Bifluorides: Human health tier II assessment

27 November 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Sodium fluoride (Na(HF2))	1333-83-1
Ammonium fluoride, ((NH4)(HF2))	1341-49-7
Potassium fluoride (K(HF2))	7789-29-9

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

This group consists of three soluble bifluoride salts with cations of low toxicity. Bifluoride ions (HF_2^-) are formed from hydrofluoric acid solutions in the presence of excess fluoride ions (F^-). When the chemicals in this group are dissolved in water, they dissociate into hydrogen fluoride (HF) and metal fluoride salts . The formation constant for the bifluoride salts is relatively small and only a minimal amount of bifluoride is formed, except in concentrated solutions. The relative concentrations of the different species of HF, F^-, and HF_2^- are dependent on the pH of the solution and involve complex equilibria (NICNAS, 2001).

These chemicals have been grouped together for assessment due to their similarity in chemical properties, uses, and toxicological profile.

When data for the bifluoride salts are not available, health hazard information for hydrogen fluoride (CAS No. 7664-39-3) has been included in this report. Aqueous solutions of bifluoride salts can produce HF in solution. The concentration of HF increases as the solution is further acidified, such as in gastric conditions; therefore, HF is considered to be a suitable analogue for the chemicals.

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified.

The National Pollutant Inventory (NPI) holds data for all sources of emissions of fluoride compounds in Australia.

International

The following international uses have been identified through the European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers, Galleria Chemical, Substances in preparations in Nordic countries (SPIN) database, and other data sources via eChemPortal including the United States Environmental Protection Agency's (US EPA) Aggregated Computer Toxicology Resource (ACToR) and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

The chemicals have reported domestic uses including:

- as cleaning/washing agents; and
- as etching creams or solutions.

The chemicals have reported commercial uses including:

- as corrosion inhibitors;
- as electroplating agents;
- as flux agents for casting or joining materials;
- as fixing agents;
- as welding and soldering agents;
- in drilling;
- in glass and non-metal product etching;
- in metal extraction and refining; and
- in metal surface treatment.

Restrictions

Australian

These chemicals are listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in Schedules 5, 6, and 7 (SUSMP, 2014).

Schedule 7:

'BIFLUORIDES (including ammonium, potassium and sodium salts) except when included in Schedule 5 or 6.'

Schedule 6:

'BIFLUORIDES (including ammonium, potassium and sodium salts) in preparations containing 3 per cent or less of total bifluorides except when included in Schedule 5.'

Schedule 5:

‘BIFLUORIDES (including ammonium, potassium and sodium salts), in preparations containing 0.3 per cent or less of total bifluorides.'

Schedule 7 chemicals are described as 'Substances with a high potential for causing harm at low exposure and which require special precautions during manufacture, handling or use. These poisons should be available only to specialised or authorised users who have the skills necessary to handle them safely. Special regulations restricting their availability, possession, storage or use may apply.' Schedule 7 chemicals are labelled with 'Dangerous Poison' (SUSMP, 2014).

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, 2014).

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, 2014).

International

The chemicals are listed on the following (Galleria Chemica):

- EU Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products;
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain; and
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient 'Hotlist').

Existing Worker Health and Safety Controls

Hazard Classification

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

- T; R25 (acute toxicity); and
- C; R34 (irritation).

Exposure Standards

Australian

No specific exposure standards are available for the chemicals. Hydrogen fluoride (CAS No. 7664-39-3) has an exposure standard of 2.6 mg/m^3 peak limitation (3 ppm peak limitation) time weighted average (TWA). Fluorides (as F) have an exposure standard of 2.5 mg/m^3 TWA.

International

The following exposure standards are identified for the fluoride (as F) content of the chemicals (Galleria Chemica).

An exposure limit of 0.2–4 mg/m^3 TWA and 1–10 mg/m^3 short-term exposure limit (STEL)/MAK/occupational exposure limit (OEL) in different countries such as the USA, Mexico, Belgium, Finland, Norway, Switzerland, Turkey, Thailand and Philippines.

Health Hazard Information

Toxicokinetics

No data are available for the chemicals.

Hydrogen fluoride (CAS No. 7664-39-3) and soluble fluoride compounds are readily absorbed in animals and humans via the oral, dermal and inhalational routes (ECB, 2001; ATSDR, 2003).

Once absorbed, hydrogen fluoride is distributed throughout body of the animals, with the highest levels found in the skeleton (NICNAS, 2001; ATSDR, 2003).

From animal and human studies, approximately 50 % of the the absorbed fluoride accumulates in the bone and teeth (NICNAS, 2001) and the remainder is excreted in the urine (ECB, 2001; ATSDR, 2003).

Acute Toxicity

Oral

The chemicals are classified as hazardous with the risk phrase 'Toxic if swallowed' (T; R25) in HSIS (Safe Work Australia).

The available data for ammonium bifluoride (CAS No. 1341-49-7) (median lethal dose (LD50) in a study using the Organisation for Economic Co-operation and Development's Test Guideline (OECD TG) 401 is 130 mg/kg bw in Sprague Dawley (SD) rats) support this classification. Reported signs of toxicity include dyspnoea, decreased cutaneous circulation, ataxia, decreased body tone, prone position, sedation, cyanosis, salivation, lacrimation, mydriasis, and haemorrhagic discharge from the nose. All surviving rats showed deteriorating conditions 24 hours after administration of the chemical (REACH). The acute oral toxicity of the sodium and potassium bifluoride salts are expected to be similar.

Dermal

No data are available for the chemicals.

Inhalation

No data are available for the chemicals.

Observation in humans

Mortalities and serious illnesses were reported from unintentional ingestion of household cleaning products, such as toilet stain removers and wheel cleaners, containing ammonium bifluoride (CAS No. 1341-49-7) (HSDB).

Corrosion / Irritation

Corrosivity

The chemicals are classified as hazardous with the risk phrase 'Causes burns' (C; R34) in HSIS (Safe Work Australia).

Multiple sources imply that the chemicals are known corrosive chemicals in humans (Cheremisinoff, 2000; ATSDR, 2003; HSDB).

Respiratory Irritation

No data are available for the chemicals.

Skin Irritation

Solid (0.5 g) potassium bifluoride (CAS No. 7789-29-9) (purity not reported) produced no skin irritation after occlusive application in New Zealand White rabbits in a study conducted in accordance with a US EPA method on skin irritation/corrosion (REACH).

Eye Irritation

No data are available for the chemicals.

Sensitisation

Respiratory Sensitisation

No data are available for the chemicals.

Skin Sensitisation

No data are available for the chemicals. The chemicals are not expected to be skin sensitisers.

Hydrogen fluoride (CAS No. 7664-39-3) does not react with and/or bind to proteins.

Repeated Dose Toxicity

Oral

No data are available for the chemicals.

While the fluoride ion gives rise to effects on the skeleton of animals and humans from repeated oral dosing (WHO, 2002), exposure to the soluble bifluoride salts in humans will be limited by local irritation effects (see **Repeated dose toxicity: Observations in humans**) due to the corrosive nature of the chemicals.

Dermal

No data are available for the chemicals. Exposure to the soluble bifluoride salts in humans will be limited by local irritation effects (see **Repeated dose toxicity: Observations in humans**) due to the corrosive nature of the chemicals.

Inhalation

No data are available for the chemicals. Exposure to the soluble bifluoride salts will be limited by local irritation effects due to the corrosive nature of the chemicals.

The repeated dose inhalation toxicity of hydrogen fluoride (HF) (CAS No. 7664-39-3) has been considered. In a 91-day repeated dose inhalation toxicity study similar to OECD TG 413, the no observed adverse effect concentration (NOAEC) for hydrogen

fluoride (CAS No. 7664-39-3) in male and female rats (strain not specified) was reported to be 0.72 mg/m^3. Local irritation effects were observed from repeated inhalation exposures to HF (ECB, 2001; NICNAS, 2001).

Observation in humans

No data are available for the chemicals.

Systemic effects were not observed in five human volunteers exposed to gaseous HF at concentrations up to 1.64 mg/m^3 for six hours/day for 15 days. The study reported local effects such as a stinging sensation in the eyes and facial skin, as well as slight irritation of the nasal mucosa (ECB, 2001).

Genotoxicity

Based on the weight of evidence from the available in vitro and in vivo genotoxicity studies, the chemicals are not considered to be genotoxic.

Ammonium bifluoride (CAS No. 1341-49-7) produced negative results in a bacterial gene mutation test (OECD TG 471) in *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 (20 to 4800 µg/plate) with or without metabolic activation (REACH).

In a non-guideline study, sodium fluoride (CAS No. 7681-49-4) and potassium fluoride (CAS No. 7789-23-3) were tested in an L5178Y mouse lymphoma cell forward-mutation assay and resulted in three-fold increases in mutant frequency, reducing the relative total growth to approximately 10 % with and without metabolic activation. In the same study, similar mutagenic activity was observed when a sample of 70 % sodium bifluoride (CAS No. 1333-83-1) was tested in the same assay. No other details were provided (REACH).

Available in vivo studies for hydrogen fluoride (CAS No. 7664-39-3) are inconclusive and are not considered reliable due to the poor reporting of the non-guideline studies (OECD, 2002; REACH).

Carcinogenicity

No data are available for the chemicals. Based on the weight of evidence, the chemicals are not considered to be carcinogenic.

The International Agency for Research on Cancer (IARC) has classified the inorganic fluorides used in drinking water as ‘Not classifiable as to its carcinogenicity to humans’ (Group 3), based on inadequate evidence for carcinogenicity in humans and animals.

Hydrogen fluoride (CAS No. 7664-39-3) does not bind to DNA.

Reproductive and Developmental Toxicity

No data are available for the chemicals.

Risk Characterisation

Critical Health Effects

The main critical effects to human health are corrosivity and acute oral toxicity. The chemicals in this group will liberate toxic gas when in contact with acid and, therefore, may cause effects in individuals who have a high acid content in their stomach.

Public Risk Characterisation

The chemicals are currently listed on Schedules 5, 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in preparations. At various concentration cutoffs, a number of warning statements, first aid instructions and safety directions relating to the chemicals apply.

Occupational Risk Characterisation

Based on the available data, the hazard classification in the HSIS (Safe Work Australia) is considered appropriate.

NICNAS Recommendation

Current risk management measures are considered adequate to protect public and workers' health and safety, provided that all requirements are met under workplace health and safety, and poisons legislation as adopted by the relevant state or territory. No further assessment is required.

Regulatory Control

Public Health

Products containing the chemicals should be labelled in accordance with state and territory legislation (SUSMP, 2014).

Work Health and Safety

The chemicals are recommended for classification and labelling under the current approved criteria and adopted GHS as below. This assessment does not consider classification of physical and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Toxic if swallowed (T; R25)*	Toxic if swallowed - Cat. 3 (H301)
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 risks from oral, dermal and ocular 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 local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemicals, if valid techniques are available to monitor the effect on the worker's health;
- 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.

References

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Chemical Identities

Chemical Name in the Inventory and Synonyms	**Sodium fluoride (Na(HF2))** Sodium bifluoride
CAS Number	1333-83-1
Structural Formula	

	
Molecular Formula	F2H.Na
Molecular Weight	61.9939

Chemical Name in the Inventory and Synonyms	**Ammonium fluoride, ((NH4)(HF2))** Ammonium hydrogen fluoride
CAS Number	1341-49-7
Structural Formula	
Molecular Formula	F2H.H4N
Molecular Weight	57.0425

Chemical Name in the Inventory and Synonyms	**Potassium fluoride (K(HF2))** Potassium bifluoride

CAS Number	7789-29-9
Structural Formula	
Molecular Formula	F2HK
Molecular Weight	78.1019

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