Soluble Sulfide Salts: Human health tier II assessment

24 April 2015

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Potassium sulfide (K2S)	1312-73-8
Sodium sulfide (Na2S)	1313-82-2
Ammonium sulfide, (NH4)(SH)	12124-99-1
Ammonium sulfide ((NH4)2S)	12135-76-1
Sodium sulfide (Na(SH))	16721-80-5
Calcium sulfide (CaS)	20548-54-3
Barium sulfide (BaS)	21109-95-5

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

These chemicals are assessed together based on their relative solubility in water. Sulfide salts are generally insoluble except for a few including ammonium (NH_4^+), alkali metal and alkali earth metal salts (Morgan, 2011). Ammonium was reported to behave like an alkali metal (Bernal & Massey, 1954).

Under normal physiological conditions (pH~7), the chemicals in this group will dissociate into hydrogen sulfide anion (HS^-) and hydrogen sulfide (H_2S; CAS No. 7783-06-4). Under very acidic conditions (e.g. in gastric juice), the formation of H_2S will predominate. It is very unlikely that the sulfide anion (S^{2-}) will be present under normal physiological conditions given the second dissociation constant of hydrogen sulfide (pKa_2 >15) (Meyer, 1983).

No added toxicity is expected from the cations calcium, sodium, potassium and ammonium. However, the barium cation (Ba^{2+}) is reported to be toxic to humans at high doses (ATSDR, 2007). The systemic behaviour of the chemicals will, therefore, be determined by the physiological conditions influencing dissociation and not by the type of sulfide salt, justifying read-across between these chemicals.

Import, Manufacture and Use

Australian

Sodium sulfide salts (Na_2S and NaSH) are listed on the 2006 High Volume Industrial Chemicals List (HVICL) within the total reported volume range of 1000–9999 tonnes for site-limited use as flotation agents in mining and metal extraction (HVICL, 2006).

Sodium bisulfide is listed for other site-limited applications including paper pulping, dyestuff processing, removing hair from hides, rayon and cellophane desulfurising and bleaching (Orica Chemicals, 2013).

For the other chemicals (ammonium bisulfide, ammonium sulfide, calcium and barium sulfide) no specific Australian use, import, or manufacturing information has been identified.

The following non-industrial uses have been identified in Australia:

- sodium sulfide and calcium sulfide as active constituents in pesticides and veterinary medicines (Australian Pesticides and Veterinary Medicines Authority—APVMA); and
- sodium sulfide for treating hides for use in gelatine and collagen manufacture (Food Standards Australia New Zealand—FSANZ).

International

The following international uses have been identified through: the European Union (EU) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; the European Commission Cosmetic Ingredients and Substances (CosIng) database; the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); and the Agency for Toxic Substances and Disease Registry (ATSDR).

Four of the chemicals (calcium, barium, sodium and potassium sulfide) have reported cosmetic use as a depilatory (hair removal) agent (see **Restrictions: International** for concentration limits).

Calcium sulfide has reported domestic use in luminous paints.

Ammonium and sodium sulfide and bisulfide salts have reported commercial uses in the textile industry, photography, engraving and lithography. Sodium sulfide salts also have reported use in heavy metal removal from wastewater.

All these chemicals have reported site-limited use in manufacturing other chemicals. For some of the chemicals, other site-limited applications include pulp and paper manufacture, textile manufacture and mining industry.

Ammonium sulfide salts (NH_4SH and $(NH_4)_2S$) have reported non-industrial uses in food flavouring and additives, while calcium sulfide has a reported non-industrial use in pesticides.

Restrictions

Australian

Some of the chemicals in this group are listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) as follows:

Potassium sulfide in Schedule 5:

- 'in preparations for metal treatment in containers each containing 50 g or less of potassium sulfide'

Sodium sulfide in Schedules 5 and 6:

- Schedule 5—'in preparations for metal treatment in containers each containing 50 g or less of sodium sulfide'; and
- Schedule 6—'in preparations for use as insect lures'.

Barium sulfide in Schedule 6:

- 'BARIUM SALTS **except**: (a) when included in Schedule 5; (b) barium sulfate; or (c) in paints or tinters containing 5 per cent or less of barium calculated on the non-volatile content of the paint or tinter'.

Schedule 5 chemicals are described as 'Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.' Schedule 5 chemicals are labelled with 'Caution' (SUSMP, 2015).

Schedule 6 chemicals are described as 'Substances with a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label'. Schedule 6 chemicals are labelled with 'Poison' (SUSMP, 2015).

No known restrictions have been identified for the other chemicals in this group.

International

The following restrictions are applicable for all or some of these chemicals (Galleria Chemica):

- Use of calcium, barium, sodium or potassium sulfide in cosmetics in the European Union is subject to the restrictions described in the Annex III of the Cosmetic Regulation (EC) No. 1223/2009. These chemicals may be used in depilatory products at a maximum concentration of 2 % (as sulfur) for alkali (sodium and potassium) sulfides and 6 % (as sulfur) for alkali earth (calcium and barium) sulfides (CosIng).
- Ammonium sulfide and bisulfide are on Annex XVII of REACH, prohibiting their use 'in jokes and hoaxes or in mixtures or articles intended to be used as such, for instance as a constituent of sneezing powder and stink bombs'.
- As the chemicals release hydrogen sulfide when in contact with acid and water, the following restriction from Annex XVII of REACH applies to all chemicals in this group: 'Substances classified as flammable gases category 1 or 2, flammable liquids categories 1, 2 or 3, flammable solids category 1 or 2, substances and mixtures which, in contact with water, emit flammable gases, category 1, 2 or 3, pyrophoric liquids category 1 or pyrophoric solids category 1, regardless of whether they appear in Part 3 of Annex VI to Regulation (EC) No 1272/2008 or not.

1. Shall not be used, as substance or as mixtures in aerosol dispensers where these aerosol dispensers are intended for supply to the general public for entertainment and decorative purposes such as the following: metallic glitter intended mainly for decoration, artificial snow and frost, ‘whoopee’ cushions, silly string aerosols, imitation excrement, horns for parties, decorative flakes and foams, artificial cobwebs, stink bombs.

2. Without prejudice to the application of other Community provisions on the classification, packaging and labelling of substances, suppliers shall ensure before the placing on the market that the packaging of aerosol dispensers referred to above is marked visibly, legibly and indelibly with: ‘For professional users only’.

3. By way of derogation, paragraphs 1 and 2 shall not apply to the aerosol dispensers referred to Article 8 (1a) of Council Directive 75/324/ EEC.

4. The aerosol dispensers referred to in paragraphs 1 and 2 shall not be placed on the market unless they conform to the requirements indicated.'

Existing Worker Health and Safety Controls

Hazard Classification

Four of the chemicals in this group are classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

Sodium sulfide (Na_2S; CAS No. 1313-82-2):

- T; R24 (acute toxicity)

- Xn; R22 (acute toxicity)
- C; R34 (corrosivity)
- R31 (toxic gas release in acidic conditions)

Potassium sulfide (K_2S; CAS No. 1312-73-8):

- C; R34 (corrosivity)
- R31 (toxic gas release in acidic conditions)

Calcium sulfide (CaS; CAS No. 20548-54-3):

- Xi; R36/37/38 (irritation)
- R31 (toxic gas release in acidic conditions)

Barium sulfide (BaS; CAS No. 21109-95-5):

- Xn; R20/22 (acute toxicity)
- R31 (toxic gas release in acidic conditions)

The other three chemicals are not listed on HSIS.

Exposure Standards

Australian

No specific exposure standards are available for the chemicals.

All chemicals in this group release hydrogen sulfide when in contact with water or in acidic conditions. Hydrogen sulfide has an exposure standard of 14 mg/m^3 (10 ppm) time weighted average (TWA) and 21 mg/m^3 (15 ppm) short-term exposure limit (STEL) (Safe Work Australia).

International

No specific exposure standards are available for the chemicals.

Hydrogen sulfide has an exposure standard of 7–14 mg/m^3 (5–10 ppm) TWA and 14–21 mg/m^3 (15 ppm) STEL in several countries including Canada, Chile, France, Denmark, Germany, Norway, the United Kingdom, the United States of America (USA) and South Africa.

The American Conference of Governmental Industrial Hygienists (ACGIH) recommends 1 ppm TWA and 5 ppm STEL for hydrogen sulfide (Galleria Chemica).

Health Hazard Information

The main hazards of these chemicals are their corrosivity due to the basic sulfide anions and their potential to release hydrogen sulfide, a highly toxic gas. Hydrogen sulfide is a direct-acting metabolic poison, which can inhibit the cytochrome oxidase (CO) activity affecting oxidative metabolism in respiratory and cardiovascular systems (Brenneman et al., 2002).

Toxicokinetics

Soluble sulfides are reported to be rapidly hydrolysed to produce hydrogen sulfide in body fluids. Therefore, the systemic toxicokinetic profile for these chemicals is considered similar to that for hydrogen sulfide (Health Canada, 1987).

Hydrogen sulfide is metabolised through three distinct pathways:

1. oxidation in the liver to thiosulfate then sulfate, which is excreted in the urine;
2. methylation; and
3. reaction with metalloproteins or disulfide-containing proteins, which is responsible for the toxic action of hydrogen sulfide (Health Canada, 1987; CICAD, 2003).

Oxidation to sulfate is the major metabolic pathway for sulfides. A study showed that an oral, intraperitoneal (i.p.) or intravenous (i.v.) doses of sodium sulfide administered to rats was mostly excreted in the urine 6–12 hours after dosing (Health Canada, 1987).

Acute Toxicity

Oral

Sodium and barium sulfide are classified as hazardous with the risk phrase 'Harmful if swallowed' (Xn; R22) in the HSIS. The available data on these two chemicals support this classification. Based on the available data, sodium and ammonium bisulfide have moderate and high acute oral toxicity, respectively, warranting hazard classification. No data are available on ammonium, potassium and calcium sulfide. Based on the the available information and common potential of alkali sulfides to cause acute toxic effects, all seven chemicals should be classified as 'Harmful if swallowed'.

The following median lethal dose (LD50) values were reported:

- 307 mg/kg bw for barium sulfide in Sprague Dawley (SD) rats (275 mg/kg bw for females and 336 mg/kg bw for males). Signs of toxicity included: congested liver and spleen; red colouration of the glandular mucous membrane of the stomach; red coloured contents in the ileum or milky white ileum contents; mucous membrane of the stomach congested and/or haemorrhaged (REACH);
- 208 mg/kg bw for sodium sulfide and bisulfide in rats (ChemIDPlus);
- 1122 mg/kg bw for sodium sulfide in Crj: CD(SD) rats. No deaths occurred at 1000 mg/kg bw, but all rats died at 1260 and 2000 mg/kg bw, 20 minutes after dosing (REACH); and
- 168 mg/kg bw for ammonium sulfide in rats (ChemIDPlus).

The LD50 for 70 % sodium bisulfide was calculated to be 115 mg/kg bw in Wistar rats, based on 30 % and 100 % mortality at oral gavage doses of 100 and 215 mg/kg bw, respectively (REACH). The LD50 was 253.8 mg/kg bw in Wistar rats for 60 % sodium sulfide (REACH). An LD50 of 184 mg/kg bw in female Wistar rats was reported for 30 % sodium bisulfide (REACH).

Dermal

Sodium sulfide is classified as hazardous with the risk phrase ‘Toxic in contact with skin’ (T; R24) in the HSIS (Safe Work Australia). Based on the available data (LD50 <340 mg/kg bw in rabbits for a 60 % concentration of sodium sulfide), this classification is supported for sodium sulfide.

Based on the available data for sodium and ammonium bisulfides, a lower hazard classification is warranted for these two chemicals. As all seven chemicals are corrosive and expected to have similar systemic availability through the dermal route of exposure, the other four chemicals in this group are considered to have at least moderate acute dermal toxicity, warranting a hazard classification.

Data are available only for sodium sulfide, sodium and ammonium hydrosulfide, indicating moderate to high acute dermal toxicity.

Following a single application of 340 mg/kg bw sodium sulfide (60 %) on the abraded skin of New Zealand White rabbits (n = 5/sex), the LD50 was determined to be <340 mg/kg bw, as 4/5 male and 4/5 female rabbits died six hours after exposure. Signs of toxicity included immediate distress of the animals, oral and nasal discharge, haemorrhagic lungs and acute skin necrosis. The surviving male rabbit exhibited black eschar formation (REACH).

Sodium bisulfide was applied at doses of 100, 200, 400, 800, 1600 mg/kg on the shaved skin of female Wistar rats. The LD50 was estimated to be 632 mg/kg bw, based on the mortality rates of 1/6, 4/6 and 6/6 animals given 400, 800 and 1600 mg/kg bw, respectively. Symptoms included a lack of balance and mild reddening and eschar of the skin in all groups. The study results were reported as questionable due to the known corrosivity of the chemical (REACH).

An LD50 of 1682 mg/kg bw was reported in rabbits for ammonium bisulfide. No details of the study were available (ChemIDPlus).

Inhalation

Barium sulfide is classified as hazardous with the risk phrase ‘Harmful by inhalation’ (Xn; R20) in the HSIS (Safe Work Australia). No median lethal concentration (LC50) values for barium sulfide or any other sulfides in this group are available to support or amend this classification. The only supportive information available is that high concentrations of airborne barium have been reported to cause severe health effects in humans (ATSDR, 2007) (see **Observation in humans**).

These chemicals have the potential to release hydrogen sulfide (H_2S) gas when in contact with acids. Four of the chemicals in this group (barium, calcium, sodium and potassium sulfide) are classified as hazardous with the risk phrase 'Contact with acids liberates toxic gases' (R31) in the HSIS (Safe Work Australia). This classification is recommended for all the chemicals in this group.

Hydrogen sulfide is classified as hazardous with the risk phrase ‘Very toxic by inhalation’ (T+; R26) in the HSIS (Safe Work Australia). Hydrogen sulfide affects the upper respiratory tract, the nose and the sense of smell, in humans and in animals. Hydrogen sulfide concentrations >1000 ppm were reported to cause sudden death in humans (see **Observation in humans**). Male CD rats exposed to hydrogen sulfide at concentrations ≥80 ppm for three hours had reversible lesions in the respiratory and olfactory mucosae (Brenneman et al., 2002).

Observation in humans

An estimated oral dose of 10–15 g of sodium sulfide (form not stated) is reported to be fatal to humans (Health Canada, 1987). Oral exposure to alkali sulfides is reported to cause nausea, vomiting and epigastric pain, along with irritation to the mucous membranes (Health Canada, 1987).

Reports on poisoning from barium sulfide noted that ingestion of large amounts of the chemical (~15 g) could lead to gastrointestinal symptoms, periorbital and extremity paraesthesiae, hypertension and progressive flaccid muscular paralysis, characteristic of Ba^{2+} toxicity (Gould et al., 1973; Downs et al., 1995). Exposure to high concentrations of airborne barium can cause electrocardiogram (ECG) abnormalities, muscle weakness and paralysis, hypokalaemia, and abdominal cramps, nausea, and vomiting (ATSDR, 2007).

Workers exposed to a spill of sodium sulfide (form not stated) for less than five minutes exhibited cardiac arrhythmias due to the breakdown of the chemical into hydrogen sulfide (ATSDR, 2014). Similarly, a worker was exposed to hydrogen sulfide generated from a sodium sulfide solution spilled on acid waste material, causing severe metabolic acidosis (ATSDR, 2014).

The human odour threshold for hydrogen sulfide gas is generally <1 ppb. Exposure to 50 ppm hydrogen sulfide can cause nasal irritation, while 100 ppm hydrogen sulfide can cause a sudden loss of olfaction, which is typically reversible with removal from contaminated air (Brenneman et al., 2002). High concentrations of hydrogen sulfide (>1000 ppm) lead to respiratory paralysis and sudden death (Brenneman et al., 2000).

Corrosion / Irritation

Corrosivity

Potassium sulfide and sodium sulfide are classified as hazardous with the risk phrase 'Causes burns' (C; R34) in the HSIS (Safe Work Australia). Calcium sulfide is classified as hazardous with the risk phrase 'Irritating to skin, eyes and respiratory system' (Xi; R36/37/38) in the HSIS (Safe Work Australia). The available limited data on ammonium, potassium and barium sulfide, ammonium and sodium bisulfide indicate that these chemicals have severe irritation or corrosive properties, warranting hazard classification. No data are available on sodium sulfide or calcium sulfide.

Considering the high basicity of the sulfide anions, the sulfides are expected to have severe irritation/corrosive properties warranting hazard classification. Sodium bisulfide causes serious eye damage. As corrosivity is expected to relate to protein denaturation as well as basicity, the bisulfides are also considered best classified as corrosive in the absence of more comprehensive data.

Only limited data are available indicating corrosivity or severe irritation:

- Ammonium sulfide and bisulfide are reported as strong irritants to skin and mucous membranes (HSDB).
- Dissolved salts of ammonium sulfide can be highly corrosive (Horvath et al., 2010).
- A 30 % sodium bisulfide solution applied into the conjunctival sac of the eyes of six Himalayan rabbits caused irreversible eye effects (REACH).
- Short-term contact with potassium sulfide was reported to cause severe burns to the skin and possible damage to the eyes (NJDOH, 2001).
- In an in vitro study (OECD TG 431), barium sulfide was found corrosive to EST-1000™ tissues (multilayered, highly differentiated model of the human epidermis formed with human-derived epidermal keratinocytes), with a relative viability of 71.2 % after three minutes of exposure, decreasing to 12.5 % after one hour of exposure (REACH).

Sensitisation

Skin Sensitisation

No data are available for any of the chemicals.

Repeated Dose Toxicity

Oral

Limited information is available on sodium sulfide. No data are available for the other chemicals. As these chemicals release a toxic gas, hydrogen sulfide, when in contact with stomach acid, adverse health effects cannot be ruled out during repeated oral exposure.

Sodium sulfide was administered in the feed of Yorkshire pigs (n = 144) at 0, 225 or 450 ppm over 104 days (Cromwell et al., 1978). No signs of toxicity were reported.

In a carcinogenicity test, Charles River CD rats (n = 26/sex/dose) were administered sodium sulfide at 9 or 18 mg/kg bw, two to three times a week in drinking water for 78 weeks. Results were reported as 'ambiguous' as the significance of the observed association between mortality and dose (no details provided) was unclear (Health Canada, 1987).

Using read-across with water soluble barium chloride (REACH), no severe toxicity due to the barium cation is expected from repeated oral exposure to barium sulfide .

Dermal

No data are available.

Inhalation

No data are available for the chemicals.

Based on the available data for hydrogen sulfide, repeated exposure to these chemicals could lead to localised lung effects and nasal damage due to the release of hydrogen sulfide.

Two repeated dose inhalation studies in rats are available for hydrogen sulfide.

Male CD rats were exposed (whole-body) to concentrations of hydrogen sulfide at 0, 10, 30 or 80 ppm, six hours/day, seven days/week for 10 weeks. Dose-related olfactory neuronal loss (ONL) and basal cell hyperplasia in the olfactory region of the nasal cavity were observed in rats at the 30 and 80 ppm doses. Basal cell hyperplasia was reported as 'a regenerative response secondary to the loss of the olfactory neurons' (Brenneman et al., 2000). A no observed adverse effect concentration (NOAEC) of 10 ppm was determined based on olfactory lesions at higher concentrations (Brenneman et al., 2000).

In another study, SD rats, Fischer 344 (F344) rats and B6C3F1 mice were exposed (whole-body) to hydrogen sulfide at concentrations of 0, 10, 30 or 80 ppm (ca. 0, 14, 42 and 111 mg/m^3, respectively) for six hours/day, seven days/week for 90 days. A NOAEC of 80 ppm was determined for systemic toxicity as there were no treatment-related effects on haematology, chemistry and gross pathology parameters (REACH). A NOAEC of 10 ppm was established for local olfactory lesions. All treated animals exhibited exposure-related increased incidence of ONL at 30 ppm and above. Mice had 100 % incidence of rhinitis in the highest dose group. Bronchiolar epithelial hypertrophy and hyperplasia in the lungs were reported in male and females SD rats at 30 ppm and above and in male F344 rats at 80 ppm (Dorman et al., 2004).

Observation in humans

Repeated inhalation exposure to hydrogen sulfide was reported to cause olfactory deficits (hyposmia), with both delayed and immediate onset, in workers at a refinery construction site (Brenneman et al., 2002).

Genotoxicity

Limited data are available, only on sodium bisulfide, sodium sulfide and hydrogen sulfide, indicating negative results for genotoxicity. The available data are insufficient to derive a conclusion on the genotoxic potential of these chemicals.

The following in vitro genotoxicity studies were available for sodium bisulfide and sodium sulfide (REACH):

- sodium bisulfide gave negative results in a bacterial gene mutation test conducted according to the Organisation for Economic Co-operation and Development Test Guideline (OECD TG) 471 using *Salmonella typhimurium* strains TA 1535, TA 1537, TA 98 and TA 100, up to 500 µg/plate in a standard plate test, up to 2500 µg/plate in a preincubation test and up to 4000 µg/plate in a preincubation test (with TA100), with or without metabolic activation; and
- sodium sulfide gave negative results in a mammalian cell gene mutation test (OECD TG 476), using mouse lymphoma L5178Y cells exposed to doses up to 781 µg/mL, with or without metabolic activation.

Hydrogen sulfide was also found negative in an Ames test with *S. typhimurium* strains TA97, TA98, and TA100 at 17, 57, 175, 582, and 1750 µg/plate, either with or without metabolic activation (ATSDR, 2014).

In one in vivo study, sodium sulfide administered intraperitoneally to NMRI mice at doses of 24, 48 or 96 mg/kg bw did not induce micronuclei in bone marrow cells (REACH).

Carcinogenicity

No data are available except for a single study with sodium sulfide in rats.

Sodium sulfide was administered in drinking water to Charles River CD rats (n = 26/sex/dose) at 9 or 18 mg/kg bw/day, twice a week for 78 weeks. While there was a significant association of mortality with dose in male rats, the results were termed as 'ambiguous'. No evidence of carcinogenicity was observed (Health Canada, 1987).

Case studies in workers and people living in areas of high geothermal activity or any area with high levels of hydrogen sulfide, showed increased occurrence of respiratory effects including irritation and alterations in lung function. An increased risk of nasal cancers was reported in a population living near an area of high geothermal activity (ATSDR, 2014). However, that report noted the limitations of these studies, regarding unknown exposure levels and potential exposure to other chemicals, and concluded that hydrogen sulfide was 'unlikely to be a carcinogen' based on the results of limited genotoxicity studies available (ATSDR, 2014).

Reproductive and Developmental Toxicity

No data are available on the chemicals. However no reproductive or developmental toxicity is expected from these chemicals based on the available data on hydrogen sulfide.

Concentrations of hydrogen sulfide up to 80 ppm do not elicit any reproductive or developmental toxicity effects based on animal data (ATSDR, 2014).

In a reproductive toxicity study, SD rats (n = 12/sex/dose) were exposed (whole body) to hydrogen sulfide at doses of approximately 10, 30 or 80 ppm (14, 42 and 111 mg/m^3, respectively), six hours/day, seven days/week, for two weeks before mating, through the mating period and during gestation days (GD) 0–19. A NOAEC for reproductive toxicity of 111 mg/m^3 was established as there were no indications of impaired fertility, reproductive performance or teratogenic effects (REACH).

Maternal or parental exposure to a mix of chemicals, including hydrogen sulfide, could increase the risk of spontaneous abortion among rayon textile, paper products and petrochemical workers (ATSDR, 2014).

Other Health Effects

Neurotoxicity

Acute human exposure to hydrogen sulfide can result in nausea, headaches, delirium, disturbed equilibrium, poor memory, neurobehavioural changes, olfactory paralysis, loss of consciousness, tremors, and convulsions (ATSDR, 2014).

A study in rats intravenously injected with sodium sulfide showed that sulfide was 'incapable of producing cerebral necrosis by a direct histotoxic effect' (Baldelli et al., 1993), but affected the nervous system via an indirect mechanism associated with serious hypotension (Baldelli et al., 1993; ATSDR, 2014).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include:

- systemic acute effects (acute toxicity from oral and dermal exposure) and
- local effects (corrosivity).

These chemicals can release hydrogen sulfide when in contact with acid, water and body fluids, causing adverse inhalation/respiratory effects.

Public Risk Characterisation

Although use in cosmetic and domestic products in Australia is not known, some of the chemicals are reported to be used in depilatory (hair removal) products overseas at concentrations up to 2 % (as sulfur) for alkali (sodium and potassium) sulfides and 6 % (as sulfur) for alkali earth (calcium and barium) sulfides. The use of these chemicals in aerosol dispensers intended for the general public is also restricted in the European Union because of their ability to release hydrogen sulfide gas. Sodium sulfide and sodium bisulfide are specifically restricted for use in jokes and hoaxes or in mixtures or articles intended for such use.

There are no restrictions in Australia on using these chemicals in cosmetics. However, there are packaging and labelling requirements for sodium sulfide, potassium sulfide and barium salts in Australia for specific uses (e.g. metal treatment and in paints or tinters) (SUSMP, 2015).

Considering the corrosive nature of these chemicals and their potential to release a toxic gas with a foul odour when in contact with acid or water, these chemicals are not expected to be available in cosmetics or domestic products at sufficiently high concentrations that could cause corrosive effects. Hence, the public risk from these chemicals is not considered to be unreasonable.

Occupational Risk Characterisation

Given the critical systemic acute and local health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise exposure are implemented. The chemicals should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

The data available support hazard classification of all chemicals in this group. An amendment to the hazard classification in the HSIS (Safe Work Australia) is recommended for some chemicals (refer to **Recommendation** section).

NICNAS Recommendation

Assessment of these chemicals are considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

Regulatory Control

Public Health

Products containing the chemicals should be labelled in accordance with state and territory legislation (SUSMP, 2015).

Work Health and Safety

The chemicals are recommended for classification and labelling under the current approved criteria and adopted GHS as below.

The table below presents the hazard classifications recommended for all chemicals, except for the following:

- 'Harmful by inhalation' (Xn; R20) for barium sulfide only; and
- ‘Toxic in contact with skin’ (T; R24) for sodium sulfide instead of the 'Harmful in contact with skin'.

This assessment does not consider classification of physical and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22) Harmful in contact with skin (Xn; R21) Contact with acids liberates toxic gas (R31)	Toxic if swallowed - Cat. 3 (H301) Harmful in contact with skin - Cat. 4 (H312) Contact with acid liberates toxic gas (AUH031)
Irritation / Corrosivity	Causes burns (C; R34)	Causes severe skin burns and eye damage - Cat. 1B (H314)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for consumers

Products containing the chemicals should be used according to the instructions on the label.

Advice for industry

Control measures

Control measures to minimise the risk from oral, dermal, ocular and inhalation exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemicals are used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemicals are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of these chemicals has not been undertaken as part of this assessment.

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Last Update 24 April 2015

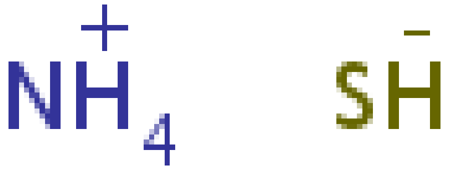
Chemical Identities

Chemical Name in the Inventory and Synonyms	**Potassium sulfide (K2S)** dipotassium monosulfide dipotassium sulfide potassium monosulfide
CAS Number	1312-73-8
Structural Formula	
Molecular Formula	K2S
Molecular Weight	110.262

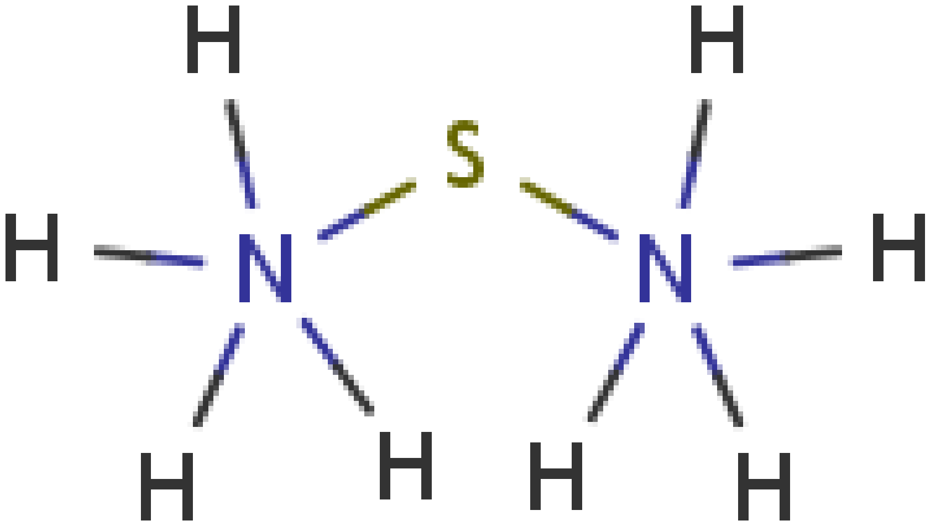
Chemical Name in the Inventory and Synonyms	**Sodium sulfide (Na2S)** disodium monosulfide disodium sulfide sodium monosulfide sodium sulphide
CAS Number	1313-82-2
Structural Formula	

	
Molecular Formula	Na2S
Molecular Weight	78.046

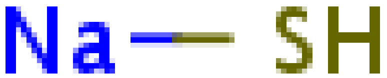
Chemical Name in the Inventory and Synonyms	**Ammonium sulfide, (NH4)(SH)** ammonium bisulfide ammonium hydrogen sulfide ammonium hydrosulfide ammonium sulfhydrate ammonium mercaptan
CAS Number	12124-99-1
Structural Formula	

	
Molecular Formula	H4N.HS
Molecular Weight	51.11

Chemical Name in the Inventory and Synonyms	**Ammonium sulfide ((NH4)2S)** ammonium monosulfide diammonium sulfide true ammonium sulfide
CAS Number	12135-76-1
Structural Formula	

	
Molecular Formula	H_8N_2S
Molecular Weight	68.143

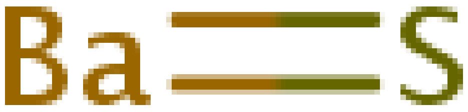
Chemical Name in the Inventory and Synonyms	**Sodium sulfide (Na(SH))** sodium bisulfide sodium hydrosulfide hydrogen sodium sulfide sodium mercaptan sodium hydrogen sulfide
CAS Number	16721-80-5
Structural Formula	

	
Molecular Formula	HNaS
Molecular Weight	56.06

Chemical Name in the Inventory and Synonyms	**Calcium sulfide (CaS)** hepar sulfuris calcareum
CAS Number	20548-54-3
Structural Formula	

	
Molecular Formula	CaS
Molecular Weight	72.144

Chemical Name in the Inventory and Synonyms	**Barium sulfide (BaS)**
CAS Number	21109-95-5
Structural Formula	

	
Molecular Formula	BaS
Molecular Weight	169.4

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