Perborates: Human health tier II assessment

02 March 2018

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Perboric acid (H3BO2(O2)), monosodium salt, trihydrate	13517-20-9
Perboric acid (HBO(O2)), sodium salt	7632-04-4
Perboric acid (HBO(O2)), sodium salt, monohydrate	10332-33-9
Perboric acid (HBO(O2)), sodium salt, tetrahydrate	10486-00-7
Perboric acid, sodium salt	11138-47-9
Perboric acid (HBO(O2)), calcium salt	54630-47-6

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**

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ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemicals in this group are salts of perboric acid. All except one are known as sodium perborates. They are produced from borax, sodium hydroxide, and hydrogen peroxide, and crystallise during production as the monohydrate, trihydrate, and tetrahydrate. The other chemical in this group is calcium perborate and is the calcium salt of perboric acid.

Sodium perborate degrades into hydrogen peroxide, sodium metaborate and water. Degradation of hydrogen peroxide to oxygen and water leads to the degradation products sodium metaborate and water. Sodium metaborate is the salt of a strong base (sodium hydroxide) and a weak acid (boric acid) and is expected to be present in aqueous solutions at the environmental temperature and pH, mainly as undissociated boric acid. Calcium perborate is also water soluble (Hawley, 1981) and undergoes degradation by the same mechanism, ultimatley producing calcium ions and boric acid in solution. Therefore, as the toxicokinetics and the toxicity of the chemicals in this group are expected to be similar, and will be predominantly driven by the peroxo group and borate ions, they are grouped together for human health risk assessment.

It is also noted that a recent opinion by the European Union (EU) Scientific Committee on Consumer Safety (SCCS) on sodium perborate and perboric acid included the group of chemicals from this assessment: CAS Nos. 13517-20-9, 7632-04-4, 10332-33-9, and 10486-00-7, and 11138-47-9 (EU RAR, 2007; SCCS, 2010).

The chemicals in this group also have similar reported uses (EU RAR, 2007; SCCS, 2010).

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information.

Sodium perborate monohydrate (CAS No. 10332-33-9) and sodium perborate tetrahydrate (CAS No. 10486-00-7) have reported domestic use as bleaching agents.

Sodium perborate monohydrate (CAS No. 10332-33-9) has reported commercial use as an oxidising agent.

Sodium perborate monohydrate (CAS No. 10332-33-9) and sodium perborate tetrahydrate (CAS No. 10486-00-7) were reported to have a total reported volume of between 100 and 1000 tonnes during the call for information for the 2006 High Volume Industrial Chemicals List (HVICL).

The National Pollutant Inventory (NPI) holds data for all sources of environmental release of boron and its compounds in Australia.

No specific Australian use, import, or manufacturing information has been identified for the other members of this group.

International

The following international uses have been identified through:

- the EU Registration, Evaluation and Authorisation of Chemicals (REACH) dossiers;
- Galleria Chemica;
- the Substances and Preparations in the Nordic countries (SPIN) database;
- the European Commission Cosmetic Ingredients and Substances (CosIng) database; and
- the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

Sodium peroxometaborate (CAS No. 7632-04-4) and sodium perborate monohydrate (CAS No. 11138-47-9) have reported cosmetic uses including:

- in oral care; and
- as oxidising agents.

The sodium perborates (CAS Nos. 7632-04-4 and 11138-47-9) have reported cosmetic uses in the United States of America (USA), with a frequency of use in 19 products (Personal Care Products Council, 2011).

The majority of the chemicals have reported domestic uses including:

- as cleaning/washing agents;
- as bleaching agents; and
- in surface treatment.

Sodium peroxometaborate (CAS No. 7632-04-4) is reported to be present in a range of domestic products (five) for interior home use up to a concentration of 30 %, in the form of tablets, granules, and powder (Household Products Database, US Department of Health and Human Services).

The majority of the chemicals have reported commercial uses including as:

- conductive agents; and
- bleaching agents for industrial laundries.

The following non-industrial uses have been identified internationally for the chemicals in this group:

- non-agricultural pesticides and preservatives;
- mild antiseptic (topical); and
- mouthwash (under medical supervision).

No specific International use, import, or manufacturing information has been identified for the other members of this group.

Restrictions

Australian

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

However, one degradation product from these chemicals, boric acid, is listed in the *Poisons Standard* (*Standard for the Uniform Scheduling of Medicines and Poisons*) (SUSMP, 2014) in Schedule 5. Boron, which includes boric acid and borax, is also listed in Schedule 4 for its non-industrial uses (NICNASa).

Another degradation product of these chemicals, hydrogen peroxide, is listed in the SUSMP (2014) in Schedules 5 and 6, at various concentrations (NICNASb).

International

The majority of chemicals in this group are listed on the following (Galleria Chemica):

- EU Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products—Annex III—List of substances which cosmetic products must not contain except subject to the restrictions laid down (CAS Nos. 7632-04-4, 10332-33-9, 10486-00-7, 11138-47-97); and
- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient "Hotlist") (CAS Nos. 7632-04-4, 10486-00-7, 11138-47-9).

Restrictions for the above chemicals for certain types of cosmetic products, according to Annex III of the REACH Regulations (List of restricted substances), are that they are not to be used:

- in products for children under three years of age; or
- on peeling or irritated skin if the concentration of free soluble borates exceeds 1.5 % (as boric acid).

The chemicals specified by CAS Nos. 13517-20-9, 10486-00-7 and 11138-47-9 in this group are also restricted by Annex XVII to the REACH Regulations. These chemicals cannot be used in substances and preparations placed on the market for sale to the general public in individual concentrations $\geq$0.5 %.

The SCCS concluded that sodium perborate and perboric acid can be considered as 'hydrogen peroxide releasing' substances, and thus are covered by entry 12 of Annex III, of the Cosmetics directive 76/768/EEC; and that the general restrictions applicable to hydrogen peroxide-releasing substances should also apply to sodium perborate and perboric acid. Using sodium perborates as an ingredient in an oxidative hair dye formulation with a maximum on-head concentration of 3 % was concluded not to pose a risk to consumers' health; while a hair dye powder formulation containing 30 % sodium perborate monohydrate would require labelling as 'Toxic' and such products should not be generally available to consumers (SCCS, 2010).

Existing Worker Health and Safety Controls

Hazard Classification

The sodium perborates in the group are classified as hazardous, with the following risk phrases for human health in the Hazardous Chemical Information System (HCIS) (Safe Work Australia):

- Reproductive toxicity – Category 1B; H360Df (May damage the unborn child. Suspected of damaging fertility)
- Specific target organ toxicity (single exposure) – Category 3; H335 (May cause respiratory irritation)
- Eye damage – Category 1; H318 (Causes serious eye damage)

Additional risk phrases have also been assigned to the following chemicals:

- Acute toxicity – Category 4; H332 (Harmful if inhaled)—Sodium perborate trihydrate (CAS No. 13517-20-9) and sodium perborate tetrahydrate (CAS No. 10486-00-7) containing ≥0.1 % (w/w) of particles with an aerodynamic diameter of below 50 micrometres.
- Acute toxicity – Category 4; H302 (Harmful if swallowed)—Sodium peroxometaborate (CAS No. 7632-04-4), sodium perborate monohydrate (CAS No. 10332-33-9) and sodium peroxoborate (CAS No. 11138-47-9).
- Acute toxicity – Category 3; H331 (Toxic if inhaled)—Sodium peroxometaborate (CAS No. 7632-04-4), sodium perborate monohydrate (CAS No. 10332-33-9) and sodium peroxoborate (CAS No. 11138-47-9) containing ≥0.1 % (w/w) of particles with an aerodynamic diameter of below 50 micrometres.

Calcium perborate (CAS No. 54630-47-6) is not listed on the HCIS (Safe Work Australia).

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

The chemicals in this group are collectively known as perborates and are salts of perboric acid. Sodium perborate degrades into sodium metaborate and water with the generation of hydrogen peroxide and oxygen. Sodium metaborate is the salt of a strong base (sodium hydroxide) and a weak acid (boric acid). Undissociated boric acid is the main species present in the blood of mammals following exposure to these chemicals (see **Grouping rationale**).

The long term toxicity of these chemicals is expected to be similar and will be driven predominantly by borate ions; the data obtained from studies with different borates can be read across for long term health effects for human health risk assessment of chemicals on this group. Local effects will arise from the peroxide functionality and will be related to the toxicity of hydrogen peroxide (EU RAR, 2007; SCCS, 2010).

Toxicokinetics

Limited data are available in humans only.

Oral and inhalation absorption of sodium perborate hydrates was assumed to be 100 % following an oral absorption study in human volunteers. The dermal absorption of 1 % was assumed as there were no data following dermal exposure, and the absorption via mucous membranes of the mouth was considered to be low. It was also noted that dermal absorption of hydrogen peroxide is negligible, and that of boron-containing ionic compounds is also very low.

Following sodium perborate ingestion, peak levels in human plasma are reached after two hours; the half-life in human plasma is about 6–10 hours. These chemicals are assumed to degrade to hydrogen peroxide and boric acid following oral application, and are excreted as boric acid in the urine (EU RAR, 2007; SCCS, 2010).

Acute Toxicity

Oral

Three chemicals in this group (sodium peroxometaborate—CAS No. 7632-04-4, sodium perborate monohydrate—CAS No. 10332-33-9, and sodium peroxoborate—CAS No. 11138-47-9) are classified as hazardous with hazard category 'Acute toxicity – category 4' and hazard statement 'Harmful if swallowed (H302) in the HCIS (Safe Work Australia).

While the available data support this classification for sodium perborate monohydrate (CAS No. 10332-33-9), information is not available for the other two sodium perborates (CAS Nos.7632-04-4, 11138-47-9). The lack of data in this case is not sufficient to recommend amendment of the current HCIS classification.

Although no data are available for calcium perborate, it will have higher perborate concentration per mass of chemical, when compared with sodium perborate monohydrate (CAS No. 10332-33-9) for which data exist. As perborate is expected to be the driver of acute toxicity for the chemicals in this group, the hazard classification should be extended to calcium perborate (CAS No. 54630-47-6).

The reported median lethal dose (LD50) for sodium perborate monohydrate (CAS No. 10332-33-9) is 1120 mg/kg bw. Reported signs of toxicity included diarrhoea, hypoactivity, and ataxia (REACH).

Although the available data (LD50—2567 mg/kg bw) for sodium perborate tetrahydrate (CAS No. 10486-00-7) do not support classification, information was not available for sodium perborate trihydrate (CAS No. 13517-20-9). It has been suggested that the higher toxicity of the monohydrate, compared with the tetrahydrate, is due to the lower water content of the salt and; therefore, higher boron/g content of the molecule. Therefore, based on the above, HCIS classification is not warranted for sodium perborate tetrahydrate (CAS No. 10486-00-7) or sodium perborate trihydrate (CAS No. 13517-20-9) (EU RAR, 2007; SCCS, 2010; REACH).

Dermal

Based on the limited available information, the chemicals in this group are likely to have low acute toxicity following dermal exposure. It is also noted that the dermal absorption through intact skin is very low; a dermal absorption rate of 1 % was considered appropriate (see **Toxicokinetics**).

The LD50 in rabbits is >2000 mg/kg bw for sodium perborate monohydrate (CAS No. 10332-33-9). Observed sub-lethal effects included diarrhoea, yellow nasal discharge and soiled anogenital area (EU RAR, 2007; SCCS, 2010; REACH).

Inhalation

Two chemicals in this group (sodium perborate trihydrate—CAS No. 13517-20-9, sodium perborate tetrahydrate—CAS No. 10486-00-7), containing ≥0.1 % (w/w) of particles with an aerodynamic diameter of below 50 micrometres, are classified as hazardous with hazard category 'Acute Toxicity – Category 4' and hazard statement 'Harmful if inhaled' (H332) HCIS (Safe Work Australia).

Three chemicals in this group (sodium peroxometaborate—CAS No. 7632-04-4, sodium perborate monohydrate—CAS No. 10332-33-9, and sodium peroxoborate—CAS No. 11138-47-9) that contain ≥0.1 % (w/w) of particles with an aerodynamic diameter of below 50 micrometres, are classified as hazardous with hazard category 'Acute Toxicity – Category 3' and hazard statement 'Toxic if inhaled' (H331) in the HCIS (Safe Work Australia).

While the available data support the classification for sodium perborate tetrahydrate (CAS No. 10486-00-7), information is not available for the other chemicals. The lack of data in this case is not sufficient to recommend amendment of the current HCIS classification.

In the absence of data, the potential for inhalation toxicity cannot be determined for calcium perborate (CAS No. 54630-47-6). No hazard classification is warranted for this chemical.

The available data (median lethal concentration—LC50) for sodium perborate tetrahydrate (CAS No. 10486-00-7) is 1.65 mg/L. Reported signs of toxicity included gasping, red nasal discharge, and compound-covered faeces (EU RAR, 2007; SCCS, 2010; REACH).

Corrosion / Irritation

Respiratory Irritation

The chemicals in the group are classified as hazardous, with hazard category Specific Target Organ Toxicity (Single Exposure) – Category 3 and hazard statement 'May cause respiratory irritation' (H335) in the HCIS (Safe Work Australia). This classification should be extended to calcium perborate (CAS No. 54630-47-6).

While the appropriate data are limited for chemicals in this group, in the absence of more comprehensive information, the available data in animal (acute and repeated dose inhalation studies) and human reports are sufficient to support the current HCIS classification (EU RAR, 2007).

Signs of respiratory tract irritation have been noted in acute inhalation studies (see **Acute toxicity: Inhalation**).

Skin Irritation

Although slight skin irritant effects were reported in animal studies, the effects were not sufficient to warrant a hazard classification for the chemicals in this group.

In a skin irritation study conducted according to the Organisation for Economic Co-operation and Development Test Guideline (OECD TG) 404, sodium perborate monohydrate (CAS No. 10332-33-9) caused mild skin irritation when applied at 0.5 g/animal to the intact skin of New Zealand White rabbits for four hours. In another skin irritation study conducted according to OECD TG 404, sodium perborate tetrahydrate (CAS No. 10486-00-7) was found to not irritate the intact skin of New Zealand White rabbits when applied at 0.5 g/animal for four hours (EU RAR, 2007; SCCS, 2010; REACH).

Eye Irritation

The sodium perborates in this group are classified as hazardous with hazard category 'Eye Damage – Category 1' and the hazard statement 'Causes serious eye damage' (H318) in the HCIS (Safe Work Australia). The available data support this classification. Although no data are available for calcium perborate (CAS No. 54630-47-6), it is expected to have comparable potential for ocular irritation associated with the perbrate ion compared with the sodium perborates and the classification should be extended to the chemical.

In an eye irritation study conducted according to OECD TG 405, 0.1 mL of sodium perborate monohydrate (CAS No. 10332-33-9) was placed into the conjunctival sac of one eye each of three New Zealand White rabbits. As the effects were irreversible in one animal up to 21 days post application, the chemical was considered to cause serious damage to the eyes. Although corneal opacity and iritis were noted in 3/3 eyes, iritis was cleared by day 21, but corneal opacity persisted in one animal to day 21.

Similarly, moderate to severe conjunctival irritation (noted in 3/3 eyes) was cleared by day 21 in 2/3 eyes. However, pale areas in the conjunctivae were still noted through to day 21 (EU RAR, 2007; SCCS, 2010; REACH).

In an eye irritation study conducted according to Federal Hazardous Substances Act Regulations 191.12 (1964-09) of the USA, 0.1 mL of sodium perborate tetrahydrate (CAS No. 10486-00-7) was placed once into the right eyes of six albino rabbits. The chemical was judged to be corrosive as severe corneal damage, severe iritis and severe conjunctivitis were observed in all animals (EU RAR, 2007; SCCS, 2010; REACH).

In another eye irritation study conducted according to OECD TG 405, sodium perborate tetrahydrate (CAS No. 10486-00-7) was placed once into the one eye each of two New Zealand White rabbits. In one animal, the chemical caused mild corneal opacity, slight iritis and conjunctival effects, which consisted of severe redness, moderate chemosis and severe discharge. Slight corneal opacity and slight redness of the conjunctiva were still present at the end of the study (21 days). Additional observations included a necrotic nictitating membrane, bulging cornea, convoluted eyelids, vascular pannus, thickened eyelids and Harderian discharge. The second animal was euthanised for humane reasons three days after the chemical was applied due to the severity of the observed response. This animal had moderate corneal opacity that covered up to the whole surface of the cornea, slight iritis and conjunctival effects, which were severe redness, moderate chemosis and severe discharge. Haemorrhagic conjunctiva and a nictitating membrane, bulging cornea, necrotic conjunctiva and mucoid and Harderian discharge were also noted. The chemical was; therefore, considered to be a severe eye irritant (EU RAR, 2007; SCCS, 2010; REACH).

Observation in humans

Sodium perborate monohydrate (CAS No. 10332-33-9) was concluded to not irritate human skin in a human patch test study in 26 volunteers when the chemical was applied between one to four hours. The chemical was applied at 0.2 g onto a 25 mm plain Hilltop chamber containing a moist Webril pad to the upper outer arm. While 1/26 subjects showed a positive skin reaction to the chemical, 21/26 reacted to the positive control (20 % solution of sodium dodecyl sulphate in distilled water) (EU RAR, 2007; SCCS, 2010; REACH).

Slight reversible irritative effects on the mucosa of the nose have been reported in a questionnaire covering four production plants for sodium perborate (EU RAR, 2007).

Sensitisation

Respiratory Sensitisation

Although limited information is available on the respiratory sensitisation potential of these chemicals, based on the available information, the chemicals in this group are not likely to be respiratory sensitisers.

In a respiratory sensitation study, 10 guinea pigs were exposed to sodium perborate tetrahydrate (CAS No. 10486-00-7) either at one hour intervals for four hours at 9 mg/m^3, or for one hour/week for six consecutive weeks to 11 mg/m^3. Both groups were challenged with the same concentrations as above for one hour, six weeks after the first exposure. Only one guinea pig responded with retracted breathing (a sign of difficult breathing). There was no indication that the chemical could cause respiratory sensitisation as skin tests, a passive cutaneous anaphylaxis and agar gel diffusion test, and histological evaluation of lung tissue did not show an effect in any of the animals (EU RAR, 2007; REACH).

Skin Sensitisation

Although limited information is available on the skin sensitisation potential of the chemicals in this group, based on the available information, the chemicals are not likely to be skin sensitisers.

Sodium perborate monohydrate (CAS No. 10332-33-9) tested negative in a skin sensitisation test (Buehler test) conducted according to OECD TG 405. Ten Dunkin-Hartley guinea-pigs (five/sex) were exposed (epicutaneous, occlusive) three times to the chemical (0.5 mL/animal (applying 0.5 ml/animal (dose not further specified, presumed powder as it is, 6 hours/day,

occlusive)) (six hours/day, once every seven days for three weeks). Animals were challenged (epicutaneous, occlusive) 14 days after the last induction with 0.5 mL of a 5 % solution in distilled water (maximum non-irritant concentration). Very slight erythema was noted in one of test group animals as well as one of control group animals (EU RAR, 2007; SCCS, 2010; REACH).

Repeated Dose Toxicity

Oral

The limited available information indicates that the chemicals in this group are not likely to cause serious damage to health from repeated oral exposure. It is also noted that the main target organs for repeated dose oral toxicity were the stomach, the blood, and possibly the testes. The degradation products (boric acid and hydrogen peroxide) possibly contributed to these health effects.

In a repeated dose toxicity study, sodium perborate tetrahydrate (CAS No. 10486-00-7) was administered (by gavage) to rats at 1000 mg/kg bw/day (70 mg boron/kg bw/day) for 28 days (see **Reproductive and developmental toxicity**). Acanthosis and hyperkeratosis in the forestomach, and hyperplasia of the fundic mucosa were noted. At the end of the study, the red blood cell count, haemoglobin, haematocrit and number of lymphocytes were significantly decreased; the number of platelets was significantly increased. The spleen size and splenic parenchyma were reduced. Although a significant (18 %) decrease in absolute testicular weights was recorded, the authors attributed this to a generalised weight reduction of 15 %; histological examination of the testes revealed no adverse effects. The lowest observed adverse effect level (LOAEL) was 1000 mg/kg bw/day (70 mg boron/kg bw/day), based on effects on the stomach, spleen and the haematopoietic system. It was concluded that the no observed adverse effect level (NOAEL) for males or females was below 1000 mg/kg bw/day (EU RAR, 2007; SCCS, 2010; REACH).

Dermal

The limited available information indicates that the chemicals in this group are not considered to cause serious damage to health from repeated dermal exposure.

In a repeated dose toxicity study, sodium perborate tetrahydrate (CAS No. 10486-00-7) was applied at 200 mg/kg bw/day (as a 10 % aqueous solution) to the abraded skin of New Zealand White rabbits for three weeks. After exposure, the skin was near normal (signs of mild irritation in some cases) and there were no adverse microscopic findings in different organs. An NOAEL of 200 mg/kg bw/day was established, being the highest tested dose (EU RAR, 2007; SCCS, 2010; REACH).

In another repeated dose toxicity study, sodium perborate tetrahydrate (CAS No. 10486-00-7) was applied at 50 mg/kg bw (as a 2.5 % aqueous solution) to the intact skin of New Zealand White rabbits (three/sex), five days/week for 13 weeks. The treatment caused no skin irritation and there were no adverse effects on blood parameters or on the gross histopathology of selected organs. An NOAEL of 50 mg/kg bw/day was established, being the highest tested dose (EU RAR, 2007; SCCS, 2010; REACH).

Inhalation

No data are available.

Observation in humans

Health surveillance data for workers in perborate production plants do not indicate obstructive lung effects such as asthma or chronic bronchitis. This conclusion was reached following spirometric examinations of about 100 workers in the production plants, even at workplaces with presumed high exposure. Workers that were followed up for several years and up to more than 20 years, also did not show deterioration of the lung function, measured as forced vital capacity (FVC), forced expiratory volume 1 (FEV1), vital capacity (VC), and peak expiratory flow (PEF). It was also noted that the measured parameters are not very sensitive, especially for small airway disease. However, the absence of effects in a large number of workers, and even in

workers exposed for more than 20 years, leads to the conclusion that there is no concern that the production workers showed obstructive lung effects (asthma or chronic bronchitis) (EU RAR, 2007; REACH).

Genotoxicity

The available information indicates that the chemicals in this group are not considered to have mutagenic or genotoxic potential.

Although sodium perborate demonstrated genotoxic potential in three different in vitro assays, this was concluded to be due to the generation of hydrogen peroxide (CAS No. 7722-84-1), as responses were reduced by the presence of catalase. Although hydrogen peroxide (CAS No. 7722-84-1) gave a positive response in some in vitro tests without metabolic activation, in vivo genotoxicity studies employing modern methodologies were all negative, probably due to effective inactivation mechanisms. It was concluding that hydrogen peroxide (CAS No. 7722-84-1) is not considered to be genotoxic (NICNASb). Boric acid (CAS No. 10043-35-3) was also not considered to have mutagenic or genotoxic potential (NICNASa). Therefore, the chemicals in this group are not considered to have mutagenic or genotoxic potential (EU RAR, 2007; SCCS, 2010).

Sodium perborate induced weak but reproducible mutagenic effects in *Salmonella typhimurium* strains TA100 and TA102, without metabolic activation. There was no response with strain TA98. However, mutagenic activity as well as toxicity disappeared completely in the presence of metabolic activation (S9 mix). The clastogenic potential of sodium perborate was noted at a concentration of 10 ug/mL and up, without metabolic activation, in Chinese hamster ovary cells (CHO-K1). However, following pre-incubation with rat liver S9, the clastogenic activity of the chemical was reduced to zero within the tested concentration ranges (EU RAR, 2007; SCCS, 2010; REACH).

Carcinogenicity

No data are available on the chemicals in this group.

Information available on the degradation products, boric acid (CAS No. 10043-35-3) and hydrogen peroxide (CAS No. 7722-84-1), indicates that the chemicals in this group are not likely to have any carcinogenic potential (EU RAR, 2007; SCCS, 2010; NICNASa; NICNASb).

Reproductive and Developmental Toxicity

The sodium perborate chemicals in this group are classified as hazardous with hazard category ‘Reproductive Toxicity – Category 1B' and hazard statement 'May damage the unborn child. Suspected of damaging fertility' (H360Df) in the Hazardous Chemical Information System (HCIS) (Safe Work Australia). The available data support this classification. As the borate ion resulting from perborate is expected to be the driver of acute toxicity for the chemicals in this group, the hazard classification should be extended to calcium perborate (CAS No. 54630-47-6).

A classification of perborates as 'Repr. Cat 3; R62' (possible risk of impaired fertility) has been recommended, based on the repeated dose toxicity study (see below) and the data on borates. An LOAEL for fertility of 70 mg boron/kg bw/day has been established for perborates. Similarly, a classification of sodium perborate as 'Repr. Cat 2; R61' (may cause harm to the unborn child) has also been recommended. This was based on the developmental effects of sodium perborate in one rat study, for which the effects were not considered to be as a consequence of general systemic toxicity. It was also noted that the boric acid data were supportive of this classification and an NOAEL for developmental effects for perborates of 100 mg/kg bw/day (7 mg boron/kg bw/day) was established (EU RAR, 2007; SCCS, 2010).

Although no data are available for calcium perborate, it has higher perborate concentration per mass of chemical when compared with the sodium perborates in this group. On this basis, it is recommended that hazard classification is extended to this chemical.

Sodium perborate has also been suggested as having embryotoxic effects due to the release of boron, as the malformations induced at the highest dose of 1000 mg/kg bw/day were similar to those induced by boric acid in other experiments. It was also agreed that, based on the pattern of malformations, both chemicals (sodium perborate and boric acid) have developmental effects, with slightly different mechanisms based on different kinetics following administration (EU RAR, 2007).

In a repeated dose toxicity study, sodium perborate tetrahydrate (CAS No. 10486-00-7) was administered (by gavage) to rats at 1000 mg/kg bw/day (70 mg boron/kg bw/day) for 28 days (see **Repeat dose toxicity: Oral**). The authors recorded a significant (18 %) decrease in absolute testicular weights but this was attributed to a generalised weight reduction of 15 %. A histological examination of the testes revealed no adverse effects. It has also been argued that more sensitive methods of histopathology than used in this study (fixed with formalin) could have revealed more subtle effects. Therefore, using reduced testes weights as early signs of testicular toxicity cannot be dismissed in view of the known testicular toxicity of the borates. It was concluded that the NOAEL for males or females was below 1000 mg/kg bw/day (EU RAR, 2007; SCCS, 2010; REACH).

In a developmental toxicity study, sodium perborate tetrahydrate (CAS No. 10486-00-7) was administered (by gavage) to 25 pregnant Crl:Cd (SD) rats on gestation days (GD) 6–15 at doses of 0, 100, 300 and 1000 mg/kg bw/day. The NOAEL for maternal toxicity was established as 100 mg/kg bw/day (7 mg boron/kg bw/day), based on significant reductions in body weight gain at the two highest doses. It is also noted that even though reduced maternal weight gain might partly be due to an increased number of resumptions and reduced foetal weights, other toxicological studies have supported the view that doses above 100 mg/kg bw/day administered via gavage are toxic to the dams. A dose-related effect was found on the ossification and bone system. While various incomplete ossifications and wavy ribs occurred at 300 mg/kg bw/day, malformations (fused ribs) were observed at 1000 mg/kg bw/day. The NOAEL for developmental toxicity was established as 100 mg/kg bw/day (7 mg boron/kg bw/day) (EU RAR, 2007; SCCS, 2010; REACH).

Degradation products

The data available on one degradation product, hydrogen peroxide (CAS No. 7722-84-1), were judged insufficient/inadequate to evaluate reproductive and developmental toxicity (NICNASb).

With respect to the second degradation product, boric acid (CAS No. 10043-35-3), the testes and developing foetus have been identified as the most sensitive targets of boron toxicity in animal studies, with the rat being the most sensitive species. The reported testicular effects included reduced organ weight and organ to body-weight ratio; atrophy and degeneration of the spermatogenic epithelium; impaired spermatogenesis; and reduced fertility. The reported developmental effects included high prenatal mortality; reduced foetal body weight; and malformations and variations of the eyes, central nervous system, cardiovascular system, and axial skeleton. The NOAEL for fertility of 100 mg/kg bw/day of boric acid (equivalent to 17.5 mg boron/kg bw/day) has been determined (based on testicular effects) from two-year and three-generation studies in rats. The critical endpoint NOAEL for developmental effects has been established at 55 mg/kg bw/day of boric acid (equivalent to 9.6 mg boron/kg bw/day) in rats (NICNASa). This would correspond to an NOAEL of 88.7 mg/kg bw/day for sodium perborate monohydrate (CAS No. 10332-33-9) and an NOAEL of 136.8 mg/kg bw/day for sodium perborate tetrahydrate (CAS No. 10486-00-7), in a similar range as described above (EU RAR, 2007).

Other Health Effects

Neurotoxicity

Information is not available on the chemicals in this group.

Although data are also not available on one the degradation product (hydrogen peroxide—CAS No. 7722-84-1), information available on the other degradation product (boric acid—CAS No. 10043-35-3) indicates that the chemicals in this group are not likely to have neurotoxic properties (EU RAR, 2007; SCCS, 2010; NICNASa; NICNASb).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (reproductive toxicity, developmental toxicity), systemic acute effects (acute toxicity from oral/inhalation exposure) and local effects (respiratory and eye irritation).

Public Risk Characterisation

The chemicals in this group have reported specialised use in cosmetic and domestic products as bleaching agents. Use in cosmetic products is subject to the *Poisons Standard* control on hydrogen peroxide; the SCCS has concluded that use in hair dye formulation up to 3 % in the final mixed product does not pose risk to consumers.

Use in domestic products for bleaching is not expected to lead to exposure via routes other than dermal contact, so systemic toxicity and respiratory irritation are not likely.

Occupational Risk Characterisation

During product formulation, oral, dermal, ocular and inhalation exposure of workers to the chemicals in this group can occur, particularly where manual or open processes are used. These might include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemicals at lower concentrations could also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

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

Based on the available data, the current hazard classification for the sodium perborate chemicals in this group in the HCIS is considered appropriate. The data available support an amendment to the hazard classification in the HCIS (Safe Work Australia) for calcium perborate (CAS No. 54630-47-6) (see **Recommendation** section).

NICNAS Recommendation

Current risk management measures are considered adequate for the sodium perborate chemicals in this group, 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.

Assessment of these chemicals is considered to be sufficient, provided that the recommended amendment to the classification for calcium perborate (CAS No. 54630-47-6) 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

Work Health and Safety

The chemicals are recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below.

The hazard classifications: Reproductive toxicity – category 1B; H360Df (May damage the unborn child. Suspected of damaging fertility), Specific target organ toxicity (single exposure) – category 3; H335 (May cause respiratory irritation), Eye damage – category 1; H318 (Causes serious eye damage) and Acute toxicity – category 4; H302 (Harmful if swallowed) should be extended to calcium perborate (CAS No. 54630-47-6). No classification for acute inhalation toxicity is warranted for calcium perborate. This assessment does not consider classification of physical and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Not Applicable	Harmful if swallowed - Cat. 4 (H302) Toxic if inhaled - Cat. 3 (H331)* Harmful if inhaled - Cat. 4 (H332)*
Irritation / Corrosivity	Not Applicable	Causes serious eye damage - Cat. 1 (H318) May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335)
Reproductive and Developmental Toxicity	Not Applicable	May damage the unborn child. Suspected of damaging fertility - Cat. 1B (H360Df)

[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;
- health monitoring for any worker who is at risk of exposure to the chemical[s], 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.

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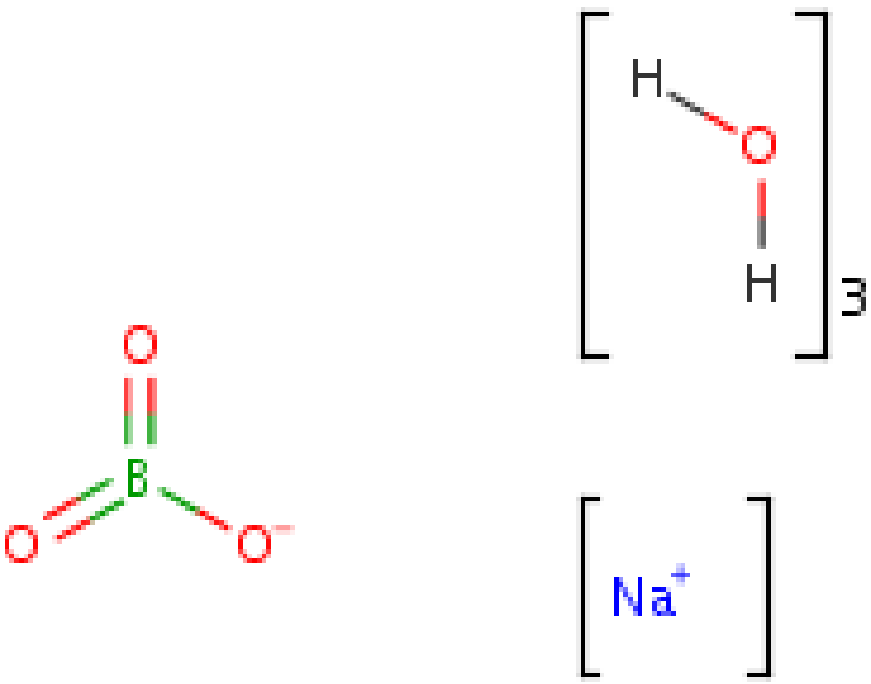
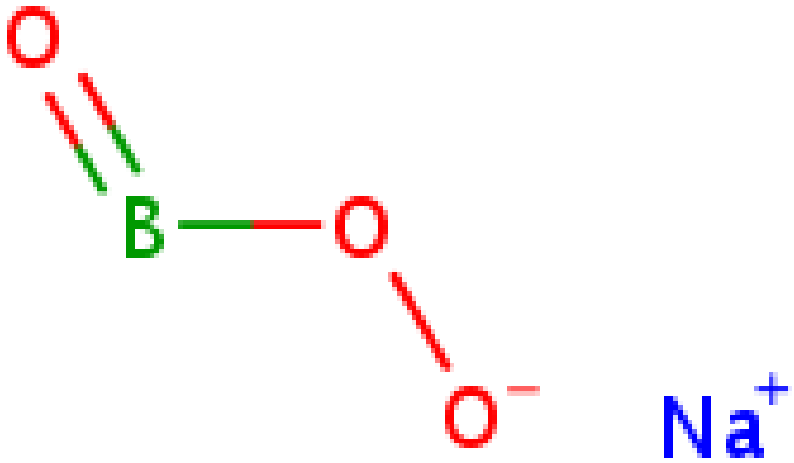
Last Update 02 March 2018

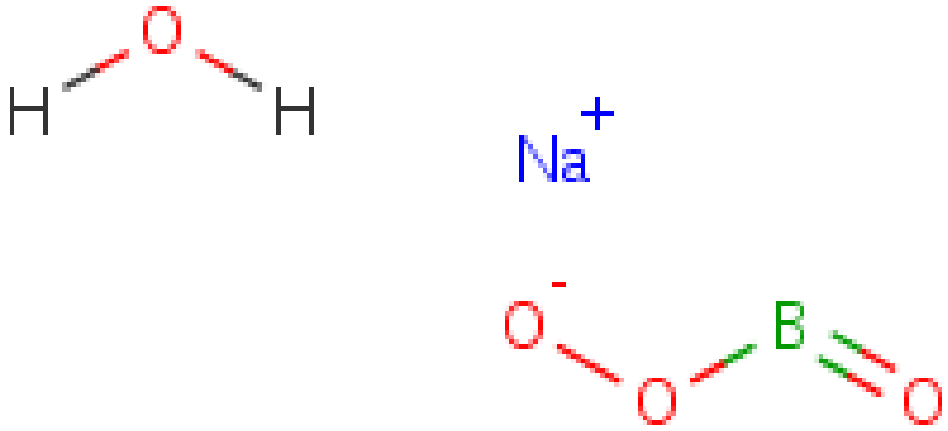
Chemical Identities

Chemical Name in the Inventory and Synonyms	**Perboric acid (H3BO2(O2)), monosodium salt, trihydrate** sodium perborate trihydrate sodium perborate
CAS Number	13517-20-9
Structural Formula	
Molecular Formula	BH3O4.3H2O.Na

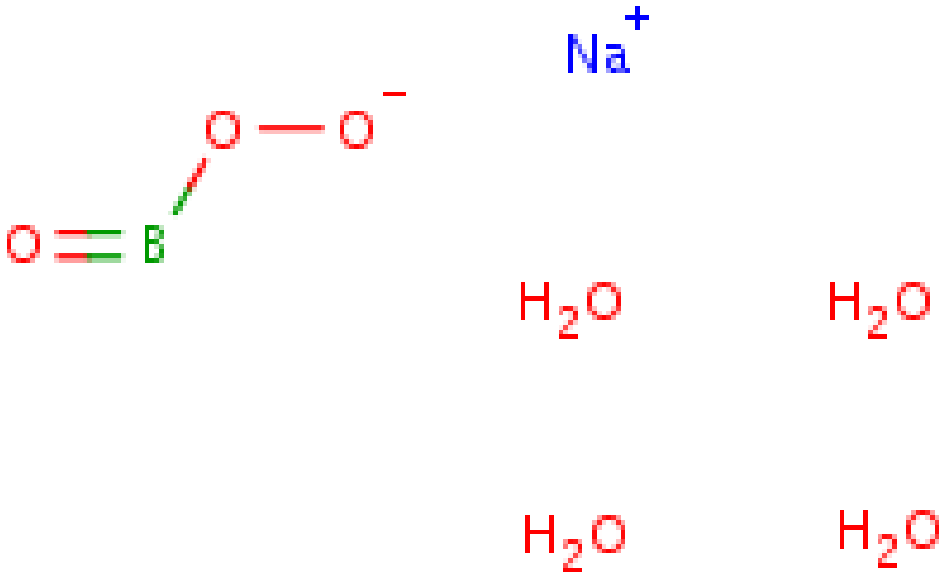
Molecular Weight	135.84

Chemical Name in the Inventory and Synonyms	**Perboric acid (HBO(O2)), sodium salt** sodium perborate sodium peroxometaborate
CAS Number	7632-04-4
Structural Formula	
Molecular Formula	BHO3.Na
Molecular Weight	81.80

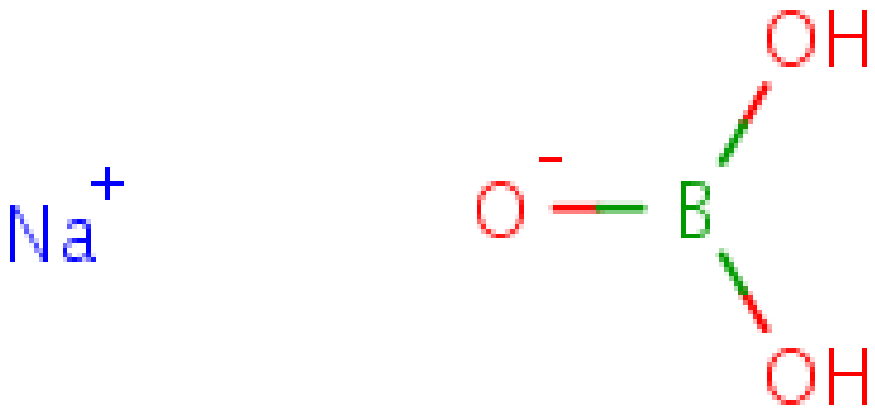
Chemical Name in the Inventory and Synonyms	**Perboric acid (HBO(O2)), sodium salt, monohydrate** sodium perborate monohydrate sodium perborate
CAS Number	10332-33-9

Structural Formula	
Molecular Formula	BHO3.H2O.Na
Molecular Weight	99.81

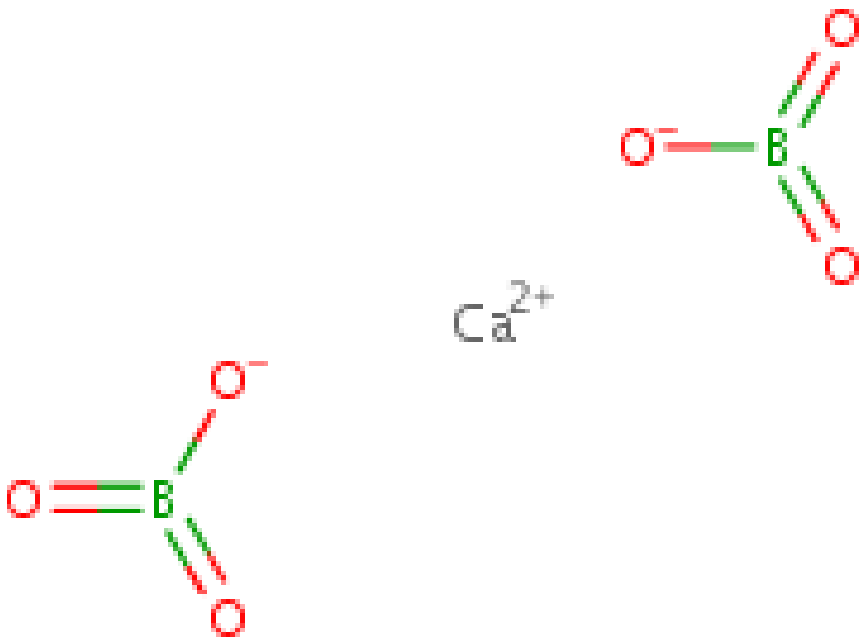
Chemical Name in the Inventory and Synonyms	**Perboric acid (HBO(O2)), sodium salt, tetrahydrate** sodium perborate tetrahydrate
CAS Number	10486-00-7
Structural Formula	

	
Molecular Formula	BHO3.4H2O.Na
Molecular Weight	153.86

Chemical Name in the Inventory and Synonyms	**Perboric acid, sodium salt** sodium perborate sodium peroxoborate sodium perborate anhydrous
CAS Number	11138-47-9
Structural Formula	

	
Molecular Formula	Unspecified
Molecular Weight	83.81

Chemical Name in the Inventory and Synonyms	**Perboric acid (HBO(O2)), calcium salt** calcium perborate
CAS Number	54630-47-6
Structural Formula	

	
Molecular Formula	BHO3.1/2Ca
Molecular Weight	79.86

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