Chromates and dichromates (soluble): Human health tier II assessment

04 July 2014

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Chromic acid (H2CrO4), diammonium salt	7788-98-9
Chromic acid (H2CrO4), dipotassium salt	7789-00-6
Chromic acid (H2CrO4), disodium salt	7775-11-3
Chromic acid (H2Cr2O7), dipotassium salt	7778-50-9
Chromic acid (H2Cr2O7), diammonium salt	7789-09-5
Chromic acid (H2Cr2O7), disodium salt, dihydrate	7789-12-0
Chromic acid (H2CrO4), disodium salt, tetrahydrate	10034-82-9
Chromic acid (H2Cr2O7), disodium salt	10588-01-9
Chromic acid (H2CrO4), magnesium salt (1:1)	13423-61-5
Chromic acid (H2CrO4), dilithium salt	14307-35-8

Chemical Name in the Inventory	CAS Number
Chromic acid (H2CrO4), chromium(3+) salt (3:2)	24613-89-6

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**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

This group consists of water-soluble chromium compounds that contain chromium in the hexavalent or +6 oxidation state. Compounds covered by this document are likely to behave in a similar manner in respect of toxicokinetics. The toxicity of chromium compounds

depends principally on valency, as well as the physical/chemical properties of the specific compounds, with hexavalent chromium being generally more toxic than trivalent (III) chromium. For this group, the toxicity is considered to be as a result of the chromium component, while the cation components are not considered to contribute significantly to toxicity. The chemicals in this group will all readily dissolve in aqueous environments in the body to release chromate (CrO_4^{2-}) or dichromate ($Cr_2O_7^{2-}$) ions. These two ions co-exist in equilibrium, regardless of the particular chromium compound involved. The chromate/dichromate ions produced from all the compounds will behave similarly in biological tissues and hence the potential toxicity will be similar.

Import, Manufacture and Use

Australian

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

The chemical chromic acid ($H_2Cr_2O_7$) disodium salt (CAS No. 10588-01-9) has reported excluded use in timber preservation.

No specific Australian use, import, or manufacturing information has been identified for other chemicals in this group.

International

The following international uses have been identified through the European Union Registration, Evaluation and Authorisation of Chemicals (EU REACH) dossiers, the Organisation for Economic Cooperation and Development Screening Information Dataset Initial Assessment Report (OECD SIAR), Galleria Chemica and Substances in Preparations in Nordic Countries (SPIN) database:

The majority of the chemicals of this group have the following reported domestic uses including:

- as corrosion inhibitors; and
- as a surface treatment.

Some of the chemicals of this group have the following reported potential domestic uses including:

- as colouring agents;
- in paints, lacquers and varnishes; and
- in cleaning/washing agents.

Some of the chemicals in this group have the following reported commercial uses, including as:

- lubricants and additives;
- absorbents and adsorbents;
- impregnation materials;
- electroplating agents; and
- photographic chemicals.

Some chemicals of the group have the following reported site-limited uses including:

- as laboratory chemicals.

The chemical chromic acid ($H_2Cr_2O_7$) disodium salt (CAS No. 10588-01-9) has reported non-industrial use in timber preservation.

Restrictions

Australian

The chemicals in this group are listed in the Poisons Standard (Standard for the Uniform Scheduling of Medicines and Poisons—SUSMP, 2012) in:

Schedule 6

As 'chromates (including dichromates) **except** in paints or tinters containing 5 per cent or less of chromium as the ammonium, barium, potassium, sodium, strontium or zinc chromate calculated on the non-volatile content of the paint or tinter'.

Schedule 6 includes substances with a moderate potential for causing harm, the extent of which can be reduced by using distinctive packaging with strong warnings and safety directions on the label.

The chemicals in this group are also subject to exemptions or additional restrictions as described in the Appendices of the above Standard (SUSMP, 2012):

Appendix I

As 'chromium—as chromates of ammonia, barium, potassium, sodium, strontium or zinc—more than 5 per cent'.

The chemicals are also listed under **Appendix E** (first aid instructions for poisons) and **Appendix F** (warning statements and general safety directions for poisons).

International

The chemicals in this group appear internationally in the following:

- Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient "Hotlist").
- The EU Cosmetic Directive 76/768/EEC Annex II: List of substances which must not form part of the composition of cosmetic products.
- The New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain.

Existing Worker Health and Safety Controls

Hazard Classification

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

CAS No.: **7789-00-6:**

Carc. Cat. 2; R49, Muta. Cat. 2; R46, Xi; R36/37/38, R43.

CAS No.: **24613-89-6:**

Carc. Cat. 2; R45, C; R35, R43.

CAS Nos: **7775-11-3, 7789-09-5, 7778-50-9, 10588-01-9:**

Carc. Cat. 2; R45, Muta. Cat. 2; R46, Repr. Cat.2; R60-61, T+; R26, T; R25-48/23, Xn; R21, C; R34, R42/43.

No specific classifications are available for the remaining chemicals of the group (CAS Nos: 7788-98-9, 7789-12-0, 10034-82-9).

Exposure Standards

Australian

The chromium (VI) compounds have the following exposure standard in the Hazardous Substances Information System (HSIS) (Safe Work Australia). These exposure standards apply to all the compounds in this assessment:

- Time weighted average (TWA): 0.05 mg/m³ for chromium (VI) compounds (as Cr), water soluble compounds.
- Short-term exposure limits (STEL): No specific exposure standards are available.

International

The following exposure standards are identified (Galleria Chemica):

CAS Nos: **7788-98-9, 7775-11-3, 7789-09-5, 7789-12-0, 10034-82-9, 10588-01-9, 24613-89-6:**

- TWA = 0.005−2.0 mg/m³ [Denmark, Sweden, USA, Estonia];
- STEL = 0.015−0.3 mg/m³ [Sweden, Poland]; and
- Ceiling limit = 0.1 mg/m³ [USA].

CAS Nos: **7789-00-6, 7778-50-9:**

- TWA = 0.005−0.5 mg/m³ [Denmark, Sweden, USA, Egypt, Greece, USA]
- STEL = 0.015−0.3 mg/m³ [Sweden, Poland]; and
- Ceiling limit = 0.1 mg/m³ [USA].

Health Hazard Information

Toxicity of the Cr (VI) compounds depends on solubility. Highly water soluble Cr (VI) compounds are very toxic by ingestion, and exposure via the dermal and inhalation routes. In this group of chemicals, the main concern regarding effects on human health is expected to be driven by the chromium (VI) component of the compound. The cation component is not expected to contribute to the toxicity of the compound.

Toxicokinetics

The soluble hexavalent chromium compounds have similar absorption, distribution, and excretion patterns (EC, 2005).

The extent of absorption of the ingested hexavalent chromium [Cr (VI)] compounds from the gastrointestinal (GI) tract is determined by its solubility and how rapidly it is reduced to trivalent chromium [Cr (III)]. While the Cr (III) does not readily diffuse across cell membranes, Cr (VI) does, due to its ability to use existing sulphate and phosphate anion transport mechanisms. Once formed, Cr (III) is stable, as the conversion back to the hexavalent state is not a favourable reaction due to the high energy required (EC, 2005).

Following inhalation exposure, animal studies have shown that 20–30 % of the administered Cr (VI) is absorbed via the respiratory tract. Highly water-soluble Cr (VI) is poorly absorbed via the gastrointestinal tract (only 2–9 % of the dose was absorbed in human studies) due to reduction to the relatively poorly absorbed Cr (III). Only limited dermal absorption takes place through intact skin, with 1–4 % Cr (VI) from an aqueous solution crossing the skin in guinea pig studies. According to the results of animal testing, chromium derived from these compounds can remain in the lungs for several weeks after inhalation exposure (EC, 2005).

Generally, absorbed Cr (VI) is distributed throughout the body, but the blood, liver, kidney, and spleen are the primary sites of distribution, in addition to local deposition either in the respiratory or the GI tract. Bone is also a site of distribution, and this may contribute to the long-term retention kinetics of chromium. Absorbed chromium can be transferred to foetuses through the placenta and to infants via breast milk. Hexavalent chromium penetrates red blood cells, where it is reduced by glutathione to trivalent chromium, which binds to haemoglobin and tends to stay for the lifespan of the cells. Chromium interacts with iron by affecting its binding to transferrin, and has been shown to impair iron metabolism and storage (EC, 2005).

Absorbed chromium is mainly excreted via urine, with only small amounts being eliminated in perspiration and bile. Inhaled or intratracheal instilled Cr (VI) is excreted in urine and faeces in similar amounts (in the range 20–70 % of the administered dose). When orally administered, most appears in faeces, due to poor gastrointestinal tract absorption. Chromium in urine and faeces is in the form of Cr (III) complexes, with glutathione for example. Chromium can also be eliminated in hair, nails, and breast milk (EC, 2005).

Acute Toxicity

Oral

The following chemicals in this group are currently classified as hazardous with the risk phrase ‘Toxic if swallowed’ (T; R25) in HSIS (Safe Work Australia): potassium dichromate (CAS No. 7778-50-9), sodium chromate (CAS No. 7775-11-3), sodium dichromate (CAS No. 10588-01-9) and ammonium dichromate (CAS No. 7789-09-5). Based on the information available, this hazard classification is supported for all the chemicals in this group.

Available oral LD50 values in rats exposed to chromium (VI) compounds varied with the compound and the sex of the rat. LD50 values for the soluble chromium (VI) compounds (sodium chromate, sodium dichromate, potassium dichromate, and ammonium dichromate) ranged from 13 to 19 mg Cr (VI)/kg in female rats and from 21 to 28 mg Cr (VI)/kg in male rats. Toxic effects included hypoactivity, lacrimation, mydriasis, diarrhoea, change in body weight, pulmonary congestion and corrosion of mucosa in the gastrointestinal tract (EC, 2005).

Dermal

The following chemicals in this group are currently classified as hazardous with the risk phrase ‘Harmful in contact with skin’ (Xn; R21) in HSIS (Safe Work Australia): potassium dichromate (CAS No. 7778-50-9), sodium chromate (CAS No. 7775-11-3), sodium dichromate (CAS No. 10588-01-9), ammonium dichromate (CAS No. 7789-09-5).

Based on the information available, this hazard classification is supported for all the chemicals in this group.

Dermal LD50 values in New Zealand rabbits exposed to the soluble chromium (VI) as sodium chromate, sodium dichromate, potassium dichromate, and ammonium dichromate ranged from 960 to 1330 mg/kg bw/day. Signs of toxicity included dermal necrosis, eschar formation, dermal oedema and erythema, and diarrhoea and hypoactivity (EC, 2005).

Although acutely harmful or toxic by the dermal route, more severe responses may be observed if there is any prior or simultaneous damage to the skin (due to greater uptake via the skin). Depending upon the pH of the Cr (VI) solution, corrosive effects can occur on contact (EC, 2005).

Inhalation

The following chemicals in this group are currently classified as hazardous with the risk phrase ‘Very toxic by inhalation’ (T+; R26) in HSIS (Safe Work Australia): potassium dichromate (CAS No. 7778-50-9), sodium chromate (CAS No. 7775-11-3), sodium dichromate (CAS No. 10588-01-9) and ammonium dichromate (CAS No. 7789-09-5).

Based on the information available, this hazard classification is supported for all the chemicals in this group.

Acute inhalation LC50 values in rats for several soluble chromium (VI) compounds (sodium chromate, sodium dichromate, potassium dichromate, and ammonium dichromate) ranged from 99 to 200 mg/m^3 with a 4-hour aerosol exposure period (equivalent to 0.09 to 0.2

mg/L). Signs of toxicity included reduced body weight, respiratory distress and irritation of the respiratory tract, lung oedema, inflammation and tracheal epithelium necrosis (EC, 2005).

Observation in humans

Accidental or intentional ingestion of generally unknown, but probably extremely high doses of chromium (VI) compounds by humans has resulted in severe respiratory, cardiovascular, gastrointestinal, haematological, hepatic, renal, and neurological effects. After dermal application of potassium chromate as treatment of scabies, renal failure, fatty degeneration of the heart, hyperaemia and necrosis of kidney tubules, and hyperaemia of the gastric mucosa have been described (ATSDR, 2012).

Corrosion / Irritation

Corrosivity

The following chemicals in this group are currently classified as hazardous with the risk phrase ‘Causes burns’ (R34) in HSIS (Safe Work Australia): potassium dichromate (CAS No. 7778-50-9), sodium chromate (CAS No. 7775-11-3), sodium dichromate (CAS No. 10588-01-9), ammonium dichromate (CAS No. 7789-09-5) and dichromium tris(chromate) (CAS No. 24613-89-6). Based on the information available, this hazard classification is supported for all the chemicals in this group.

Corrosive effects with the soluble Cr (VI) chemicals strongly depend upon the concentration and the pH of the solution. Concentration-dependent erythema was observed in guinea pigs when repeated applications were made daily for four days on non-abraded skin using potassium dichromate solution. A more severe response was observed in skin traumatised by wax depilation or non-scarring abrasion, where chrome ulcers with thick eschar and underlying tissue necrosis were observed (REACH; IPCS, 1988). Similar results have been shown in rabbits where dermal application of chromium (VI) compounds to the clipped, non-abraded skin of rabbits (at 42 –55 mg/kg bw/day) resulted in skin inflammation, oedema, and necrosis (ATSDR, 2012).

Repeated intratracheal instillation of sodium dichromate resulted in lung inflammation, fibrosis and emphysema (EC, 2005).

In workers regularly exposed to Cr (VI) in solution, chrome ulcers developed after some initial damage to the skin. This has been described for dye workers handling sodium or potassium dichromate solutions, and frequently in exposed workers in the chromate production and chrome plating industries. The severity of the ulcer depends upon the frequency and duration of skin contamination and the condition of the skin and the pH of the solution (EC, 2005). Favoured sites for ulcer development are the nail root areas, the creases over the knuckles, finger webs, the backs of the hands, and the forearms. Ordinarily, a chrome sore, if not deep, persists for about three weeks after exposure is discontinued (IPCS, 1988). Exposure of the skin to airborne fumes and mists of chromium(VI) compounds may also contribute to the development of chrome sores apart from direct dermal contact (ATSDR, 2012).

Respiratory Irritation

It is recommended that the R37 classification be removed as the chemicals in this group are recommended for classification with the risk phrase 'Causes burns' (R34). When a substance is classified with R34, the risk of damage by irritation is implicit and they are considered as if R36/37/38 has been assigned.

Skin Irritation

Potassium chromate (CAS No. 7789-00-6) is currently classified as hazardous with the risk phrase ‘Irritating to eyes, respiratory system and skin’ (R36/37/38) in HSIS (Safe Work Australia). It is recommended that this classification be removed as the chemicals in this group are recommended for classification with the risk phrase 'Causes burns' (R34). When a substance is classified with R34, the risk of damage by irritation is implicit and they are considered as if R36/37/38 has been assigned.

Dermal effects observed in animals after direct application of potassium dichromate to their skin include inflammation, necrosis, corrosion, eschar formation, and oedema in rabbits and skin ulcers in guinea pigs (ATSDR, 2012).

Eye Irritation

It is recommended that the R36 classification be removed as the chemicals in this group are recommended for classification with the risk phrase 'Causes burns' (R34). When a substance is classified with R34, the risk of damage by irritation is implicit and they are considered as if R36/37/38 has been assigned.

Sensitisation

Respiratory Sensitisation

The following chemicals in this group are currently classified as hazardous with the risk phrase ‘May cause sensitisation by inhalation’ (R42) in HSIS (Safe Work Australia): potassium dichromate (CAS No. 7778-50-9), sodium chromate (CAS No. 7775-11-3), sodium dichromate (CAS No. 10588-01-9), ammonium dichromate (CAS No. 7789-09-5).

Based on the information available, this hazard classification is supported for all the chemicals in this group.

Sensitisation of workers, resulting in respiratory and dermal effects, has been reported in numerous occupational exposure studies (EC, 2005). The exposure route for the initial sensitisation in an occupational setting is most likely a combination of inhalation, oral and dermal exposures (ATSDR, 2012).

Symptoms of asthma and signs of respiratory distress consistent with a type I allergic response (decreased forced expiratory volume, facial erythema, nasopharyngeal pruritus, blocked nasal passages, cough, and wheeze) are produced in individuals previously sensitised to chromium compounds (ATSDR, 2012).

Chromium-sensitive patients, when challenged with chromium compounds via a nebuliser, displayed anaphylactoid reactions characterised by dermatitis, facial angioedema and erythema, nasopharyngeal pruritus, cough, wheezing, bronchospasms, increased plasma histamine levels, urticaria, and decreased forced expiratory volume (ATSDR, 2012).

Skin Sensitisation

The following chemicals in this group are currently classified as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (R43) in HSIS (Safe Work Australia): potassium chromate (CAS No. 7789-00-6), potassium dichromate (CAS No. 7778-50-9), sodium chromate (CAS No. 7775-11-3), sodium dichromate (CAS No. 10588-01-9), ammonium dichromate (CAS No. 7789-09-5) and dichromium tris(chromate) (CAS No. 24613-89-6).

Based on the information available, this hazard classification is supported for all the chemicals in this group.

In animals, soluble Cr (VI) chemicals produced positive skin sensitisation response in guinea pig maximisation studies and a mouse ear swelling test (EC, 2005).

In humans working with the chemicals, skin sensitisation resulting from contact with Cr (VI) is relatively common (EC, 2005). Sensitisation may occur from inhalation, oral, and/or dermal exposure. The acute response phase lasts for a few days to a few weeks and is characterised by erythema, oedema, and small and large blisters. The chronic phase exhibits similar clinical features, but may also include thickened, scaly, and fissured skin (ATSDR, 2012).

Several studies have estimated that the exposure levels of 4–25 ppm are required to elicit a dermal response in chromium-sensitised individuals (ATSDR, 2012). It has also been reported that at concentrations of 0.5 % and below, potassium dichromate elicited a response in patch testing studies. In one study a minimum (10 % reacting) elicitation concentration of 0.09 µg Cr (VI)/cm^2 was calculated after Cr (VI)-sensitive volunteers were exposed to potassium dichromate (EC, 2005).

However, it is anticipated that the exposure level required to elicit a dermal response in sensitised individuals will be highly variable due to individual sensitivity and, therefore, it is not possible to reliably determine a threshold for either induction or elicitation in an exposed population using the available data.

The mechanism involved in the sensitisation indicates that Cr (III) could be the ultimate hapten. Skin contact with Cr (VI) leads to penetration of Cr (VI) into the skin where it is reduced to Cr (III). There is some evidence for cross-reactivity between Cr (III) and Cr (VI), i.e., Cr (VI)-sensitised subjects may also react to Cr (III) (EC, 2005).

Repeated Dose Toxicity

Oral

The chemicals in this group are not currently classified as hazardous in HSIS (Safe Work Australia). Based on the information available, no hazard classification is recommended for the chemicals in this group.

In the rat, testicular degeneration was observed (at 40 mg/kg bw/day—14 mg Cr (VI)/kg bw/day), which caused a large decrease in body weight gain following gavage administration of the chemical for 90 days. A NOAEL of 20 mg/kg bw/day (7 mg/kg bw/day Cr (VI)) was determined for effects on the testis, the only organ examined (EC, 2005).

In a two-year study, F344/N rats exposed to the chemical in drinking water (up to 516 mg/L, equivalent to 5.95 mg/kg bw/day Cr (VI) for males and 7.0 mg/kg bw/day Cr (VI) for females) showed no effect on survival (NTP, 2008).

In a two-year study, B6C3F1 mice exposed to the chemical (up to 516 mg/L, equivalent to 5.95 mg/kg bw/day Cr (VI) for males and 7.0 mg/kg bw/day Cr (VI) for females) in drinking water showed increased epithelial hyperplasia in the duodenum at all doses in both sexes of mice. Mice also displayed histiocytic infiltration of the duodenum at the two highest doses in both sexes; in the jejunum of females at the highest dose; in the liver at 0.39 mg Cr (VI)kg/day in females; of the mesenteric lymph nodes in both sexes at all doses; and of the pancreatic lymph nodes at the two highest doses in male and female mice (NTP, 2008).

Dermal

No repeated dermal studies are available, although these substances are recognised as being corrosive on repeated dermal exposure.

Inhalation

The following chemicals in this group are currently classified as hazardous with the risk phrase ‘Toxic: danger of serious damage to health by prolonged exposure through inhalation' (R48/23) in HSIS (Safe Work Australia): potassium dichromate (CAS No. 7778-50-9), sodium chromate (CAS No. 7775-11-3), sodium dichromate (CAS No. 10588-01-9), and ammonium dichromate (CAS No. 7789-09-5).

Based on the information available, this hazard classification is supported for all the chemicals in this group.

Inhaling the chemical as dust for eight months caused reduction in bodyweight gain, and deaths in mice exposed to 0.3–3.7 mg/m^3 (0.1 –1.2 mg Cr (VI)/m^3). Rats appeared to be less sensitive (no deaths after 16 months at the same concentrations (EC, 2005).

Inhaling the chemical as an aerosol (0.06 mg/m^3—0.025 mg Cr(VI)/m^3) for 90 days in rats produced increased alveolar macrophage and spleen lymphocyte activities. At a higher dose of 0.57 mg/m^3 (0.2 mg Cr(VI)/m^3) much of this enhancement was lost. It was not possible to determine the NOAEL from the repeated exposure inhalation studies (EC, 2005).

Repeated intratracheal instillation of the chemical resulted in lung inflammation, fibrosis and emphysema (EC, 2005).

Observation in humans

Workers exposed to dissolved chromium (VI) aerosols and chromium trioxide mists (mean exposure duration of 2.5 years), reported effects on the respiratory, renal, and gastrointestinal systems.

Respiratory effects included bleeding from the nasal septum, nasal mucosal atrophy, nasal septal ulceration and perforation, epistaxis, rhinorrhoea, and decreased lung function, with LOAEL values ranging from 0.002 to 0.414 mg chromium (VI)/m^3.

Effects indicative of renal toxicity included increased retinol binding protein and tubular antigen, and increased urinary β-2μ-globulin. LOAEL values for these effects range from 0.004 to 0.05 mg chromium (VI)/m^3.

Gastrointestinal effects reported in workers included stomach pains, cramps, and ulcers, with a LOAEL value of 0.004 mg chromium (VI)/m^3.

Based on a comparison of LOAEL values for respiratory, renal and gastrointestinal effects in workers, the respiratory tract was identified as the most sensitive target of chronic-duration inhalation exposure to dissolved chromium (VI) aerosols and mists (ATSDR, 2012).

Genotoxicity

The following chemicals in this group are currently classified as hazardous as a Category 2 mutagen with the risk phrase ‘May cause heritable genetic damage' (R46) in HSIS (Safe Work Australia): potassium chromate (CAS No. 7789-00-6), potassium dichromate (CAS No. 7778-50-9), sodium chromate (CAS No. 7775-11-3), sodium dichromate (CAS No. 10588-01-9), and ammonium dichromate (CAS No. 7789-09-5).

Based on the information available (in vivo somatic and germ cell mutagenicity), this hazard classification is supported for all the chemicals in this group.

Hexavalent chromium (VI) compounds are mutagenic as shown in gene mutation assays (including reverse mutations, frame shift mutations, and base pair substitutions), and DNA damage (including DNA interstrand crosslinks, DNA strand breaks and DNA-protein crosslinks), in bacterial cells (such as *Salmonella typhimurium*, *Escherichia coli* and *Bacillus subtilis*) (ATSDR, 2012).

Chromium (VI) compounds also showed positive results in forward mutations and mitotic gene conversion in yeast (*Saccharomyces cerevisiae*), DNA damage (such as DNA strand breaks, fragmentation, DNA-protein crosslinks and DNA-DNA crosslinks), chromosomal damage (including sister chromatid exchanges and chromosomal aberrations), and DNA synthesis inhibition in mammalian cell lines and primary cultures (including primary cultures of human gastric mucosal cells, respiratory tract cells and lymphocytes) (ATSDR, 2012).

In in vivo studies, hexavalent chromium (VI) compounds also tested positive for mutations in *Drosophila melanogaster* and for DNA damage (such as DNA-protein crosslinks and DNA strand breaks), mutations (in mice exposed in utero, in mouse germ cells, and in transgenic mice), chromosomal damage (sister chromatid exchanges, chromosomal aberrations, and micronuclei), and DNA synthesis inhibition in rats and mice (IARC, 1990 and 2012).

Results of an occupational exposure study in humans showed that lymphocytes of workers exposed to dusts of chromium (VI) compounds showed elevated frequencies of DNA strand breaks, sister chromatid exchange, and micronuclei (ATSDR, 2012). Findings from occupational exposure studies are supported by the above mentioned in vivo studies in animals, in vitro studies in mammalian cells, yeast and bacteria, and studies in cell-free systems.

Carcinogenicity

The following chemicals in this group are currently classified hazardous as a Category 2 carcinogen with the risk phrase ‘May cause cancer' (T; R45) in HSIS (Safe Work Australia): potassium dichromate (CAS No. 7778-50-9), sodium chromate (CAS No. 7775-11-3), sodium dichromate (CAS No. 10588-01-9), ammonium dichromate (CAS No. 7789-09-5) and dichromium tris(chromate) (CAS No. 24613-89-6).

The following chemical in this group is currently classified hazardous as a Category 2 carcinogen with the risk phrase ‘May cause cancer by inhalation' (T; R49) in HSIS (Safe Work Australia): potassium chromate (Cas No. 7789-00-6).

The data available support an amendment to the classification (refer to the Recommendation section below).

Based on the information available (epidemiological and animal data on carcinogenicity by inhalation, and also some animal data on oral tumour induction), all the chemicals in this group should be classified as a Category 1 carcinogens (based on sufficient evidence in humans and experimental animals) with the risk phrase ‘May cause cancer' (T; R45) in HSIS (Safe Work Australia).

Chronic inhalation studies provide evidence that soluble chromium (VI) compounds are carcinogenic in animals. The chemical produced lung tumours in rats when administered by continuous inhalation of aqueous aerosol or long-term repeated intratracheal instillation in saline (EC, 2005). Also, there was a single incidence of a squamous cell carcinoma of the pharynx in a rat after inhaling the chemical as an aerosol (EC, 2005). Mice exposed to 4.3 mg chromium (VI)/m^3 had a 2.8-fold greater incidence of lung tumours, compared with controls (ATSDR, 2012).

In addition, numerous animal studies (rats and mice) using the intratracheal, intrapleural, and intrabronchial routes of exposure show that soluble chromium (VI) compounds produce respiratory tract tumours (EC, 2005). Local tumours in rats exposed by intrapleural or intramuscular administration has also been documented (IARC, 1990).

Chronic exposure to the chromium (VI) compounds in drinking water resulted in a dose-dependent increase in the incidence of neoplasms of the digestive tract in B6C3F1 mice (increased incidences of neoplasms of the duodenum, jejunum, or ileum in males at 7 mg/kg bw/day and females at 9 mg/kg bw/day), and F344/N rats (increased incidences of squamous cell neoplasms of the oral cavity increased in males at 17 mg/kg bw/day and at females at 20 mg/kg bw/day) (NTP, 2008).

Data for dermal route carcinogenicity studies on the chemicals are not available.

Occupational exposure to chromium (VI) compounds (based on retrospective studies) in various industries such as those involved in chromate production, chromate pigment production and use, chrome plating, stainless steel welding, and ferrochromium alloy production, have been associated with increased risk of respiratory system cancers, primarily bronchogenic and nasal (ATSDR, 2012). One study also found significantly higher stomach cancer death rates in areas where well-water chromium levels had been elevated (ATSDR, 2012).

The International Agency for Research on Cancer (IARC) classified chromium (VI) as known to be a human carcinogen (Group 1) based on sufficient evidence of carcinogenicity from studies in humans and experimental animals (IARC, 2012).

Reproductive and Developmental Toxicity

The following chemicals in this group are currently classified as hazardous as a Category 2 reproductive toxin with the risk phrases ‘May impair fertility’ (R60) and ‘May cause harm to the unborn child’ (R61) in HSIS (Safe Work Australia): potassium dichromate (CAS No. 7778-50-9), sodium chromate (CAS No. 7775-11-3), sodium dichromate (CAS No. 10588-01-9) and ammonium dichromate (CAS No. 7789-09-5).

Based on the information available, this hazard classification is supported for all the chemicals in this group.

A number of studies have reported reproductive effects in rats and mice orally exposed to the chemical (63–333 mg/kg bw/day) in the drinking water. The chemical resulted in increased pre-implantation and post-implantation losses, resorptions, stillbirths and decreased numbers of corpora lutea and numbers of foetuses, both live and dead (NTP, 2008).

Following a 6-day gavage administration of the chemical (0, 10 and 20 mg/kg bw/day) to Wistar rats, decreased sperm count, increased percentage of abnormal sperm, and morphological changes to seminiferous tubules (decreased diameter of seminiferous tubules and germ cell rearrangement) were observed at six weeks after completion of the treatment. A NOAEL was not determined in this study as effects were seen at all doses (Li et al., 2001).

In the rat, testicular degeneration was observed at a dose level (40 mg/kg bw/day) that caused a large decrease in body weight gain following gavage administration of the chemical for 90 days. A NOAEL of 20 mg/kg bw/day was determined for effects on the testes (EC, 2005). Other studies found no effects on the testes, following administration of potassium dichromate in the diet for nine weeks. The highest dose levels in these studies were 24 mg/kg bw/day in the rat and 92 mg/kg bw/day in the mouse (EC, 2005).

The male reproductive system was identified as a target for oral chromium(VI) exposure in intermediate-duration studies in monkeys and rabbits. Decreased sperm count and motility, and histopathological changes to the epididymis (ductal obstruction, development of micro canals, depletion of germ cells, hyperplasia of Leydig cells, and Sertoli cell fibrosis) have been reported in monkeys exposed to 2.1 mg chromium (VI)/kg bw/day as potassium dichromate in drinking water for 180 days (ATSDR, 2012).

In addition to the studies reported above, the chemical is a developmental toxicant in rats and mice. Foetuses were consistently reported to have retarded development, decreased foetal body weight and crown-rump length, and higher incidences of subdermal haemorrhagic patches and kinky short tails. There was also a significant reduction in ossification in caudal, parietal, and interparietal bones of the foetuses (NTP, 2008).

Foetotoxicity was observed in mice following administration of the chemical in drinking water during gestation (days 0–19). Significant developmental effects in the absence of maternal toxicity (increased incidence of post-implantation losses and resorptions, reduced foetal weight, decreased crown-rump length and delayed cranial ossification) occurred at the lowest dose level tested, 60 mg/kg bw/day. Therefore, no developmental NOAEL was determined (EC, 2005).

In a pre-gestational study in female mice, foetotoxic effects were seen starting from the lowest dose level tested, 250 ppm (63 mg/kg bw/day) in the absence of maternal toxicity. Significant levels of total chromium were found in treated animals at necropsy. No NOAEL could be identified for the developmental effects, which included increased post-implantation losses and resorptions, reduced litter size, foetal weight and crown-rump length, increased incidence of kinky tail, short tail and subdermal haemorrhagic patches, and delayed ossification of the parietal, interparietal and caudal bones. These foetal effects were seen in the absence of maternal toxicity (EC, 2005).

Overall, highly water-soluble chromium (VI) compounds should be considered to be developmental toxicants in the mouse. These findings can be regarded as relevant to humans. It is noted that some of the adverse effects on reproduction observed in animal studies may be related to the germ cell mutagenicity of these chromium (VI) compounds (see Mutagenicity section).

Observations in humans

Studies on the effects of exposure of humans to the chemical are inconclusive.

Increased incidence of 'toxicosis', and 'complications during pregnancy and childbirth' were reported among female workers of a dichromate production facility (EC, 2005). The nature of the complications and toxicosis was not specified. The poor quality and reporting of these studies preclude their use for drawing conclusions regarding potential reproductive effects.

The effect of the chemical on sperm quality was studied in 21 electroplating workers in Henan, China. Significant ($p<0.05$) decreases in sperm count, sperm motility, concentrations LDH and LDH-x, and significantly increased follicle stimulating hormone (FSH) concentrations were found in the exposed workers compared with the controls. Duration of employment for all study participants ranged from 1 to 15 years; no information on exposure levels or demographics of the exposed and control groups were reported (Li et al., 2001).

Other Health Effects

Neurotoxicity

Exposure of humans to high levels of airborne chromium (VI) in occupational and environmental settings produced symptoms of dizziness, headache, and weakness when they were working over the chromate tanks. Cerebral oedema was found in a case of fatal poisoning by ingestion. More recently, patients with 8–25-fold higher chromium blood levels that resulted from parenteral feeding, did not have increased signs of somatopsychic responses. However, the number of patients studied was small and they were suffering from serious clinical diseases. Additional studies are needed to provide further information on the effect of hexavalent chromium compounds on the neuro/behavioural changes in humans.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects (carcinogenicity, mutagenicity, reproductive toxicity, developmental toxicity), systemic acute effects (acute toxicity by the oral, dermal and inhalation route of exposure) and local effects (corrosivity, skin sensitisation, respiratory sensitisation). The chemical may also cause harmful effects following repeated exposure through inhalation.

Public Risk Characterisation

The use of chromium (VI) compounds in products available to the public in Australia is restricted as a Schedule 6 chemical in the Poisons Standard (SUSMP, 2012). Domestic use of the compounds relevant to Australia or internationally were not identified. Therefore, it is unlikely that the public will be exposed to the chemical.

Occupational Risk Characterisation

Given the critical systemic long-term, systemic acute and local health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise dermal, 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.

NICNAS Recommendation

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

Regulatory Control

Public Health

Considering that the available information indicates low public exposure to the chemicals, no regulatory controls are recommended.

Work Health and Safety

The health risk to workers from these chemicals is controlled when correct classification and labelling are considered, and adequate control measures to minimise occupational exposure and protective equipment are implemented.

The chemical is recommended for classification and labelling under the current approved criteria and adopted Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This assessment does not consider classification of physical hazards and environmental hazards.

Note: * in the table below indicates existing hazard classification for one or more compounds in the group. It is proposed that the current classification is applied to all members of the group.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Toxic if swallowed (T; R25)* Harmful in contact with skin (Xn; R21)* Very toxic by inhalation (T+; R26)*	Toxic if swallowed - Cat. 3 (H301) Harmful in contact with skin - Cat. 4 (H312) Fatal if inhaled - Cat. 2 (H330)
Irritation / Corrosivity	Causes burns (C; R34)*	Causes severe skin burns and eye damage - Cat. 1 (H314)
Sensitisation	May cause sensitisation by inhalation (Xn, R42)* May cause sensitisation by skin contact (Xi; R43)*	May cause allergy or asthma symptoms or breathing difficulties if inhaled - Cat. 1 (H334) May cause an allergic skin reaction - Cat. 1 (H317)

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Repeat Dose Toxicity	Toxic: danger of serious damage to health by prolonged exposure through inhalation (T; R48/23)*	Causes damage to organs through prolonged or repeated exposure - Cat. 1 (H372)
Genotoxicity	Muta. Cat 2 - May cause heritable genetic damage (T; R46)*	May cause genetic defects - Cat. 1B (H340)
Carcinogenicity	Carc. Cat 1 - May cause cancer (T; R45)	May cause cancer - Cat. 1A (H350)
Reproductive and Developmental Toxicity	Repro. Cat 2 - May impair fertility (T; R60)* Repro. Cat 2 - May cause harm to the unborn child (T; R61)	May damage fertility. May damage the unborn child - Cat. 1B (H360FD)

[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 dermal, ocular and inhalation exposure to the chemical 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 storage, handling and use of a hazardous chemical are dependent 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:

- using closed systems or isolation of operations;
- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemical 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 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 selection of 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 hazardous chemical are prepared; and
- managing risks arising from storage, 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 physical hazards of the chemical has not been undertaken as part of this assessment.

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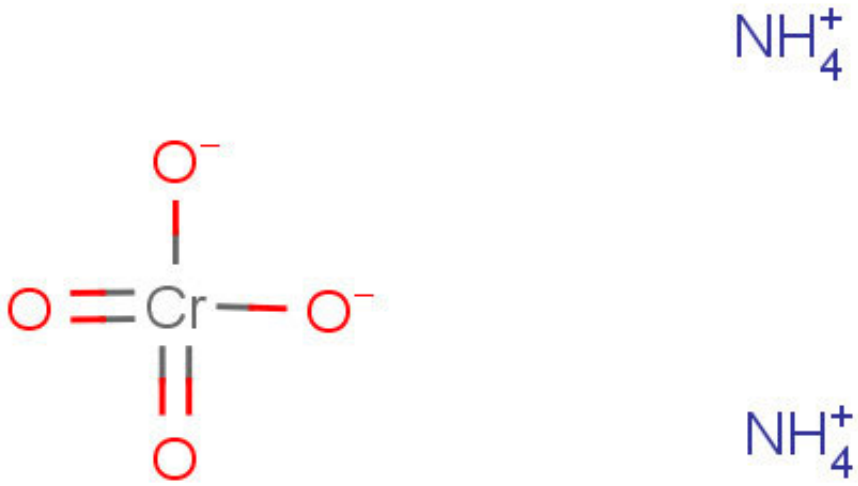
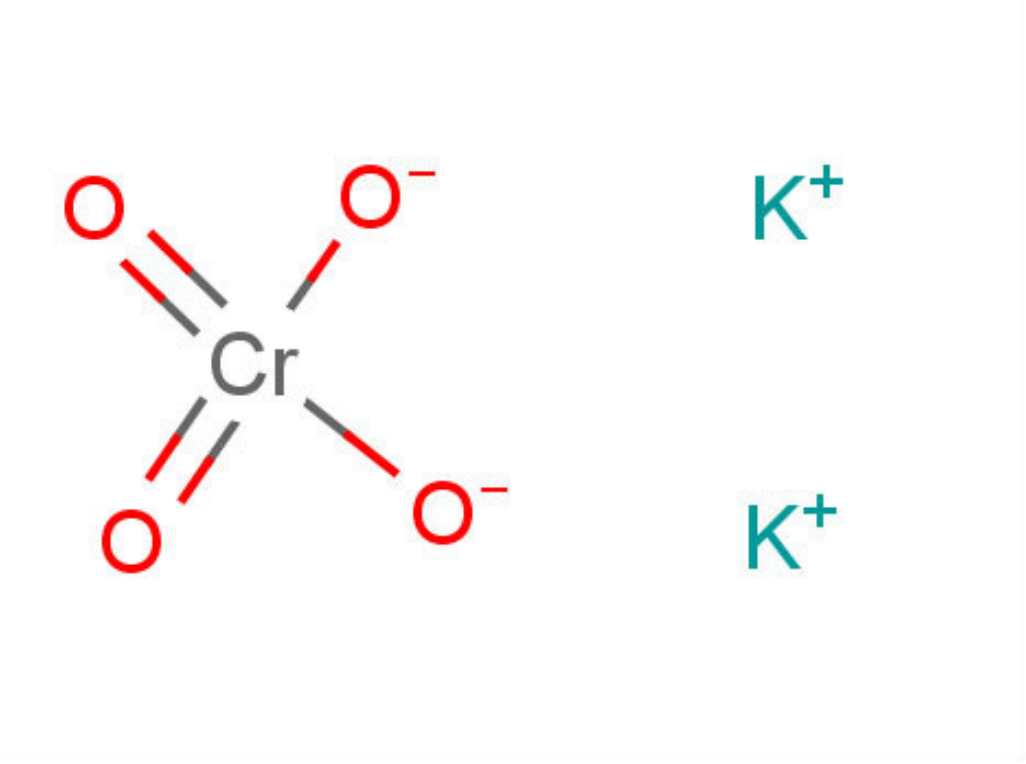
Last Update 04 July 2014

Chemical Identities

Chemical Name in the Inventory and Synonyms	**Chromic acid (H2CrO4), diammonium salt** Ammonium chromate Ammonium chromate(VI) Diammonium chromate Chromic acid, diammonium salt Chromic acid (H2CrO4), ammonium salt (1:2)
CAS Number	7788-98-9
Structural Formula	
Molecular Formula	CrH2O4.2H3N
Molecular Weight	152.07

Chemical Name in the Inventory and Synonyms	**Chromic acid (H2CrO4), dipotassium salt** Potassium chromate Bipotassium chromate Dipotassium chromate Dipotassium monochromate Tarapacaite
CAS Number	7789-00-6

Structural Formula	
Molecular Formula	CrH2O4.2K
Molecular Weight	194.19

Chemical Name in the Inventory and Synonyms	**Chromic acid (H2CrO4), disodium salt** Sodium chromate Chromitope Sodium Chromium disodium oxide Disodium chromate Rachromate
CAS Number	7775-11-3
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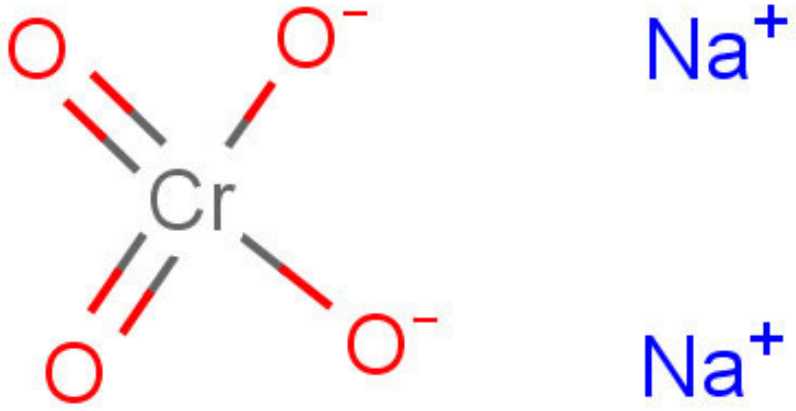
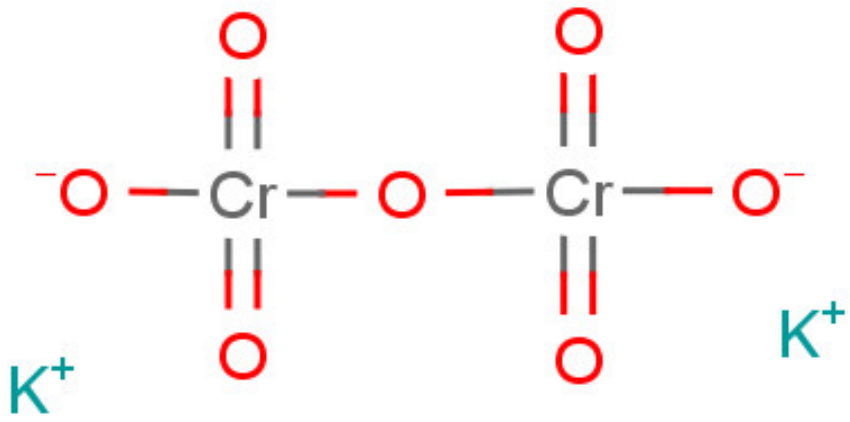
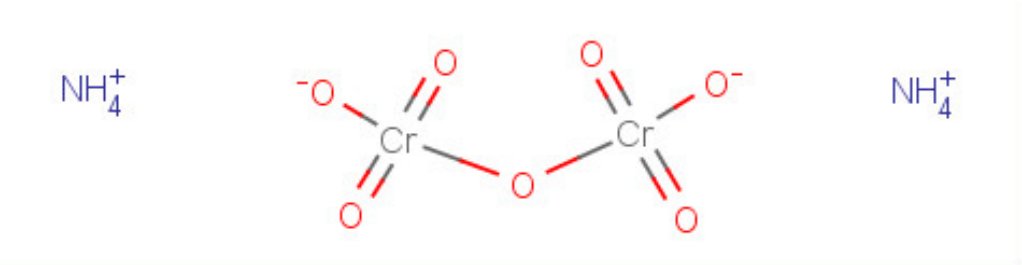
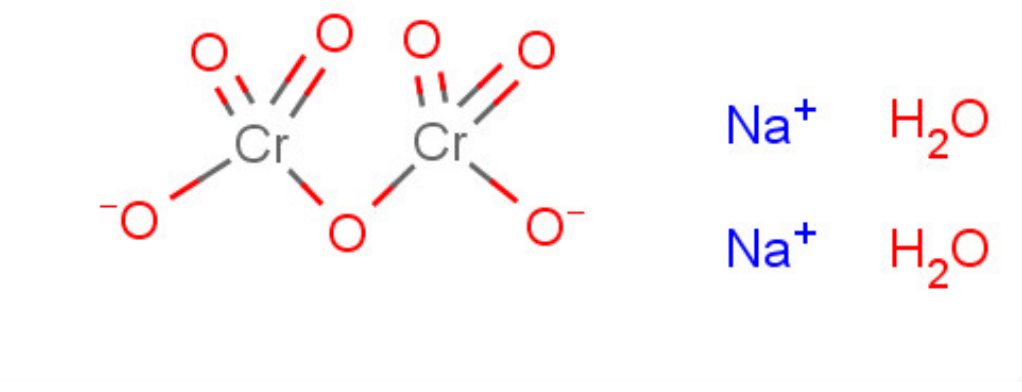
	
Molecular Formula	CrH2O4.2Na
Molecular Weight	161.97

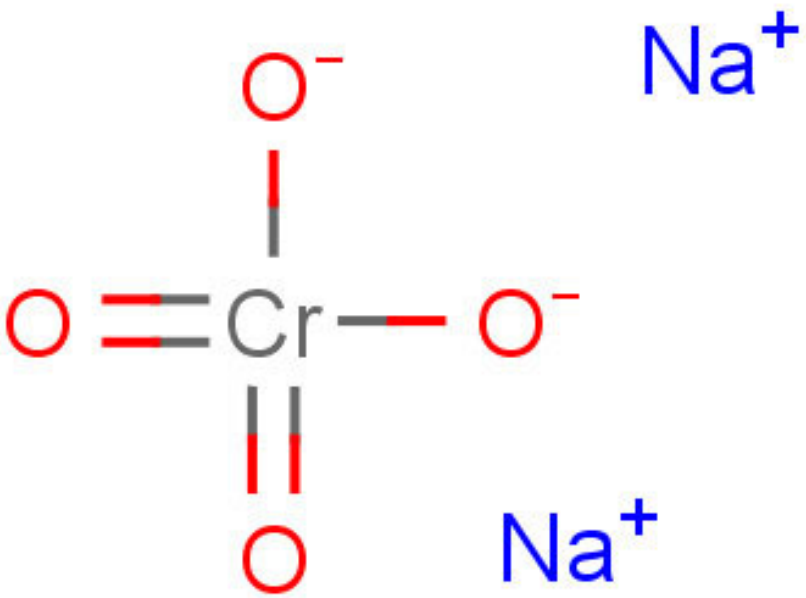
Chemical Name in the Inventory and Synonyms	**Chromic acid (H2Cr2O7), dipotassium salt** Potassium dichromate Potassium bichromate Dipotassium bichromate Dipotassium dichromate Lopezite
CAS Number	7778-50-9
Structural Formula	

Molecular Formula	Cr2H2O7.2K
Molecular Weight	294.18

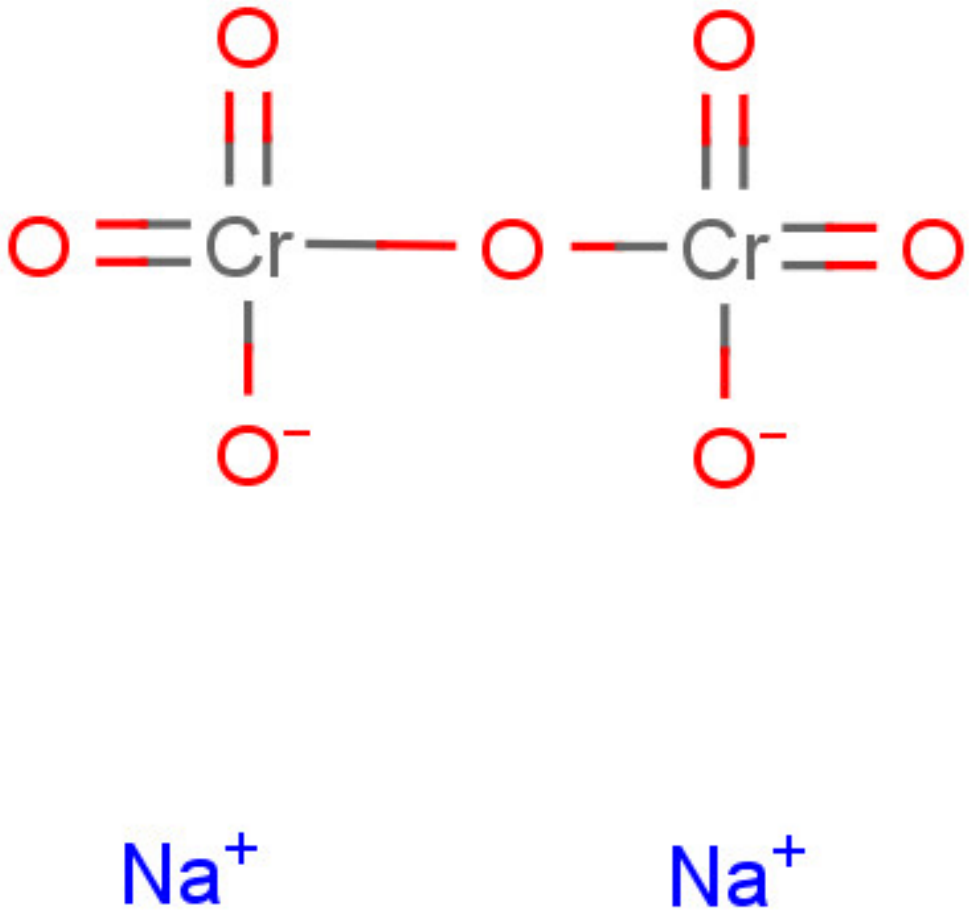
Chemical Name in the Inventory and Synonyms	**Chromic acid (H2Cr2O7), diammonium salt** Ammonium bichromate Ammonium dichromate Diammonium dichromate Dichromic acid (H2Cr2O7), diammonium salt Dichromic acid, diammonium salt
CAS Number	7789-09-5
Structural Formula	
Molecular Formula	Cr2H2O7.2H3N
Molecular Weight	252.06

Chemical Name in the Inventory and Synonyms	**Chromic acid (H2Cr2O7), disodium salt, dihydrate** Sodium Dichromate Dihydrate Disodium dichromate dihydrate Chromic acid (H2Cr2O7), disodium salt, dihydrate (9CI)
CAS Number	7789-12-0
Structural Formula	
Molecular Formula	Cr2H2O7.2H2O.2Na

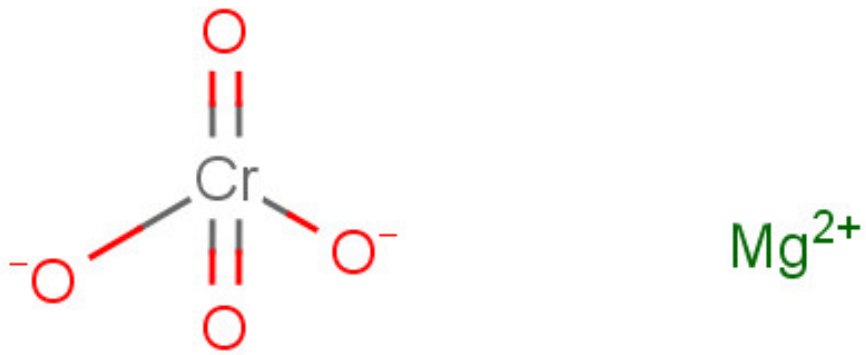
Molecular Weight	298.00

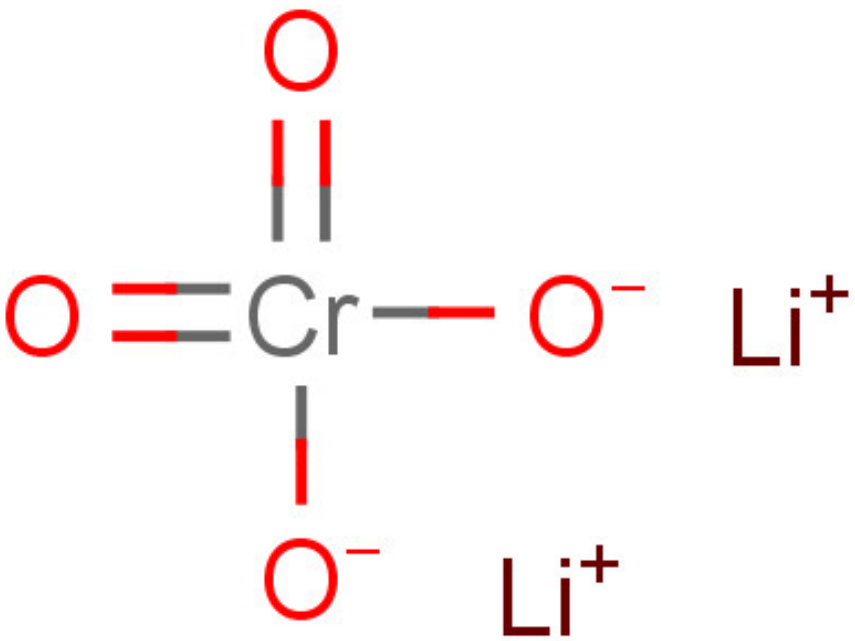
Chemical Name in the Inventory and Synonyms	**Chromic acid (H2CrO4), disodium salt, tetrahydrate** Sodium chromate(VI), tetrahydrate Sodium chromate tetrahydrate Chromic acid, disodium salt, tetrahydrate Sodium chromate tetrahydrate
CAS Number	10034-82-9
Structural Formula	
Molecular Formula	CrH2O4.4H2O.2Na
Molecular Weight	161.97

Chemical Name in the Inventory and Synonyms	**Chromic acid (H2Cr2O7), disodium salt** Sodium bichromate Sodium dichromate Bichromate of soda Chromium sodium oxide (Cr3Na2O7) Dichromic acid (H2Cr2O7), disodium salt

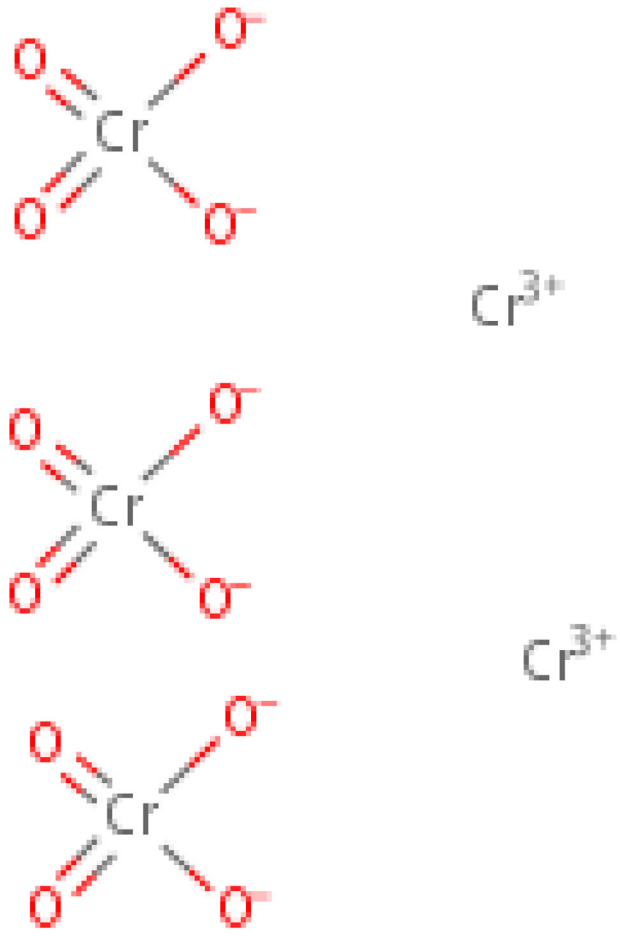
CAS Number	10588-01-9
Structural Formula	
Molecular Formula	Cr2H2O7.2Na
Molecular Weight	261.97

Chemical Name in the Inventory and Synonyms	**Chromic acid (H2CrO4), magnesium salt (1:1)** Magnesium chromate Chromic acid, magnesium salt (1:1)
CAS Number	13423-61-5
Structural Formula	

	
Molecular Formula	CrH2O4.Mg
Molecular Weight	140.30

Chemical Name in the Inventory and Synonyms	**Chromic acid (H2CrO4), dilithium salt** Lithium chromate Chromium lithium oxide (CrLi2O4) Dilithium chromate Lithium chromate(VI) Chromic acid (H2CrO4), lithium salt (1:2)
CAS Number	14307-35-8
Structural Formula	

Molecular Formula	CrH2O4.2Li
Molecular Weight	129.87

Chemical Name in the Inventory and Synonyms	**Chromic acid (H2CrO4), chromium(3+) salt (3:2)** Chromium(III) chromate Cr2(CrO4)3 Chromic chromate Chromium chromate Dichromium tris(chromate) Dichromium(3+) trichromate
CAS Number	24613-89-6
Structural Formula	
Molecular Formula	CrH2O4.2/3Cr
Molecular Weight	452

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