Perchlorates: Human health tier II assessment

18 September 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Perchloric acid, sodium salt	7601-89-0
Perchloric acid, potassium salt	7778-74-7
Perchloric acid, ammonium salt	7790-98-9
Perchloric acid, sodium salt, monohydrate	7791-07-3
Perchloric acid, magnesium salt	10034-81-8

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

The chemicals in this group are inorganic salts of perchloric acid that only differ in the cation component: sodium perchlorate (CAS No. 7601-89-0), sodium perchlorate monohydrate (CAS No. 7791-07-3), potassium perchlorate (CAS No. 7778-74-7), ammonium perchlorate (CAS No. 7790-98-9), and magnesium perchlorate (CAS No. 10034-81-8).

The chemicals in this group have similar physicochemical properties, routes of exposure, and reported uses. They are also grouped together based on their expected similar toxicology profile due to the perchlorate anion (US EPA, 2002; ATSDR, 2008). The cations are considered to have low toxicity (NICNAS, 2013).

Import, Manufacture and Use

Australian

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

Sodium perchlorate (CAS No. 7601-89-0) is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of 1000–9999 tonnes. The chemical has reported commercial use as an oxidising agent in explosives.

No specific Australian use, import, or manufacturing information has been identified for potassium perchlorate (CAS No. 7778-74-7), sodium perchlorate monohydrate (CAS No. 7791-07-3), ammonium perchlorate (CAS No. 7790-98-9) or magnesium perchlorate (CAS No. 10034-81-1-8).

International

The following international uses have been identified through European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (EU REACH) dossiers; Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database; and eChemPortal: Organisation for Economic and Co-operative Development (OECD) High Production Volume chemical program (OECD HPV), the US Environmental Protection Agency's Aggregated Computational Toxicology Resource (ACToR), and the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

Sodium perchlorate (CAS No. 7601-89-0) has reported domestic use as a colouring agent. The US Household Products Database did not indicate any cosmetic or domestic use of the chemicals in this group and, given that sodium perchlorate is colourless, it is probable that its use is in producing a colouring agent.

The chemicals in this group have reported commercial use including in explosives, photography, pyrotechnics, smokeless powder and rocket propellant.

The chemicals in this group have reported site-limited use including:

- as stabilisers;
- as intermediates in synthesis; and
- in manufacturing machinery and equipment.

Chemicals in this group have reported non-industrial use as therapeutic agents (thyroid inhibitors).

Restrictions

Australian

Potassium perchlorate (CAS No. 7778-74-7) is listed in the *Poisons Standard* (Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP, 2013)) in Schedule 4 for non-industrial uses (prescription only medicine, or prescription animal remedy).

International

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

- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient "Hotlist").

Existing Worker Health and Safety Controls

Hazard Classification

Sodium perchlorate (CAS No. 7601-89-0) and potassium perchlorate (CAS No. 7778-74-7) are classified as hazardous, with the following risk phrase for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

Xn; R22 (Acute toxicity)

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Toxicokinetics

As perchlorate salts readily dissolve in water, the perchlorate anion is easily absorbed (>90 %) from the gastrointestinal tract. As vapour pressure of perchlorate salts is low at room temperatures, absorbing vapours through inhalation is considered negligible. However, absorbing particles through inhalation would depend on the particle size distribution. The potential for dermal absorption through intact skin is low, as perchlorates cannot readily penetrate the skin due to their ionic nature. Absorption through the skin is typically less than 10 % and frequently less than 1 % (Mattie, 2006; ATSDR, 2008).

Although perchlorates bind to serum proteins (bovine and human serum albumin), they do not undergo metabolism in adult rats or humans and are eliminated unchanged. Perchlorates can be taken up in relatively large amounts by the thyroid, breast tissue, and salivary glands, but generally leave these organs in a few hours. Absorbed perchlorates are eliminated rapidly through the urinary tract (>90 %), with urinary half-lives around four hours in the rat and six hours in humans. The cations do not influence the pattern of excretion (ATSDR, 2008).

The thyroid is the main target organ for perchlorate toxicity in animals and humans. Studies in rats have shown that perchlorate is readily taken up into the thyroid by an active transport mechanism, reaching a maximum concentration level (>3 % of the administered dose/g tissue) in four hours. An elimination half-time for the thyroid has been estimated to be 10–20 hours. Perchlorates have also been found in breast milk, without any evidence of abnormal thyroid function in the babies or the children (Mattie, 2006; ATSDR, 2008).

Studies have shown that perchlorate can cross the placental barrier in rats. Following exposure to perchlorate through drinking water in rats at 1 mg/kg bw/day or lower, a foetal:maternal serum concentration ratio of approximately one was established. However, this ratio fell to less than one when the maternal dosage was 10 mg/kg bw/day, suggesting the possibility of a dose-dependent limitation in the capacity of transplacental transfer (ATSDR, 2008).

Perchlorate was also found to competitively inhibit the active uptake of iodine from the blood into the thyroid follicle cells. This results in reduced thyroid hormone production (triiodothyronine T3 and thyroxine T4) and increased thyroid stimulating hormone (TSH) secretion via a negative feedback loop. Therefore, the majority of animal and human toxicity studies available are associated with thyroid histopathology evaluation (US EPA, 2002; Mattie, 2006; ATSDR, 2008; HSDB)

Acute Toxicity

Oral

Sodium perchlorate (CAS No. 7601-89-0) and potassium perchlorate (CAS No. 7778-74-7) are classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in HSIS (Safe Work Australia). While the limited available data do not support this classification, in the absence of more comprehensive information, there are insufficient data to recommend amendment of the current HSIS classification.

In an acute oral toxicity study conducted according to OECD Test Guideline (TG) 423, female Sprague Dawley (SD) rats were administered (gavage) sodium perchlorate at doses of 300 or 2000 mg/kg bw and observed for 14 days. Hypoactivity was observed at the highest dose level for all animals within two hours of treatment. No other abnormalities were reported. A median lethal dose (LD50) of >2000 mg/kg bw was established (REACHa).

While data are not available for the other chemicals in this group, similar results could be expected.

Dermal

Sodium perchlorate (CAS No. 7601-89-0) had low acute toxicity in animal tests following dermal exposure. The LD50 in rats is >2000 mg/kg bw. Even though data are not available for the other chemicals in this group, similar results could be expected. The low dermal absorption potential through intact skin supports this finding (see **Toxicokinetics**).

In an acute dermal toxicity study conducted according to OECD TG 402, undiluted sodium perchlorate was applied (semi-occlusive) to the skin of SD rats (male/female) for 24 hours with observation up to 14 days. There were no deaths and systemic clinical signs were also not observed during the study. Crusts were observed at the site of application in 1/5 males from day 10 until day 15. A dermal LD50 of >2000 mg/kg bw was established (REACHa).

Inhalation

No data are available.

Corrosion / Irritation

Respiratory Irritation

Although specific information is not available, the chemicals in this group have been reported to be respiratory irritants during short-term exposure (ICSC).

Skin Irritation

Sodium perchlorate (CAS No. 7601-89-0) is reported to be a slight skin irritant in animal studies. The effects were not sufficient to warrant a hazard classification.

In a dermal irritation study (OECD TG 404), solid sodium perchlorate (500 mg) was applied (semi-occlusive) on the shaved skin of three New Zealand White rabbits for four hours, with observation up to 72 hours. Following the four-hour exposure, very slight erythema was observed in all three animals on day one; this persisted to day two in one animal. The mean scores over 24, 48 and 72 hours for each animal were 0.3, 0.0, and 0.0 for erythema and 0.0, 0.0, 0.0 for oedema respectively. Effects were fully reversible within 72 hours (REACHa).

Eye Irritation

Sodium perchlorate (CAS No: 7601-89-0) has been reported to produce irritant effects in an eye irritation study in rabbits. Although limited data are available for chemicals in this group, eye irritation was sufficiently marked in this study to support the need for classification (refer to **Recommendation** section). Lesser results are not expected for the other chemicals in this group.

In an eye irritation study (OECD TG 405), the solid chemical (100 mg) was applied to one eye of each of three male New Zealand White rabbits with observation up to 12 days. The mean score values at 24, 48 and 72 hours were 2.67, 2.3 and 2.4 for chemosis; 2.3, 2.3 and 2.3 for redness of the conjunctivae; 1.0, 0.67 and 0.33 for iris lesions; and 2.0, 1.67 and 0.67 for corneal opacity respectively. While chemosis and conjunctival redness persisted until day 12, all other parameters were fully reversible within 72 hours to six days. The chemical is considered to be an eye irritant (REACHa).

Sensitisation

Skin Sensitisation

The available data on sodium perchlorate (CAS No: 7601-89-0) indicate that the chemicals in this group are not likely to be skin sensitisers.

In a skin sensitisation study conducted according to OECD TG 429 (local lymph node assay—LLNA), sodium perchlorate (CAS No. 7601-89-0) at 1 %, 2.5 %, 5 %, 10 % and 25 % concentration in dimethylformamide was applied to the dorsal surface of female CBA mice ears at 25 µL on days one, two, and three. Irritant effects were not observed at the highest concentration (25 %) during the preliminary test. Clinical signs, mortality, and cutaneous reactions, and any noteworthy increase in ear thickness were not observed during the study. The stimulation index (SI) values obtained were 1.59, 1.49, 1.71, 1.21, and 0.54 corresponding to 1.0, 2.5, 5.0, 10 and 25 % concentrations respectively. Therefore, an EC3 (the effective concentration inducing an SI of 3) value can not be determined from this study (REACHa).

Repeated Dose Toxicity

Oral

Although thyroid effects were noted in animal studies following repeated oral exposure, the available human data showed no evidence of adverse haematological, hepatic, renal, or clinically significant thyroid effects following consumption of perchlorate at low doses (≤0.04 mg/kg bw/day for six months) (see **Repeat dose toxicity: observation in humans**).

The thyroid is the main target organ for perchlorate toxicity in animals and humans following repeated oral exposure. The first observed biological effect of perchlorate exposure is the alteration of hormone levels (T4, T3, TSH) due to reversible chemically induced iodine deficiency (see **Toxicokinetics**). Although thyroid changes (thyroid hyperplasia) can lead to thyroid tumours in rodents, this only occurred following exposure to high amounts (928 to 2573 mg perchlorate/kg bw/day) in rodents for a long period (see **Carcinogenicity**). However, the relevance of these rodent tumours to humans has been questioned and it has been concluded that perchlorate is unlikely to pose a risk of thyroid cancer in humans (Matte, 2006; ATSDR, 2008).

In a repeated dose toxicity study (OECD TG 408), groups of SD rats (male/female, 10/sex/dose level) were administered ammonium perchlorate (CAS No: 7790-98-9) in drinking water at doses of 0.01, 0.05, 0.2, 1.0 and 10 mg/kg bw/day (0.009, 0.04, 0.17, 0.85, or 8.5 mg perchlorate/kg bw/day) for 90 days. Another group (10 rats/sex) were administered the chemical at doses of 0.0, 0.05, 1.0 and 10 mg/kg bw/day for 90 days and kept for a 30 day treatment-free period to evaluate the reversibility of perchlorate toxicity. At the highest dose level, adverse effects observed in the thyroid after 90 days of exposure were redness, increased thyroid weight, follicle hypertrophy and minimal hyperplasia. These effects were reversible after the treatment-free period. Although thyroid hormone (T3/T4/TSH) levels were significantly affected at the highest tested dose, hormone levels approached control levels (except for T4 in males, TSH in females) following the 30-day treatment-free period. No other toxicologically relevant effects were observed. A no observed adverse effect level (NOAEL) of 1 mg/kg bw/day was established in this study (ATDSR, 2008; HSDB; REACHb).

In another repeated dose toxicity study (with limited information), female NMRI mice were administered potassium perchlorate (CAS No: 7778-74-7) at 0 or 1 % concentrations in their diet (estimated dose of 2011 mg/kg bw/day) for up to 160 days. Although increased body weights were noted during the first two months of treatment, increased thyroid weight, nuclei volumes and height of epithelial follicles were noted throughout the exposure period. Examinations of the thyroid showed progressive changes in the histological appearance followed by hypertrophy and hyperplasia. Hyperplastic follicles, adenomatic tissues and secreting cystadenomas were observed at later stages of the treatment period; however, there was no apparent progression to malignancy. The lowest observed adverse effect level (LOAEL) was 2011 mg/kg bw/day (US EPA, 2002).

Dermal

No data are available.

Inhalation

No data are available.

Observation in humans

Occupational studies and studies in volunteers who ingested daily doses of perchlorate ≤0.05 mg/kg bw/day for 14 days or ≤0.04 mg/kg bw/day for six months showed no evidence of adverse haematological, hepatic, renal, or clinically significant thyroid effects.

In a study in workers in production facilities for ammonium perchlorate (CAS No: 7790-98-9), the workers (n = 37) were exposed to the chemical at a respirable concentration averaging 0.86 mg/m^3. The average airborne exposure for the highest exposure group was 8.6 mg/day (particle size 0.1–10 µm) or 59.4 mg/day (total particulate perchlorate). No significant haematological, hepatic or renal effects were observed. Cumulative exposure measurements were not considered in this study.

Another study in Nevada compared data between exposed and unexposed workers from the same industrial complex. The cumulative dose in the high exposure group was estimated to be 38 mg/kg bw, which corresponds to a daily dose of 0.01 mg/kg bw/day, based on the approximate average exposure duration of nine years for high dose workers. There were no adverse effects on the thyroid, kidney, liver or function of the bone marrow. A cross-sectional health study in Utah also reported no effects on blood and clinical chemical parameters at exposure values of up to 34 mg/day. However, thyroid hormones were observed to have increased (Matte, 2006; ATSDR, 2008).

In a case study, a patient with severe hyperthyroidism was treated with an average of 1068 mg of sodium perchlorate/day (CAS No: 7601-89-0) for 3.5 months. Although the patient developed nephrotic syndrome (decreased serum albumin and increased serum cholesterol), these effects were reversible at the end of treatment (ATSDR, 2008).

Several human deaths have been reported among hyperthyroid patients (Graves' disease) following treatment with potassium perchlorate (CAS No. 7778-74-7) at 600–1000 mg/day (perchlorate doses of 5–12 mg/kg bw/day) for 2–8 months. All of the dead patients were females and died due to aplastic anaemia or severe agranulocytosis. Symptoms of gastrointestinal distress were also reported in a small percentage of hyperthyroid patients.

Another review of 250 cases reported a 1.5 % incidence of nausea among patients administered 600 or 1000 mg of the chemical/day and 4 % among patients administered 1500 or 2000 mg/day (ATSDR, 2008).

In another study, 3 % of 180 patients were administered the chemical at doses of 400–1000 mg/day (6–14 mg/kg bw/day) and 18 % of 67 patients were administered the chemical at doses of 1200–2000 mg/day (17–29 mg/kg bw/day). Symptoms observed within two to three weeks of exposure included skin rash, sore throat and gastrointestinal irritation (US EPA, 2002).

Genotoxicity

Although limited data are available, the available information indicates that the chemicals in this group and perchlorate as an anion are not considered to have either mutagenic or genotoxic potential.

Ammonium perchlorate (CAS No. 7790-98-9) gave negative results in several in vitro tests such as an Ames assay with *Salmonella typhimurium* strains and a mouse lymphoma gene mutation assay. Magnesium perchlorate (CAS No. 10034-81-8) was also negative in *S. typhimurium* strain 1535 and in a test to produce DNA-protein cross links in cultured human lymphocytes (US EPA, 2002; ATDSR, 2008).

Ammonium perchlorate (CAS No. 7790-98-9) was negative in a bone marrow erythrocyte micronucleus test in rats following exposure to 8.5 mg/kg bw/day in drinking water for 90 days.

Similar results were reported in a bone marrow micronucleus assay in mice following intraperitoneal injection of ammonium perchlorate of 500 mg/kg bw/day for three consecutive days; higher doses were lethal to the mice (US EPA, 2002; ATDSR, 2008).

Carcinogenicity

Although sufficient evidence is available to show that the perchlorate ion is carcinogenic in animals, the relevance of this to humans is questionable. Chemicals in this group are not considered to have mutagenic or genotoxic potential (see **Genotoxicity**); effects on thyroid hormone homeostasis have been stated as the sole mechanism for the observed thyroid tumours in rodents. The National Academy of Sciences National Research Council (NAS) has noted that 'on the basis of the understanding of the biology of human and rodent thyroid tumours, it is unlikely that perchlorate poses a risk of thyroid cancer in humans'. The US EPA also came to the conclusion that perchlorate is not likely to pose a risk of thyroid cancer in humans, at least at doses below those necessary to alter thyroid hormone homeostasis (US EPA, 2005; ATSDR, 2008).

Potassium perchlorate (CAS No. 7778-74-7) and sodium perchlorate (CAS No. 7601-89-0) have been shown to produce thyroid tumours (papillary and/or follicular adenomas and/or carcinomas) in rats and mice following long-term exposure (1–24 months). The estimated doses of perchlorate in these studies ranged from 928 to 2573 mg/kg bw/day (US EPA, 2005; ATSDR, 2008; HSDB).

In a combined carcinogenicity/two-generation reproductive toxicity study, groups of SD rats (30/sex/dose level) were administered ammonium perchlorate (CAS No.7790-98-9) in drinking water at doses of 0, 0.3, 3.0 and 30 mg/kg bw/day. Both male and female rats (P1 generation) were treated for at least 70 days before mating and through the mating period (21 days) until they were euthanised. The males were euthanised after a sufficient number of pregnancies were determined, and females after 21 days of lactation. The dosing duration was the same for the P1 and F1 groups of animals, with the exception of additional exposure of F1 pups during the gestation and lactation periods. There were follicular cell adenomas in one control male rat in the parent (P1) generation and two high-dose (30 mg/kg bw/day) males in the first offspring (F1) generation at 19 weeks of age. It was concluded that the thyroid tumours in the offspring were most likely treatment-related, but that they would be expected to be in high dose male rats in the presence of a markedly goitrogenic dosing regimen (US EPA, 2002; HSDB).

In a carcinogenicity study (non-guideline), male Wistar rats were administered potassium perchlorate (CAS No. 7778-74-7) in drinking water at concentrations of 0 or 1 % (estimated to be 1339 mg/kg bw/day) for two years. The rats were euthanised after 0, 40, 120, 220 and 730 days of exposure. After 40 days of treatment, follicular cell hyperplasia in the thyroid was observed. After 200 days of treatment, diffusely degenerative thyroid changes with fibrosis and increased colloid were observed. Some of the rats (4/11) developed benign tumours of the thyroid. The LOAEL was 1339 mg/kg bw/day, based on the effects observed at the only tested dose (ATDSR, 2008; REACHc).

Limited information was located regarding exposure to perchlorate and cancer in humans. In two ecological epidemiological studies conducted in the USA, the epidemiological evidence was not considered to be sufficient to determine any association between perchlorate exposure and thyroid cancer (US EPA, 2005; ATDSR, 2008).

Reproductive and Developmental Toxicity

The chemicals in this group do not show specific reproductive or developmental toxicity. Any reproductive and developmental effects were only observed secondary to maternal toxicity (see **Other health effects: Neurotoxicity**).

In a two-generation reproductive toxicity study, groups of SD rats (30/sex/group)were administered ammonium perchlorate (CAS No. 7790-98-9) in drinking water at doses of 0. 0.3, 3.0 and 30.0 mg/kg bw/day (perchlorate doses of 0, 0.26, 2.6, or 25.5 mg/kg bw/day). The F1 generation was given the same doses as their P1 generation (from weaning to 19 weeks of age). There were no signs of parental toxicity and male and female mating and fertility parameters were also not affected. The NOAEL for reproductive effects of perchlorate in this study was 25.5 mg/kg bw/day. Parental and offspring NOAELs of 0.3 mg/kg bw/day were established in this study, based on anti-thyroid effects at higher doses (ATDSR, 2008; HSDB; REACHb).

In a developmental toxicity study, groups of SD rats were administered ammonium perchlorate (CAS No. 7790-98-9) in drinking water at perchlorate doses of 0, 0.009, 0.09, 0.85, and 25.5 mg/kg bw/day, beginning 14 days premating and continuing to gestation day (GD) 21. There were no maternal or litter parameters clearly affected by the treatment with the chemical. Significant decrease in serum T4 was noted in dams at all doses during gestation. Although a downward trend was also noted in serum T3 in the dams during gestation, the effect was only significant at the highest dose. Serum TSH was substantially increased in the pregnant dams at all doses. For the foetuses and pups, there were dose-related increases in TSH and decreases in T3/T4. Significant reduction of ossification sites/litter for sternal centres and forelimb phalanges in the foetuses of the 25 mg/kg bw/day group were observed. No adverse effects on development occurred at levels that did not cause maternal toxicity. Based on thyroid effects, the maternal and developmental LOAELs were reported to be 0.009 mg/kg bw/day in this study (ATDSR, 2008; HSDB).

In another developmental toxicity study, pregnant New Zealand White rabbits were given ammonium perchlorate in drinking water at perchlorate doses of 0, 0.09, 0.85, 8.5, 25.5, or 85 mg/kg bw/day on GD 6–28. The incidence of hypertrophy of the follicular epithelium of the thyroid was dose related from ≥10 mg/kg bw/day. Serum T4 was significantly reduced at 25.5 and 85 mg/kg bw/day. There were no treatment-related effects on any of the litter parameters studied or on gross alterations or skeletal and soft tissue anomalies. The maternal and developmental NOAELs were reported to be 0.85 and 85 mg/kg bw/day, respectively (ATDSR, 2008; HSDB, REACHb).

In a developmental toxicity study (non-guideline), pregnant rabbits were administered potassium perchlorate (CAS No: 7778-74-7) in their diet at 100 mg/kg bw/day from conception to GD 28. As the maternal and foetal thyroid weights increased three and four fold respectively at day 21, the authors suggested that these results were evidence that the placenta is permeable to perchlorate. It was also concluded that the increase in the weight of the foetal thyroid, compared with the maternal thyroid, pointed to a foetal thyroid system that is more sensitive to iodine deficiency (US EPA, 2002; REACH). Similar effects were also observed in a guinea pig study where near-term (close to delivery) foetuses of dams were administered 1 % potassium perchlorate (~531 mg perchlorate/kg bw/day) in drinking water during the last half of the gestation period. The relative foetal thyroid weights increased 15 fold compared with controls, and hyperplasia was observed, while maternal thyroids were not affected (ATDSR, 2008).

Other Health Effects

Neurotoxicity

As thyroid hormones play a critical role in the neurological development of the foetus, there is concern that altered thyroid levels (maternal and/or foetal) during pregnancy could result in neurodevelopmental effects. Evidence for neurodevelopmental effects is not conclusive in animals; the NAS has noted that animal studies did not adequately serve as a surrogate for human studies due to species-specific differences. As rats have a smaller store of iodinated thyroglobulin, which is more quickly depleted when iodine uptake is reduced, and a more rapid clearance of T4, the response of rats to short-term oral dosages of perchlorate is quantitatively different (more sensitive) from the response observed in humans given comparable dosages (US EPA, 2002; ATSDR, 2008).

Neurodevelopmental effects have not been reported in humans despite the extensive use of these chemicals over many years. It has been suggested that as long as maternal serum levels of thyroid hormones are maintained within normal levels during pregnancy, there is no apparent developmental risk due to the placental transfer of maternal thyroid hormones. As relatively large doses of perchlorate (600–900 mg/day, 8–13 mg/kg bw/day) are required in humans to deplete thyroidal iodine stores sufficiently to decrease serum levels of T4, these doses might not be relevant during normal occupational exposure and consumers exposed by using products containing the chemicals in this group (ATSDR, 2008).

In a neurodevelopmental study, pregnant female SD rats (25/group) were administered ammonium perchlorate (CAS No. 7790-98-9) in drinking water at doses of 0.1, 1, 3, or 10 mg/kg bw/day (perchlorate doses of 0.09, 0.9, 2.6, and 8.5 mg/kg bw/day) from GD 0 (mating) to day 10 of lactation. No changes in behavioural effects (passive avoidance, watermaze swimming, motor activity or auditory startle) were observed at the highest tested dose. Hormone changes (decreased T4, increased TSH) occurred at lower doses (≤2.6 mg/kg bw/day). The most prominent effect was an increase in the thickness of the corpus callosum of the brain in pups at day 12 of lactation at the highest dose administered (Matte, 2006; ATSDR, 2008, HSDB).

To further examine the brain morphometry observations in the study, a subsequent study using the same dosing as the previous study was performed to evaluate brain development with data collected at critical times—one foetal (GD 21) and three postnatal (PND) (4, 9, and 21). Significant effects (alteration of brain structures) were observed following developmental exposure to the chemical at doses of 0.01 mg/kg bw/day. However, the brain morphometry changes were not dose-dependent (US EPA, 2002).

It was concluded that the current information is still inadequate to determine whether a causal relationship exists between maternal perchlorate exposure and pup neurodevelopmental abnormalities in rodents (US EPA, 2002; Matte, 2006; ATSDR, 2008; HSDB).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include potential interference with the inhibition of iodine uptake in the thyroid which might produce neurodevelopmental effects. The chemicals in this group can also cause eye irritation.

The NAS concluded that animal studies were not relevant to humans. Rats are more sensitive to the development of thyroid tumours and their thyroid function is easily disrupted (doses that cause only 10 % iodine uptake inhibition cause changes to hormone levels). Humans are less susceptible and not likely to develop thyroid tumours (doses that cause 70 % iodine uptake inhibition have no effect on hormone levels) (US EPA, 2005; ATDSR, 2008).

Public Risk Characterisation

There are no reported Australian cosmetic or domestic uses of the chemicals in this group. The US Household Products Database also did not indicate any cosmetic or domestic use of the chemicals in this group. As chemicals in this group will have limited public uses or are unlikely to be used by the public, exposure to the public is expected to be limited.

Therefore, the risk to public health is not considered to be unreasonable and further risk management is not considered necessary for public safety.

Occupational Risk Characterisation

During product formulation, 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 chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise ocular and inhalation exposure to the chemical are implemented. The chemical 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 appropriate controls.

The data available support an amendment to the hazard classification in HSIS (refer to the **Recommendation** section).

NICNAS Recommendation

Assessment of the chemicals in this group 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

Work Health and Safety

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

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)*	Harmful if swallowed - Cat. 4 (H302)
Irritation / Corrosivity	Irritating to eyes (Xi; R36)	Causes serious eye irritation - Cat. 2A (H319)

[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 industry

Control measures

Control measures to minimise the risk from ocular and inhalation exposure to the chemicals in this group 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 chemical is used. Examples of control measures which may minimise the risk include, but are not limited to:

- 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 chemical.

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 assist with meeting 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 chemical 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 the chemical has not been undertaken as part of this assessment.

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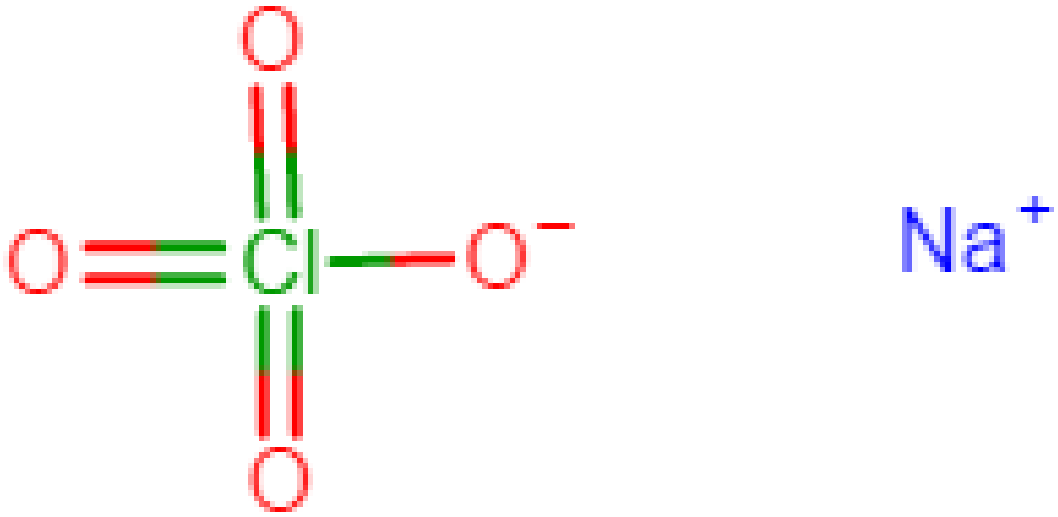
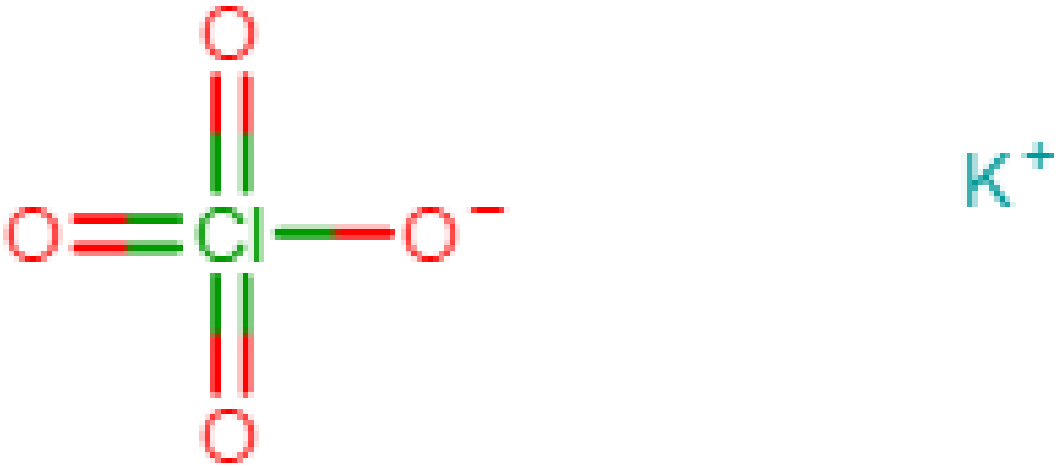
Last Update 18 September 2014

Chemical Identities

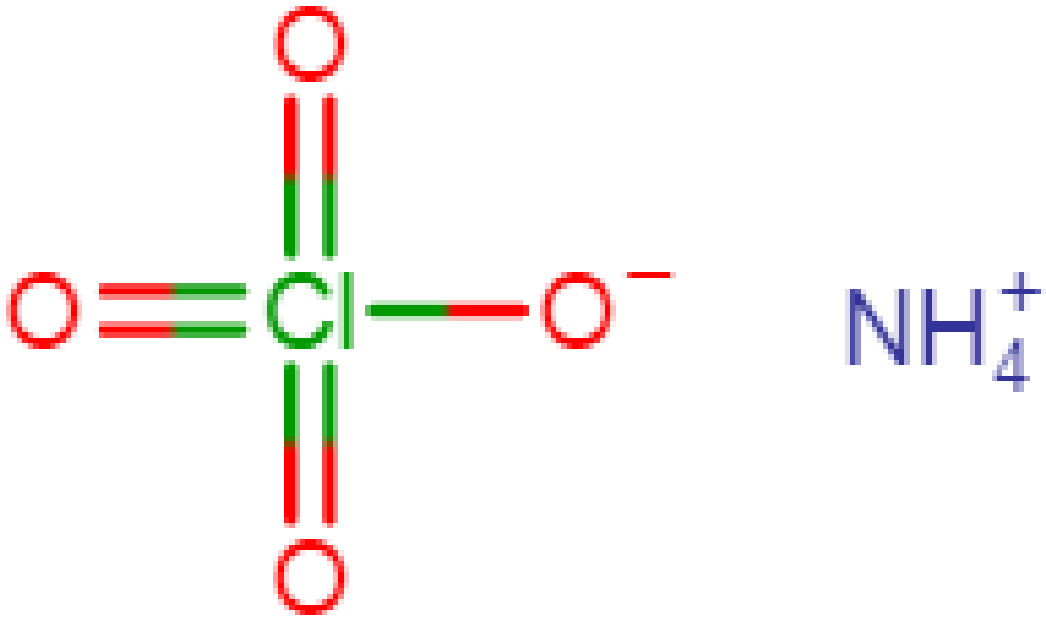
Chemical Name in the Inventory and Synonyms	**Perchloric acid, sodium salt** sodium perchlorate
CAS Number	7601-89-0
Structural Formula	

	
Molecular Formula	ClHO4.Na
Molecular Weight	122.44

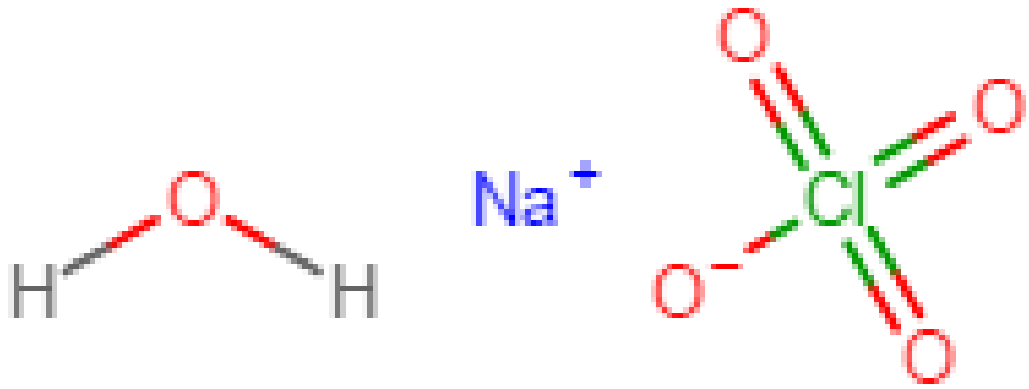
Chemical Name in the Inventory and Synonyms	**Perchloric acid, potassium salt** potassium perchlorate
CAS Number	7778-74-7
Structural Formula	

	
Molecular Formula	ClHO4.K
Molecular Weight	138.547

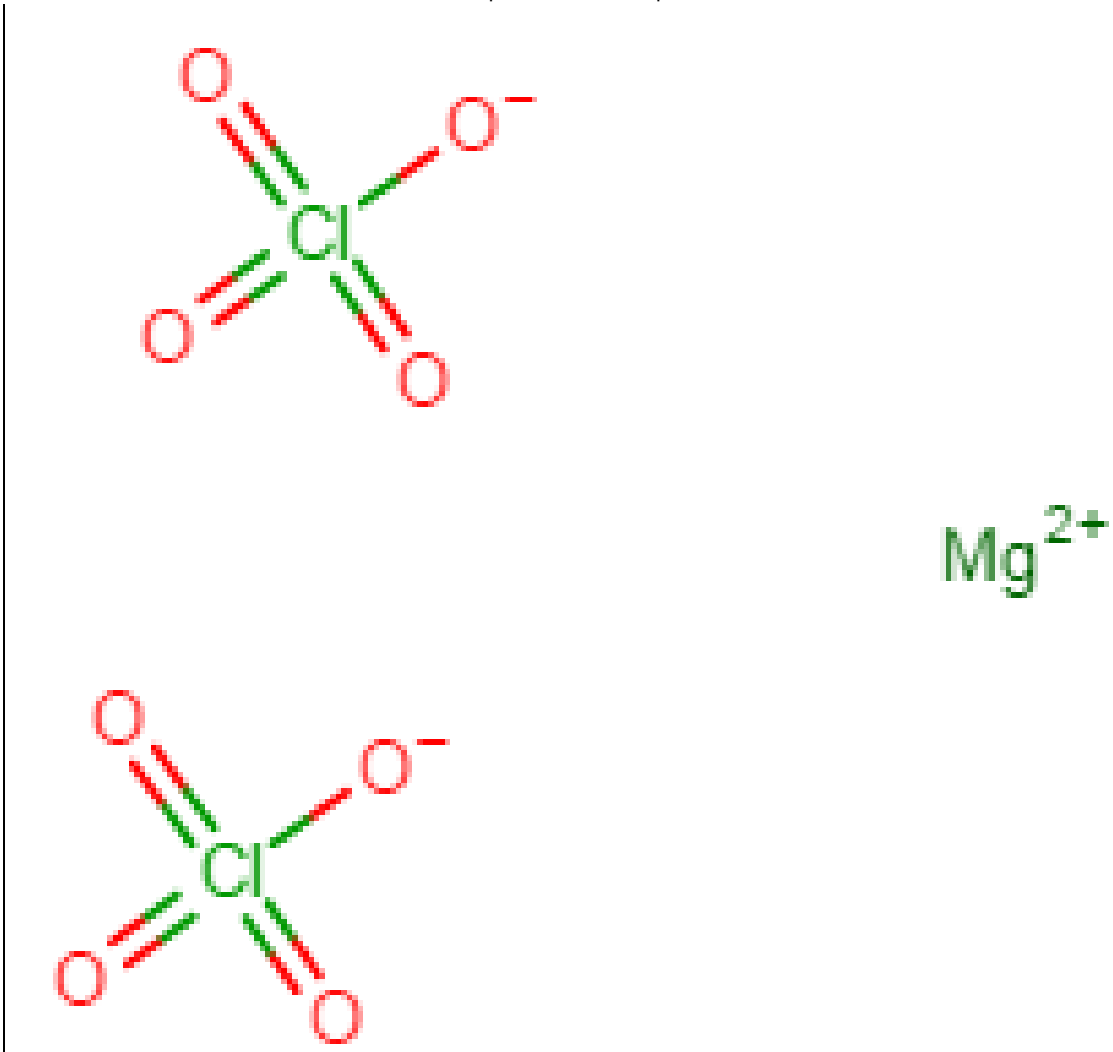
Chemical Name in the Inventory and Synonyms	**Perchloric acid, ammonium salt** ammonium perchlorate
CAS Number	7790-98-9
Structural Formula	

	
Molecular Formula	ClHO4.H3N
Molecular Weight	117.49

Chemical Name in the Inventory and Synonyms	**Perchloric acid, sodium salt, monohydrate** sodium perchlorate, monohydrate
CAS Number	7791-07-3
Structural Formula	

	
Molecular Formula	ClHO4.H2O.Na
Molecular Weight	140.454

Chemical Name in the Inventory and Synonyms	**Perchloric acid, magnesium salt** magnesium perchlorate
CAS Number	10034-81-8
Structural Formula	



Molecular Formula	ClHO4.1/2Mg
Molecular Weight	223.203

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