Dichloroisocyanurates: Human health tier II assessment

05 February 2016

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3-dichloro-, potassium salt	2244-21-5
1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3-dichloro-, sodium salt	2893-78-9
1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3-dichloro-, sodium salt, dihydrate	51580-86-0

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, sodium dichloro isocyanurate dehydrate (CAS 51580-86-0; troclosene sodium), sodium dichloro isocyanurate (CAS 2893-78-9; troclosene sodium, dihydrate), and potassium dichloro isocyanurate (CAS 2244-21-5; troclosene potassium), are synthetic organic chemicals containing a dichlorinated triazine ring. They are chlorinated derivatives of isocyanuric acid (CAS No 108-80-5) and contain approximately 60 % available chlorine. They are collectively called dichloro isocyanurates.

The different counterions (i.e. K+, Na+) or hydration status (i.e. dehydrate, dihydrate) are not expected to affect the chemical reactivity and the hazard classification for the purpose of this assessment (see ***Health Hazard Information***).

Import, Manufacture and Use

Australian

The following Australian uses have been identified through Australian Pesticides and Veterinary Medicines Authority (APVMA, 2014) and several material safety datasheets (MSDS).

The chemicals have reported domestic uses including;

- as disinfectants in cleaning products and dishwashing compounds; and
- as bleaching agents.

The chemicals have reported site-limited uses as disinfectants for industrial water treatment.

The chemicals can have non-industrial uses as swimming pool sanitisation agents, as general biocides and as topical anti-infection agents.

International

The following uses were identified through Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI), the European Commission Cosmetic Ingredients and Substances (CosIng) database, Galleria Chemica (Galleria Chemica), Substances in Preparations in Nordic Countries (SPIN), United States National Library of Medicine Household Products Database (US NLM HPD), US Occupational Health Database (HazMap), REACH dossier (REACH) and US Environmental Protection Agency - Reregistration Eligibility Decision (US EPA, 1992).

The chemical troclosene potassium (CAS No 2244-21-5) has reported use as an antimicrobial in cosmetic products.

The chemicals have reported domestic uses including;

- in dry laundry bleaches;
- as anti-freezing agents;
- as bleaching agents; and
- as disinfectants in cleaning products and dishwashing compounds.

The chemicals have reported commercial uses including;

- as chlorinating agents for wool; and
- as photochemicals

The chemicals have reported site-limited uses including in industrial deodorants.

The chemicals have reported non-industrial uses as swimming pool sanitisation agents, as disinfectants for civil sanitation, animal husbandry and plant protection, as a pesticide (slimicide) and as a topical anti-infective.

Restrictions

Australian

This chemicals are listed in the Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) in Schedules 5 and 6, under 'Chlorinating compounds' (SUSMP, 2015).

Schedule 6:

'CHLORINATING COMPOUNDS except:

(a) when included in Schedule 5;

(b) when separately specified in these Schedules;

(c) sodium hypochlorite preparations with a pH of less than 11.5;

(d) in liquid preparations containing not less than 2 per cent but not more than 4 per cent of available chlorine when labelled with the statements:

WARNING – Ensure adequate ventilation when using. Vapour may be harmful. May give off dangerous gas if mixed with other products;

(e) in liquid preparations containing less than 2 per cent of available chlorine; or

(f) in other preparations containing 4 per cent or less of available chlorine'.

Schedule 5:

'CHLORINATING COMPOUNDS containing 20 per cent or less of available chlorine, except:

(a) when separately specified in these Schedules;

(b) sodium hypochlorite preparations with a pH of less than 11.5;

(c) liquid preparations containing not less than 2 per cent but not more than 4 per cent of available chlorine when labelled with the statements:

WARNING – Ensure adequate ventilation when using. Vapour may be harmful. May give off dangerous gas if mixed with other products;

(d) liquid preparations containing less than 2 per cent of available chlorine; or

(e) other preparations containing 4 per cent or less of available chlorine'.

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

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

The chemicals are listed in the Agricultural and Veterinary Chemicals Code (Listed Chemical Product – Home Swimming Pool and Spa Products) – Standard 2014. The Standard sets out requirements for formulation of a chemical product or class of chemical products to which the Standard applies, including in relation to the packaging, labelling and handling of the product or products (APVMA, 2014).

International

Council of Europe Resolution AP (92) 2 on control of aids to polymerisation for plastic materials and articles - Limits for finished articles states that the finished article(s) containing the chemicals should not release to food or any of the food simulants triazine derivatives in excess of 0.25 mg/kg (Galleria Chemica).

The chemicals are listed on the US Food and Drug Administration (US FDA) Center for Food Safety and Applied Nutrition (CFSAN) Food Additive status list (Galleria Chemica).

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):

- Xn; R22, R31 (Harmful if swollowed, contact with acids liberates toxic gas); and
- Xi; R36/37 (Irritating to eyes and respiratory system).

Exposure Standards

Australian

No exposure standards have been assigned for these chemicals.

International

No exposure standards have been assigned for these chemicals.

Health Hazard Information

The chemicals in this assessment belong to the group of chlorinated isocyanurates that are used as sources of available chlorine. In contact with water or moist surfaces, the chemicals undergo partial hydrolysis to form equilibrium of free chlorine as hypochlorous acid (HOCl; CAS No 7790-92-3) and chlorinated and non-chlorinated isocyanurates. The equilibrium depends on the pH, the temperature, and the initial dichloroisocyanuric acid concentration. As the equilibria involve all of the possible chlorinated isocyanurates, the toxicity of diisocyanurate salts in this assessment will be virtually equivalent at the same available chlorine concentration. In the body, these chemicals are expected to be hydrolysed rapidly, and the free chlorine is reduced by reaction with various inorganic, organic and biological materials of saliva and stomach fluid as fast as it is formed. Therefore, the reaction products, isocyanuric acid and its salt, sodium isocyanurate (CAS No 2624-17-1; monohydrate) as well as free chlorine as hypochlorous acid are assumed to be of toxicological significance (US EPA, 2015) and can be used to support the health hazard data available for the dichloroisocyanurates (US EPA, 1992; 2015). Human health effects of sodium salt of hypochlorous acid have been assessed by NICNAS (NICNASa).

Toxicokinetics

Toxicokinetic studies for the three chemicals are not available. Studies are available for sodium isocyanurate (CAS No 2624-17-1), a stable degradation product of dichloroisocyanuric acid.

Sodium isocyanurate is rapidly absorbed, distributed, and excreted as shown in metabolism studies in rats, dogs and human subjects (REACH).

The elimination half-life of ^{14}C-sodium isocyanurate was 30–60 minutes in Sprague Dawley (SD) rats and 90-120 minutes in beagle dogs following 5 mg/kg body weight (bw) intravenous (i.v.) or oral administration (US EPA, 2004). The half-life, after oral dosing at 500 mg/kg bw, was 120 to 150 minutes in rats as well as dogs. At the 5 mg/kg bw dose, the chemical was completely absorbed and excreted

mainly via the urine. At the 500 mg/kg bw oral dose, the chemical was incompletely absorbed and 55-70 % (rats) or 27-86 % (dogs) was excreted in the faeces and the remainder in the urine. The chemical was excreted unchanged, suggesting negligible metabolism of cyanurate (REACH).

The elimination half-life of cyanuric acid in human swimmers soaked in a pool containing isocyanuric acid for 120 minutes or following ingestion of solution containing isocyanuric acid, was estimated as 2.2–3.5 hours. Ingested isocyanuric acid was excreted mainly via urine (REACH; US EPA, 2004).

No data are available for absorption of the chemical following inhalation exposure.

Acute Toxicity

Oral

The chemicals are classified as hazardous with the risk phrase ‘Harmful if swallowed’ (Xn; R22) in HSIS (Safe Work Australia). The available data support this classification for troclosene sodium dihydrate.

The chemicals in this group are considered to have moderate acute oral toxicity.

In a study performed according to EPA OPP 81-1 (Acute Oral Toxicity) guideline, SD rats (5/sex/dose) were treated with 1500, 2000, 2500, 3000 and 4000 mg/kg bw of troclosene sodium dihydrate (CAS No 51580-86-0) via oral gavage and observed for 14 days. The estimated median lethal dose (LD50) was 1671 mg/kg bw for the dihydrate and the estimated LD50 for the anhydride was 1436 mg/kg bw (REACH).

In addition, an LD50 of 1230 mg?/kg bw was reported for troclosene sodium dihydrate in mice (SciFinder).

Dermal

The chemicals are considered to have low acute dermal toxicity.

In a study performed according to EPA OPP 81-2 (Acute Dermal Toxicity) guideline, SD rats (5/dose/sex) were treated with 500, 1000, 2500 and 5000 mg/kg bw of troclosene sodium dihydrate (CAS No 51580-86-0) in acetone via the dermal route. No mortality was observed up to 14 days after the exposure (REACH).

Inhalation

The experimental data suggest that the chemicals could be moderately toxic via inhalation with a median lethal concentration (LC50) greater than 0.27 mg/L but less than 1.17 mg/L (REACH). Based on this, classification of the three chemicals for acute inhalation toxicity is recommended.

In a guideline study (OECD 403), SD rats (5/dose/sex) were exposed to troclosene sodium (CAS No 2893-78-9) dust (whole body) at a gravimetric concentration of 0.27 and 1.17 mg/L for 4 hours. Dust particles had a mean mass median diameter of 1.93 µm with a geometric standard deviation of 2.40 µm. The rats were observed for 14 days after exposure. The dose of 1.17 mg/L was lethal to 60 % (6/10) of exposed male and female rats while 0.27 mg/L was not lethal. This suggests that the LC50 is greater than 0.27 mg/L but less than 1.17 mg/L. The clinical signs included irregular breathing, salivation, squinting, prostration, lethargy, crusty eye, alopecia, scab, opacity of the eye, gasping and poor coat quality. Lung effects were detected at necropsy in all rats that died before scheduled termination (REACH).

Observation in humans

In humans, deaths may occur after 1-8 days following ingestion of very large quantities of the chemicals. The main toxic effects include ulceration or bleeding from stomach, gastrointestinal irritation, salivation, lacrimation, dyspnoea, weakness, emaciation, lethargy, diarrhoea and coma (TOXNET).

Corrosion / Irritation

Respiratory Irritation

The chemicals are classified as hazardous with the risk phrase ‘Irritating to respiratory system’ (Xi; R37) in HSIS (Safe Work Australia).

Data for the chemicals being assessed are not available. However, a similar chemical, isocyanuric chloride (CAS No 87-90-1), was shown to be irritating to the respiratory tract in humans (NICNASb). Isocyanuric chloride belongs to the chlorinated isocyanurates group of chemicals and is expected to behave similarly to the assessed chemicals when in contact with biological solutions.

Skin Irritation

A single dermal irritation study is available for only one of the chemicals of the group, troclosene sodium dihydrate. At high concentrations, this chemical was considered a severe skin irritant. Based on this study, classification of the three chemicals for skin irritation is recommended.

In a study performed according to the EPA OPP 81-5 (Acute Dermal Irritation) guideline, New Zealand White rabbits (3/sex) were treated with a dermal application of 0.5 grams of troclosene sodium dihydrate (CAS No 51580-86-0) to intact skin for 24 hours under semiocclusive conditions. The rabbits were observed for 21 days after exposure. Very slight to moderate erythema was observed at all sites at 30 to 60 minutes after patch removal. Erythema persisted for 96 hours at two sites. Other dermal effects included thickening, blanching, necrosis, epidermal scaling, raw areas, and the compound adhered to the skin. All effects were reversible within 21 days (REACH).

Eye Irritation

The chemicals are classified as hazardous with the risk phrase 'Irritating to eyes' (Xi; R36) in HSIS (Safe Work Australia). The available data support higher classification as these chemicals are considered to be severe ocular irritants.

In a study performed according to the EPA OPP 81-4 (Acute Eye Irritation) guideline, New Zealand White rabbits (3/sex) were treated with 0.1 g of troclosene sodium (CAS No 2893-78-9) in one eye with the other eye serving as a control. The treated eye was rinsed with distilled water within 20-30 seconds after application of the chemical. The rabbits were observed for up to 21 days following application. Severe irritation including corneal opacity, iritis and conjunctivitis was noted in all treated eyes throughout the study. Corneal superficial keratitis (pannus) was also noted in five out of six rabbits between days 7 and 21. Other symptoms included haematoma and slight green discolouration of the conjunctival tissue. Ocular irritation persisted in all animals through to study termination at day 21 (REACH).

Sensitisation

Skin Sensitisation

Chlorinated isocyanurates are not known to be dermal sensitisers (IUCLID 2000; Clayton and Clayton 1993).

In a guideline maximisation test (OECD 406), Dunkin-Hartley guinea pigs (10 males/dose) were intradermally induced at 0.1 % troclosene sodium dihydrate (CAS No 51580-86-0) in distilled water. Topical induction used 1 % troclosene sodium dihydrate in distilled water for 48 hours under occluded conditions. Three weeks after topical induction, the guinea pigs were challenged via topical application of troclosene sodium dihydrate at concentrations of 0.1 or 0.5 % in distilled water for 24 hours under occluded conditions and followed up to 48 hours after challenge. Control animals received similar treatments without the chemical. Troclosene sodium dihydrate was not sensitising to guinea pig skin in this study (REACH).

Repeated Dose Toxicity

Oral

The chemicals are not expected to cause severe effects following repeated oral exposure.

Assessed chemicals are unstable in the body (particularly in the stomach) and therefore the stable degradation product isocyanuric acid (CAS No 108-80-5) or its monosodium salt (CAS No 2624-17-1) can be used as supporting chemicals for oral toxicity (see Health Hazard Information).

In a 104-week repeated-dose toxicity study comparable to OECD TG 451, Charles River CD rats (80/sex/dose) were administered 0, 400, 1200, 2400 or 5375 ppm sodium isocyanurate (average of 25, 76, 154 or 371 mg/kg bw/day for males and 1, 42, 129, 266 and 634 mg/kg bw/day for females) in drinking water. A sodium control group (80/sex) received 7768 ppm sodium hippurate (average 60 and

99 mg/kg bw/day for males and females, respectively). The lowest observed adverse effect level (LOAEL) in rats was 5375 ppm based on reduced survival and lesions in the heart and urinary tract of males. Acute nephrosis and chronic progressive nephropathy in the kidneys and inflammation were considered related to calculi found in the kidney and bladder. It is noted that the highest dose of 5375 ppm is reported to be the limit of water solubility of sodium isocyanurate (REACH).

In a 59-day study under conditions similar to OECD TG 407, Charles River CD rats (5/sex/dose, except control 10/sex) were administered isocyanuric chloride in drinking water at 0 (control), 400, 1200, 4000 or 8000 ppm (approximately 0, 62 187, 622 or 1240 mg/kg bw/day for males and approximately 0, 68, 203, 677 or 1350 mg/kg bw/day for females). The highest dose of 8000 ppm was lethal to three males and four females and 4000 ppm was lethal to one female. Treatment-related effects included reduced body weight (significant in males only), decreased water and food consumption, laboured breathing, emaciation, accumulation of yellow material on the anogenital region and a decrease in defaecation and activity. Reduced urine volume, urine creatinine (males only) and absolute liver weights were observed in high dose group. Based on death, clinical toxicity and reduced body weight, the LOAEL was approximately 622 and 677 mg/kg bw/day for males and females, respectively (REACH; US EPA, 2015).

In a 13-week study comparable to OECD TG 408, CD rats (24-40/sex/dose) were treated with 0, 896, 1792 or 5375 ppm sodium isocyanurate (approximately 0, 101, 214 or 710 mg/kg bw/day for males and approximately 0, 130, 265 or 870 mg/kg bw/day for females) in drinking water. An additional control group received sodium hippurate (approximately 916 and 1210 mg/kg bw/day for males and females, respectively) as a sodium control. No mortality or clinical signs of toxicity were reported. There were no treatment related effects on bodyweight or food consumption, or gross pathology. In males, the relative testes and heart weights were significantly reduced at the highest dose of sodium isocyanurate. Very slight to slight hyperplasia of the urinary bladder epithelium was detected in 4/20 high-dose and 1/24 mid-dose males (REACH; US EPA, 2015).

In a 13-week study comparable to OECD TG 408, B6C3F1 mice (25/sex/dose) were treated with 0, 896, 1792 or 5375 ppm sodium isocyanurate (approximately 0, 252, 522 and 1994 mg/kg bw/day for males and 0, 298, 610 and 2201 mg/kg bw/day for females) in drinking water. Five mice from each group were sacrificed at six weeks. An additional control group received sodium hippurate (approximately 1210 and 1320 mg/kg bw/day for males and females, respectively) as a sodium control. Clinical biochemistry was not analysed and only limited microscopic examination was performed on controls and high-dose animals. One mouse died in the high-dose groups but the death was considered accidental. Increased absolute and relative ovarian weights were observed in high-dose females but also in sodium controls. Hyperplasia of the transitional bladder epithelium and congestion or haemorrhage associated with the presence of calculi in the bladder were seen in the two high-dose males. In addition, five mice at the highest dose had focal hepatic necrosis that was seen only in one control male. The no observed adverse effect level (NOAEL) was approximately 522 and 2201 mg/kg bw/day for males and females, respectively (REACH; US EPA, 2015).

Dermal

No data are available.

Inhalation

The experimental data using an analogue similar to the assessed chemicals suggest that the chemicals could be moderately toxic via inhalation although the main symptoms are consistent with an irritant effect.

In a 28-day toxicity study, CD rats (10/sex/concentration) were exposed via inhalation (whole-body) to isocyanuric chloride (CAS No 87-90-1; ACL 85 Sanitiser) dust at approximately 3, 10, 30 mg/m^3 for four weeks (six hours/day, five days/week). The dust was sieved and included only respirable particles at mass median diameter (MMD) of 2.1 to 4.5 µm. The treatment did not cause mortality. The clinical signs of toxicity at two highest concentrations included rales, nasal discharge, excessive salivation, lacrimation and laboured breathing and the treatment-related changes were observed in body weights, organ weights (unspecified) and some clinical parameters (unspecified). The lowest concentration of 3 mg/m^3 was considered to be the no observable effect concentration (NOEC) (Hammond et al., 1986; REACH).

Genotoxicity

The chemicals gave the following negative results in in vitro studies (CCRIS):

- Troclosene sodium (CAS No 2893-78-9) was tested in bacterial gene mutation assay using *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 with or without metabolic activation (liver S9) at concentrations 0.33–33 µg/plate.
- Troclosene potassium (CAS No 2244-21-5) was tested in a bacterial gene mutation assay using *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 without metabolic activation (liver S9) at concentrations 0.33–33 µg/plate and with metabolic activation at concentrations 3-1000 µg/plate.

In addition, the mutagenic potential of sodium isocyanurate (CAS No 2624-17-1), a sodium salt of a stable degradation product of the chemicals (see Health Hazard Information), has been evaluated using in vitro and in vivo tests. Sodium isocyanurate was negative in following studies (Hammond et al., 1986; REACH):

- in an in vitro bacterial gene mutation assay (OECD 471) using Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 with or without metabolic activation (liver S9) tested up to concentrations of 5000 exceeding the solubility of the chemical in the incubation medium;
- in an in vitro sister-chromatid exchange assay in Chinese hamster ovary cells at concentrations up to 1500 µg/mL;
- in an in vitro chromosomal mutation test in L5178Y mouse lymphoma cells up to a concentration of 2000 µg/mL; and
- in an in vivo chromosomal aberration test of rat bone marrow cells at 24 or 48 hours following a single oral dose of 5000 mg/kg sodium cyanurate.

Based on these tests, the chemicals are not considered to be mutagenic.

Carcinogenicity

No data exist for carcinogenicity of the assessed chemicals. However, the sodium salt of a stable degradation product of the chemicals, sodium isocyanurate (CAS No 2624-17-1) is not carcinogenic in mice or in rats.

In a 104-week repeated-dose toxicity study comparable to OECD TG 451, CD rats (80/sex/dose) were treated with 0, 400, 1200, 2400 or 5375 ppm sodium isocyanurate (average of 25, 76,154 or 371 mg/kg bw/day for males and 1, 42, 129, 266 and 634 mg/kg bw/day for females) in drinking water. A sodium control group (80/sex) received 7768 ppm sodium hippurate (average 60 and 99 mg/kg bw/day for males and females, respectively). Incidence of tumours was similar in high dose groups compared to controls and no evidence for carcinogenicity of the chemical analogue was reported following histopathological examination (US EPA, 2015).

In another 104-week repeated-dose toxicity study comparable to OECD TG 451, B6C3F1 mice (80/sex/dose) were treated with 0, 400, 1200, 2400 or 5375 ppm sodium isocyanurate (average of 25, 76,154 or 371 mg/kg bw/day for males and 1, 42, 129, 266 and 634 mg/kg bw/day for females). A sodium control group (80/sex) received 7768 ppm sodium hippurate (average 60 and 99 mg/kg bw/day for males and females, respectively). Incidence of tumours was similar in high dose groups compared to controls and no evidence for carcinogenicity of the chemical analogue was reported following histopathological examination (US EPA, 2015).

Based on these studies, the three chemicals are not considered to be carcinogenic.

Reproductive and Developmental Toxicity

No data exist for reproductive or developmental toxicity of the assessed chemicals. Therefore, data from a sodium salt of a stable degradation product of the chemicals, sodium isocyanurate (CAS No 2624-17-1) is used to estimate the reproductive or developmental toxicity. The chemicals are not expected to present reproductive or developmental hazard.

Reproductive toxicity

In a three-generation reproductive toxicity study comparable to OECD TG 416, CD rats (12 males and 24 females/dose) were treated with 0, 400, 1200 or 5375 ppm sodium isocyanurate (77.05% pure) (approximately 0, 47, 130 or 614 mg/kg bw/day for males and 0, 62, 196 or 730 mg/kg bw/day for females) in drinking water for 100 days or more pre-mating. An additional group

of 12 males and 24 females was treated with sodium hippurate at approximately 946 or 1366 mg/kg bw/day, respectively, as sodium controls. A minimum of 14 days after weaning of the first litters of the first generation (F1a), parent females were mated again (to different males) to produce second litters of first generation (F1b). The F1b males and females were randomly selected to become parents for the next generation. After a minimum of 120 days of sodium isocyanurate treatment, the F1b parents were mated twice to produce first (F2a) and second (F2b) litters of the second generation. The F2b litters were mated once to produce the third generation litters. There were no treatment-related, consistent effects on fertility, gestation length, litter size, pup survival and pup weights in any generation of rats (US EPA, 2004).

Developmental toxicity

In a prenatal, developmental toxicity study comparable to OECD TG 414, Charles River CD rats (25/dose) were treated with 0, 200, 1000 or 5000 mg/kg bw/day of sodium isocyanurate in 4 % aqueous carboxymethyl cellulose via oral gavage on gestation days (GD) 6–15. Dams were sacrificed on GD20. Additional sodium control groups received 1118 and 5590 mg/kg bw/day of sodium hippurate. The high sodium control dose was lethal to 11/25 females during gestation. No mortality was seen in any other groups. No treatment-related maternal (clinical signs and body weight) or reproductive (number resorptions, implantations, corpora lutea or the duration of pregnancy) toxicity was reported. There were no treatment-related effects on mean foetal body weights, number of viable foetuses, litter size or foetal sex ratio, or foetal crown rump length in the sodium isocyanurate groups. There were no treatment-related effects on total number of litters with malformed foetuses in the sodium isocyanurate group (US EPA, 2004).

In another prenatal, developmental toxicity study comparable to OECD TG 414, pregnant New Zealand White rabbits (20/dose) were treated with 0, 50, 200 or 500 mg/kg bw/day of sodium isocyanurate in 1 % aqueous carboxymethyl cellulose via oral gavage on GDs 6–18. On GD 29, surviving dams were necropsied and foetuses analysed for developmental toxicity. One high-dose and two low-dose females aborted during the study. No treatment-related clinical signs of toxicity or gross abnormalities were detected in dams. There were no treatment-related effects on reproductive parameters including gravid uterus weight, duration of pregnancy or the mean number of corpora lutea. An increase in post-implantation loss was seen at the high dose, but the loss was within the historical control data. There were total of 3, 9, 2 and 16 late resorptions in the control, low-, mid- and high-dose groups, respectively. There were no significant treatment-related effects on foetal body weight or in foetal malformation data. However, increase in incidence of hydrocephaly was suggested, as hydrocephaly was detected in three foetuses (one litter), two foetuses (two litters) and nine foetuses (two litters) following exposure to 0, 200 or 500 mg sodium isocyanurate/kg bw/day, respectively. Therefore the NOAEL for developmental toxicity was considered as 200 mg sodium isocyanurate/kg bw/day (US EPA, 2004).

Risk Characterisation

Critical Health Effects

Critical health effects include acute oral toxicity as well as irritation of skin, eyes and respiratory system.

Public Risk Characterisation

In Australia, the chemicals are known to be used as disinfectants in cleaning products and dishwashing compounds. Therefore, public exposure is expected during handling and use of the chemicals.

This chemicals are listed in the Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) in Schedules 5 and 6, under 'Chlorinating compounds' (SUSMP, 2015).

Therefore, it is concluded that if these regulations are followed, the public health risk is not expected to be high.

Occupational Risk Characterisation

Given the critical acute and local health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise oral, dermal, ocular and inhalation exposure are implemented. The chemicals should be

appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

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

NICNAS Recommendation

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

Regulatory Control

Public Health

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

Work Health and Safety

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

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)* Contact with acids liberates toxic gas (R31)* Harmful by inhalation (Xn; R20)	Harmful if swallowed - Cat. 4 (H302) Contact with acid liberates toxic gas (AUH031) Harmful if inhaled - Cat. 4 (H332)
Irritation / Corrosivity	Risk of serious eye damage (Xi; R41) Irritating to skin (Xi; R38) Irritating to respiratory system (Xi; R37)*	Causes serious eye damage - Cat. 1 (H318) Causes skin irritation - Cat. 2 (H315) May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335)

[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 that 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 chemicals, if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- 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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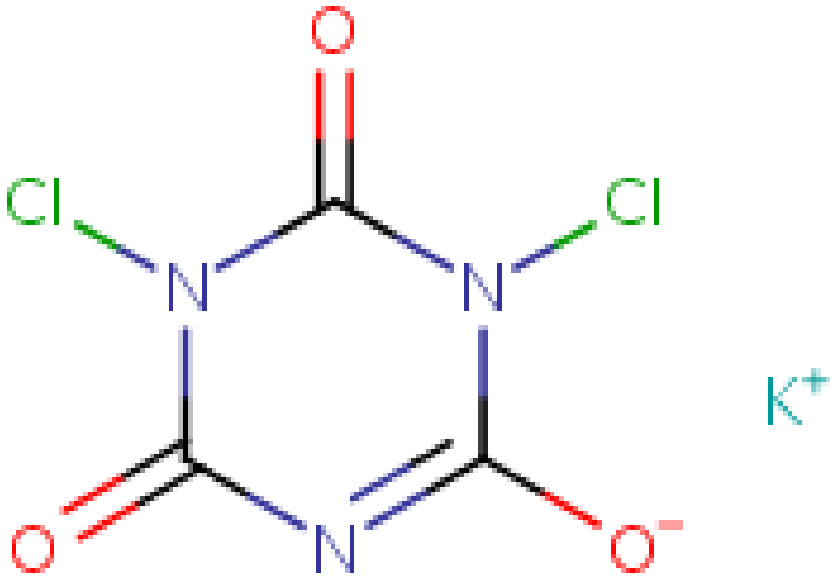
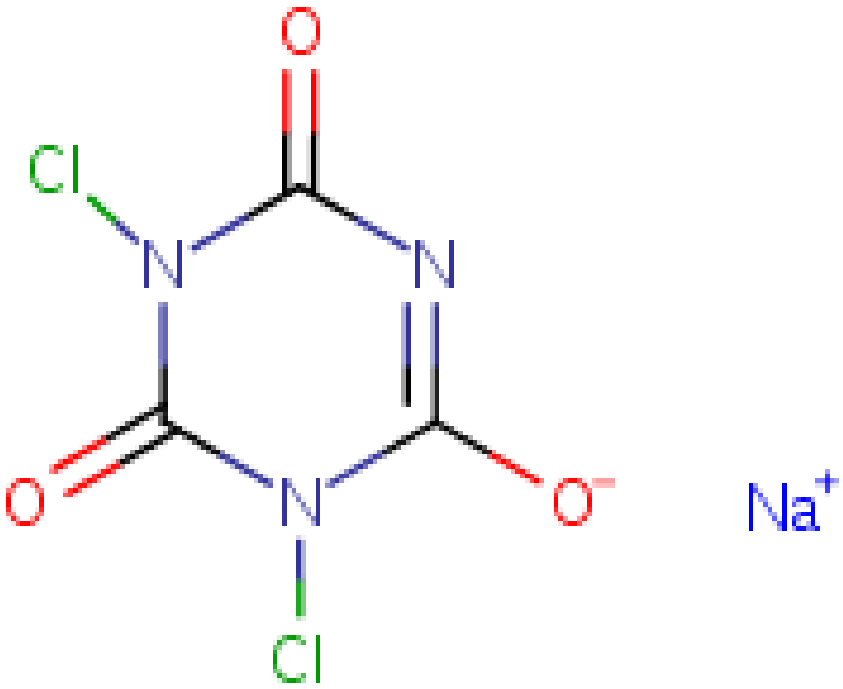
Last Update 05 February 2016

Chemical Identities

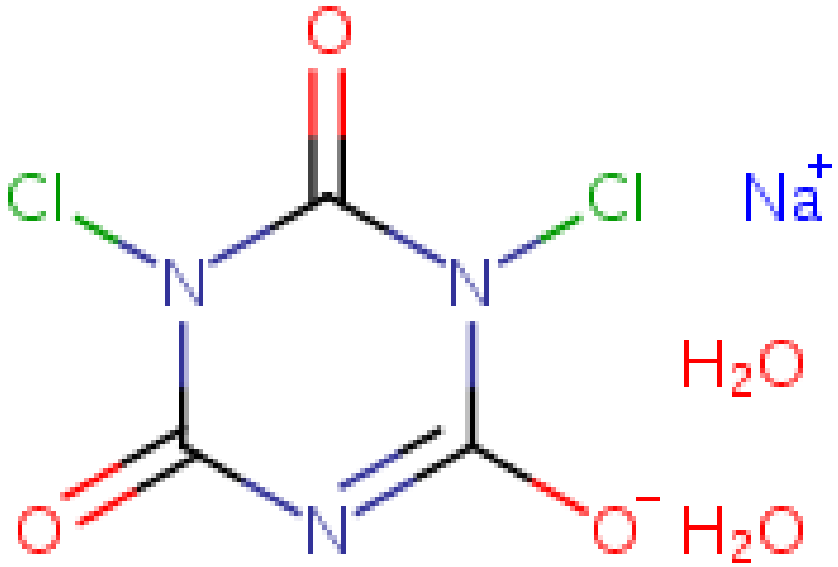
Chemical Name in the Inventory and Synonyms	**1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3-dichloro-, potassium salt** potassium dichloroisocyanurate potassium dichloro-s-triazinetrione troclosene potassium
CAS Number	2244-21-5

Structural Formula	
Molecular Formula	C3HCl2N3O3.K
Molecular Weight	236.055

Chemical Name in the Inventory and Synonyms	**1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3-dichloro-, sodium salt** sodium dichloroisocyanurate troclosene sodium sodium dichloro-s-triazinetrione
CAS Number	2893-78-9
Structural Formula	

	
Molecular Formula	C3HCl2N3O3.Na
Molecular Weight	219.947

Chemical Name in the Inventory and Synonyms	**1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3-dichloro-, sodium salt, dihydrate** sodium dichloroisocyanurate dihydrate troclosene sodium dihydrate sodium dichloro-s-triazinetrione dihydrate
CAS Number	51580-86-0
Structural Formula	

	
Molecular Formula	C3HCl2N3O3.2H2O.Na
Molecular Weight	255.9766

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