344 / male
- *No. of animals per sex per dose:* 4-6
- *Age and weight at the study initiation:* 8-10 weeks (age) + 2 weeks acclimatization, weight not specified

Administration/exposure

- *Type of inhalation exposure and test conditions):* gas inhalation (whole body exposure)
- *Duration of test/exposure period:* **4 h**
- *Doses/concentration levels:* 0, 10, 50, 200, 400, or 500-700 ppm
- *Analytical verification of test atmosphere concentrations:* yes (using gas chromatography)
- *Post exposure observation period:*
    - 0-400 ppm-exposed rats: 1, 24 and 48 h
- *Control group and treatment:* yes
- *Statistical methods:* effects of H_2S exposures compared to control treatments on the activities mitochondrial enzymes: GLM procedures contained in version 6.03 of SAS for microcomputers (SAS Institute, Inc., 1988)

  Postexposure effects of H_2S: Means of treatment combinations were compared by orthogonal contrasts

Results and reliability

- *LC50:* not specified

- *Number of deaths at each dose level:*

Concentration (ppm)	Mortality
0	0
10	0
50	0
200	0
400	0
500-700	All animals died

Additional information that may be needed to adequately assess data for reliability:

- *Time of death:* not specified
- *Clinical signs:* no symptoms in rats exposed to 10, 50, 200 ppm; transient lethargy in animals exposed to 400 ppm
- *Necropsy findings:* not specified
- *Potential target organs:* not specified
- *Other findings:* inhibition of the mitochondrial respiratory chain enzymes in lung mitochondria
- *If both sexes tested, results should be compared:* not specified

3.3.1.7 Lund and Wieland (1966)

Study reference:

Lund O.E. and Wieland H. (1966): [Pathologic-anatomic findings in experimental hydrogen sulfide poisoning (H_2S). A study on rhesus monkeys]. Int Arch Arbeitsmed 22 (1), 46-54. (Publication in German)

Detailed study summary and results:

Test type

- Acute inhalation toxicity study, no guideline followed, no GLP

Test substance

- *Test substance:* hydrogen sulphide (EC: 231-977-3)
- *Degree of purity:* not specified
- *Impurities:* not specified
- *Batch number:* not specified

Test animals

- *Species/strain/sex:* monkey / rhesus / not specified
- *No. of animals per sex per dose:* 3
- *Age and weight at the study initiation:* not specified

Administration/exposure

- *Type of inhalation exposure and test conditions:* gas inhalation (method of exposure not specified)
- *Duration of test/exposure period:*

Animal	Duration of exposure	Post-exposure observation period
1	35 min	none
2	25 min and 3 days later 17 min	5 days
3	22 min	10 days

- *Doses/concentration levels:* 500 ppm
- *Analytical verification of test atmosphere concentrations:* not specified
- *Post exposure observation period:* 0-10 days
- *Control group and treatment:* no
- *Statistical methods:* not specified

Results and reliability

- *LC50:* not specified
- *Number of deaths at each dose level:* One out of three animals died after 35 min of exposure to 500 ppm H_2S

Additional information that may be needed to adequately assess data for reliability:

- *Time of death:* animal 1 died after 35 min of exposure to 500 ppm H_2S
- *Clinical signs:* conjunctival irritation

Animal	Clinical signs + mortality
1	35 min: sudden unconsciousness, apnea, acute respiratory and cardiac arrest with lethality
2	25 min (1st exposure): sudden unconciousness + apnea (nearly lethal) during first exposure but successful reanimation 17 min (2nd exposure 3 days later): sudden unconciousness
3	22 min: sudden unconciousness but no apnea, in post-exposure observation period animal was somnolent, low locomotor activity, anorexia

- *Necropsy findings:*

Animal	Histopathological findings
1	No marked findings
2	Necrotic alterations of the cerebral cortex and basal ganglia, no changes in kidney, adrenal glands and heart
3	Necrotic alterations of the cerebral cortex, no changes in kidney, adrenal glands and heart

- *Potential target organs:* not specified
- *Other findings:* not specified
- *If both sexes tested, results should be compared:* not specified

3.3.1.8 Kage et al. (1992)

Study reference:

Kage S., Nagata T., Kimura K., Kudo K., and Imamura T. (1992): Usefulness of thiosulfate as an indicator of hydrogen sulfide poisoning in forensic toxicological examination - a study with animal experiments. Japanese Journal of Forensic Toxicology 10, 223-227.

Detailed study summary and results:

Test type

- *Acute inhalation toxicity study, no guideline followed, no GLP*

Test substance

- *Test substance:* hydrogen sulphide (EC: 231-977-3)
- *Degree of purity:* not specified
- *Impurities:* not specified
- *Batch number:* not specified

Test animals

- *Species/strain/sex:* rabbit / Japanese White / not specified
- *No. of animals per sex per dose:* 5
- *Age and weight at the study initiation:* not specified

Administration/exposure

- *Type of inhalation exposure and test conditions:* not specified
- *Duration of test/exposure period:* 14-30 min
- *Doses/concentration levels:* 100-200 ppm and 500-1000 ppm
- *Analytical verification of test atmosphere concentrations:* not specified
- *Post exposure observation period:* 2 h and 24 h
- *Control group and treatment:* not specified
- *Statistical methods:* not specified

Results and reliability

- *LD50 or LC50 value with confidence limits if calculated:* not specified
- *Number of deaths at each dose level:* all animals (5/5) died at 500-1000 ppm

Additional information that may be needed to adequately assess data for reliability:

- *Time of death:* not specified
- *Clinical signs:* not specified
- *Necropsy findings:* not specified
- *Potential target organs (if identified in the report):* blood, lung, brain
- *Other findings:* not specified
- *If both sexes tested, results should be compared:* not specified

3.4 Skin corrosion/irritation

3.5 Serious eye damage/eye irritation

3.6 Respiratory sensitisation

3.7 Skin sensitisation

3.8 Germ cell mutagenicity

3.9 Carcinogenicity

3.10 Reproductive toxicity

3.11 Specific target organ toxicity – single exposure

3.12 Specific target organ toxicity – repeated exposure

3.13 Aspiration hazard

4 ENVIRONMENTAL HAZARDS

Not provided

Kage S., Nagata T., Kimura K., Kudo K., and Imamura T. (1992): Usefulness of thiosulfate as an indicator of hydrogen sulfide poisoning in forensic toxicological examination - a study with animal experiments. Japanese Journal of Forensic Toxicology 10, 223-227. https://hero.epa.gov/hero/index.cfm/reference/details/reference_id/12026

Khan A.A., Schuler M.M., Prior M.G., Yong S., Coppock R.W., Florence L.Z., and Lillie L.E. (1990): Effects of hydrogen sulfide exposure on lung mitochondrial respiratory chain enzymes in rats. Toxicol Appl Pharmacol 103 (3), 482-490. https://www.ncbi.nlm.nih.gov/pubmed/2160136

Lopez A., Prior M.G., Reiffenstein R.J., and Goodwin L.R. (1989): Peracute toxic effects of inhaled hydrogen sulfide and injected sodium hydrosulfide on the lungs of rats. Fundamental and Applied Toxicology 12 (2), 367-373. DOI: 10.1016/0272-0590(89)90053-5

Lund O.E. and Wieland H. (1966): [Pathologic-anatomic findings in experimental hydrogen sulfide poisoning (H2S). A study on rhesus monkeys]. Int Arch Arbeitsmed 22 (1), 46-54. https://www.ncbi.nlm.nih.gov/pubmed/5957909

Prior M.G., Sharma A.K., Yong S., and Lopez A. (1988): Concentration-time interactions in hydrogen sulphide toxicity in rats. Canadian Journal of Veterinary Research 52 (3), 375-379. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1255467/

Tansy M.F., Kendall F.M., Fantasia J., Landin W.E., Oberly R., and Sherman W. (1981): Acute and subchronic toxicity studies of rats exposed to vapors of methyl mercaptan and other reduced-sulfur compounds. Journal of Toxicology and Environmental Health 8 (1-2), 71-88. DOI: 10.1080/15287398109530051

THRU Laboratories (1972): Toxic hazards research unit annual technical report: 1972. Report No. AMRL TR. Aerospace Medical Research Laboratory, Air Force Systems Command. Transportation U.D.o., Wright Patterson Air Force Base, Ohio, study report

WHO (CICAD) (2003): HYDROGEN SULFIDE: HUMAN HEALTH ASPECTS

Zwart A., Arts J.H.E., Klokman-houweling J.M., and Schoen E.D. (1990): Determination of Concentration-Time-Mortality Relationships to Replace LC50 Values. Inhalation Toxicology 2 (2), 105-117. DOI: 10.3109/08958379009145248