Persulfates: Human health tier II assessment

05 February 2016

- Chemicals in this assessment
- Preface
- Grouping Rationale
- Import, Manufacture and Use
- Restrictions
- Existing Worker Health and Safety Controls
- Health Hazard Information
- Risk Characterisation
- NICNAS Recommendation
- References

Chemicals in this assessment

| Chemical Name in the Inventory | CAS Number |
|--|------------|
| Peroxydisulfuric acid (((HO)S(O)2)2O2), dipotassium salt | 7727-21-1 |
| Peroxydisulfuric acid (((HO)S(O)2)2O2), diammonium salt | 7727-54-0 |
| Peroxydisulfuric acid (((HO)S(O)2)2O2), disodium salt | 7775-27-1 |

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

NICNAS has made every effort to assure the quality of information available in this report. However, before relying on it for a specific purpose, users should obtain advice relevant to their particular circumstances. This report has been prepared by NICNAS using a range of sources, including information from databases maintained by third parties, which include data supplied by industry. NICNAS has not verified and cannot guarantee the correctness of all information obtained from those databases. Reproduction or further distribution of this information may be subject to copyright protection. Use of this information without obtaining the permission from the owner(s) of the respective information might violate the rights of the owner. NICNAS does not take any responsibility whatsoever for any copyright or other infringements that may be caused by using this information.

ACRONYMS & ABBREVIATIONS

Grouping Rationale

Ammonium, potassium and sodium persulfates are closely related chemicals with similar chemical structure and physical-chemical properties. These inorganic substances differ only by the cationic portion of the salt, which is not likely to influence the hazardous properties of the molecules. The anionic part is identical and, therefore, the three salts are expected to display very similar toxicological and ecotoxicological behaviour based on the available data.

The similar toxicological effects identified in the acute oral, dermal and inhalation studies support the applicability of the read across approach. Accordingly, data gaps for each persulfate can be filled by read across. The three chemicals are therefore assessed as one chemical group in this report. The overall data are adequate to conduct a hazard assessment of this group.

Import, Manufacture and Use

Australian

The following Australian industrial uses were reported under previous mandatory calls for information (NICNAS, 2001).

The chemicals have reported cosmetic uses, including:

- in hair bleaches;
- in hair colouring preparations; and
- in hair lighteners.

The chemicals have reported domestic use as ingredients in adhesives.

The chemicals have reported commercial uses, including:

- as oxidising agents in metal etching;
- in dyeing and printing;
- in deodourising and bleaching oils; and
- in photography.

The chemicals have reported site-limited uses, including:

- in manufacture of rubber products;
- in manufacture of paper and paperboard industries; and
- as depolarisers in batteries.

Ammonium, potassium and sodium persulfates are not manufactured in Australia. However, several products are formulated in Australia from imported persulfates. While the majority of bleach products on the Australian market are for professional use in hairdressing salons, a small number of products are also used at home by consumers.

International

The following international uses have been identified through the Organisation for Economic Co-operation and Development Screening information data set International Assessment Report (OECD SIAR), Galleria Chemica, Substances and Preparations in Nordic countries (SPIN) database and the European Commission Cosmetic Ingredients and Substances (CosIng) database.

The chemicals have reported cosmetic uses, including:

- in hair bleaches; and
- in hair colouring preparations.

The chemicals have reported domestic uses, including:

- as bleaching agents;
- as cleaning and washing agents;
- in paints, lacquers and varnishes; and
- in flame retardants;
- in decolourising and deodourising oils; and
- in treatment of water for swimming pools and spas.

The chemicals have reported commercial uses, including:

- as oxidising agents;
- as reducers and retarders in photography;
- in textile dyeing;
- in manufacture of printed circuits;
- in metal etching;

- in electroplating; and
- in construction.

The chemicals have reported site-limited uses, including:

- in manufacture of pulp and paper boards; and
- in the manufacture of fluorocarbon elastomers.

Restrictions

Australian

The persulfates are listed in the *Poisons standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in Schedule 6 (SUSMP, 2015).

Schedule 6:

AMMONIUM PERSULFATE and POTASSIUM PERSULFATE:

in hair preparations.

SODIUM PERSULFATE:

- (a) in hair preparations; or
- (b) in products for the treatment of water for swimming pools and spas.

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).

Sodium and potassium persulphates are listed in the Australia New Zealand Food Standards Code – Schedule 18 -Processing Aids – S18.06 Permitted bleaching, washing and peeling agents and in water used as an ingredient in other foods (section 1.138): all foods under GMP conditions (FSANZ, 2012).

Ammonium persulphate is listed in Schedule 18–Processing Aids- S18.08 Permitted processing aids—Miscellaneous purposes (section 1.140): Yeast washing agent under GMP conditions (FSANZ, 2012).

International

All three persulfates are listed by the US FDA under 21CFR 176-170a as 'Indirect Food Additives- Substances for Use Only as Components of Paper and Paperboard - Components of paper and paperboard in contact with aqueous and fatty foods' with no restrictions.

Persulfate compounds are currently regulated under the Canadian Department of Justice, Hazardous Products Act, Ingredient Disclosure List (SOR/88-64) with the maximum authorised concentration of 0.1 %.

Existing Worker Health and Safety Controls

Hazard Classification

Ammonium, sodium and potassium persulfates are classified as hazardous for human health in the Hazardous Substances Information System (HSIS) with the following risk phrases (Safe Work Australia, 2015):

- Xn; R22 (acute toxicity)
- Xi; R36/37/38 (Irritation)
- R42/43 (Sensitisation)

Exposure Standards

Australian

The chemicals have exposure standards of 0.1 mg/m³ time weighted average (TWA) (Safe Work Australia, 2015).

International

The following exposure standards were identified for persulfate salts (Galleria Chemica):

An exposure limit of 0.1 mg/m³ TWA in countries such as Belgium, Canada, Ireland, Italy, Portugal, Spain and the USA.

An exposure limit of 2 mg/m³ TWA in countries such as Denmark, Iceland and Norway.

Health Hazard Information

Toxicity information on ammonium, sodium and potassium persulfate was sourced primarily from the OECD Screening Initial Assessment Report (SIAR) for Persulfates, CAS Nos. 7727-54-0, 7727-21-1, 7775-27-1 (OECD, 2005) and the NICNAS Priority Existing Chemical Assessment Report No. 18 (NICNAS, 2001). Additional sources of hazard information for the chemicals include the RIVM (National Institute for Public Health and the Environment) report on Cosmetovigilance in the Netherlands (de Wit-Bos et al., 2012) and the Final Report on the Safety Assessment of Ammonium, Potassium, and Sodium Persulfate (CIR, 2001). Unless noted, references to individual studies below are taken from these reviews.

Toxicokinetics

Persulfate salts rapidly dissociate in water into the respective cation (ammonium, potassium or sodium) and anionic persulfate. The influence of the cations on toxicity is expected to be negligible, with toxicokinetics and dynamics mainly influenced by the persulfate anion (OECD, 2005).

No data were available on the oral, dermal or inhalation absorption of the three persulfates. Ingested sodium and potassium ions will be readily taken up in the gastrointestinal tract and will enter the body's electrolyte pool. Absorption of ammonium ions increases as the pH of the contents of the lumen increases, and the ions are actively transported at lower pH levels. Ammonium ion, absorbed from the gastrointestinal tract, travels via the hepatic portal vein directly to the liver where most of it is converted to urea and glutamine and widely distributed in the body (Castell and Moore, 1971).

The persulfate ion is poorly absorbed from the gastro-intestinal tract, especially when administered in large doses, such that the capacity of specialised transport processes for this ion in the intestines is exceeded. No data were available on the distribution of the persulfate salts in the body. Based on the in vitro chemistry of persulfates, the persulfate anion is expected to decompose under in vivo conditions to form hydrogen peroxide and sulfate ions. Hydrogen peroxide is rapidly metabolised to oxygen and water by catalase and peroxidase enzymes in mammalian tissues and there is practically no potential for bioaccumulation (OECD, 2005). Sulfate ions are required by the body for the synthesis of sulfur-containing macromolecules.

Physiological studies have demonstrated that sodium, potassium and ammonium ions are mainly excreted in the urine. Inorganic sulfate is also eliminated from the body, almost entirely by renal excretion (i.e. without biotransformation).

Acute Toxicity

Oral

Persulfate salts are classified as hazardous with the risk phrase 'Harmful if swallowed' (Xn; R22) in HSIS (Safe Work Australia) The available data support this classification. Persulfate salts are considered to have moderate acute toxicity by the oral route.

The acute oral median lethal dose (LD50) values for the three persulfate salts (in rats) were reported as 495-820 mg/kg bw for ammonium persulfate (Smyth et al, 1969; FMC, 2001), 895-930 mg/kg bw for sodium persulfate (Degussa AG, 1979) and 1130 mg/kg bw for potassium persulfate (FMC, 1979a). Clinical signs for all persulfates were ocular and oral discharge, irregular breathing and loss of muscle control.

Dermal

Persulfate salts have low acute dermal toxicity.

The acute dermal LD50 was greater than 2000 mg/kg bw (rats) for ammonium persulfate (FMC, 1991b), and greater than 10,000 mg/kg bw (rabbits) for sodium and potassium persulfates (FMC, 1979c). Ocular and nasal discharge and slight irritation were reported in animals dermally exposed to high levels of persulfates (FMC, 1979b).

Inhalation

All three persulfates have low acute inhalation toxicity.

Acute inhalation studies with ammonium, sodium and potassium persulfates performed according to OECD guidelines in rats, indicated median lethal concentration (LC50) values of greater than the maximum attainable concentrations, 2.95 mg/L, 5.1 mg/L and 42.9 mg/L, respectively. Following exposure to high concentrations of persulfates, animals exhibited dyspnoea, respiratory distress and increased nasal, ocular and oral secretion (FMC 1987, FMC, 1979b; FMC 1995).

Corrosion / Irritation

Respiratory Irritation

The chemicals are classified as hazardous with the risk phrase 'Irritating to Respiratory system' (Xi; R37) in the HSIS (Safe Work Australia). No data were available for ammonium or potassium persulfates. The limited data available for sodium support this classification.

Groups of male ND4 Swiss Webster mice were exposed, head-only, to sodium persulfate dust for 30 minutes at concentrations of 0.26 to 3.22 mg/L. Mortality was observed in all except the lowest exposure group during the 7-day post-exposure period with clinical signs that included ocular and nasal discharge and decreased respiratory rate. Abnormal gait and whole body tremors were observed in animals exposed to the highest concentration of dust. The concentration of dust which produced a 50 % decrease in respiratory rate (RD50), was 2.25 mg/L, indicating that sodium persulfate was a respiratory system irritant (FMC, 1994).

Skin Irritation

Ammonium and sodium persulfates were not found to be skin irritants in animal studies. However human observations support the existing classification as skin irritants.

The dermal irritation potential of ammonium persulfate was determined (according to OECD Test Guideline TG404) using six male and female New Zealand White rabbits (CTFA, 1994). No irritation was noted within 72 hours following application.

In another study, ammonium persulfate, 0.5 g moistened with 0.1 mL of water was applied under an occlusive patch to the intact and abraded skin of three white Russian rabbits for 4 hours (BGChemie, 1994). Slight oedema, which disappeared within 24 hours, was observed on intact skin, while moderate to severe erythema, moderate oedema, and scab formation were observed at the abraded sites. Ammonium persulfate was considered non-irritating to intact skin.

Three brief study reports submitted by industry on sodium persulfate showed at most a slight skin irritant potential in rabbits (FMC, 1979d; FMC, 1980).

Eye Irritation

The chemicals are classified as hazardous with the risk phrase 'Irritating to eyes' (Xi; R36) in the HSIS (Safe Work Australia). The limited data available support this classification.

In one eye iritation study, ammonium persulfate (0.1 g) was instilled into the conjunctival sacs of the eyes of three white Russian rabbits (BG Chemie, 1996). Severe diffused reddening and swelling with hyper-secretion were noticed, and subsided within 72 hours; although clouding of the cornea was still present at this time. Ammonium persulfate was considered slightly irritating to the eye. No irritation scores were available.

In another study conducted according to the OECD TG 405 (details not available), ammonium persulfate was instilled in the eyes of nine New Zealand White rabbits. The eyes of six animals were not rinsed whereas the eyes of three animals were rinsed 30 seconds after instillation (CTFA 1994). Ammonium persulfate caused slight to mild conjunctivitis and iritis in the unrinsed eyes and was considered minimally irritating to these eyes. Ammonium persulfate was practically non-irritating to rinsed eyes. No irritation scores were available.

In a single unpublished study, sodium persulfate was instilled into the eyes of 8 rabbits. Eye irritation was scored by the Draize method at 24, 48 and 72 h. Slight conjunctivitis was noted at 48 h (FMC, 1979c).

Observation in humans

Standard patch tests have shown 5 % ammonium persulfate to be irritating to human skin (Calnan & Shuster, 1963; Cronin, 1980), although a separate study found 1/20 people exhibited an equivocal response when tested with 5 % to 10 % persulfate (Forck, 1968). Application of 17.5 % solution of the persulfate salts under an occlusive wrap for four hours was found to cause irritation in 8/46 subjects (Jordan, 1998 cited in CIR, 2001).

Workers experienced skin rashes within one month of beginning work in a factory manufacturing ammonium and potassium persulfates, occurring in 20 % to 70 % of new employees (White et al., 1982). Two cases of irritant reactions to hair bleach containing ammonium persulfate have been described, involving erythema of the scalp and forehead developing over several hours followed by crusting (Cronin, 1980; Fisher & Dooms-Goossens, 1976).

One case of corneal burns from potassium persulfate was reported (BIBRA International, 1997). Irritant effects of persulfates are reported to include pain in the eyes with conjunctivitis.

Sensitisation

Respiratory Sensitisation

The chemicals are classified as hazardous with the risk phrase 'May cause sensitisation by skin contact' (R42) in the HSIS (Safe Work Australia). The limited data available support this classification.

Ammonium persulfate has been tested in an animal model of occupational lung disease, namely, airway responsiveness to acetylcholine in rabbits. Airway hyper-responsiveness (AHR) is regarded as an initial step in the development of obstructive lung

disease (Vandenplas et al., 1996). Ammonium persulfate at approximately 50 mg/m³ for four hours induced AHR (Mensing et al., 1995).

Skin Sensitisation

The chemicals are classified as hazardous with the risk phrase 'May cause sensitisation by inhalation contact' (R43) in the HSIS (Safe Work Australia). The limited data available support this classification.

There was evidence of delayed contact hypersensitivity in two maximisation tests (OECD TG 406) using ammonium and sodium persulfate in guinea pigs. All test animals reacted positively following challenge by intradermal injection of 0.1 % ammonium persulfate and 80 % of animals were positive following dermal challenge with 1 % ammonium persulfate 14 days later. The corresponding figures for sodium persulfate were 90 % positive for test animals positive following an (non-standard) intracutaneous challenge and 60 % of the test animals were positive following topical challenge (CIR, 2001; BIBRA International, 1997).

Sodium persulfate was not sensitising when applied to the skin of guinea pigs in an unpublished Buehler Test, conducted to guideline standards (FMC, 1990b). In a murine local lymph node assay (LLNA), investigators concluded that both ammonium and sodium persulfate were moderate to strong sensitisers with EC3 values (amount of chemical required to elicit a stimulation index of 3) calculated to be 1.9 % and 0.9 % respectively (Cruz et al., 2009 cited in HSDB).

Observation in humans

Many patch test studies is human volunteers gave positive response to sodium and ammonium persulfates (Fisher et al., 1976; Pepys et al, 1976).

There are strong indications that ammonium, sodium and potassium persulfate are linked to a variety of skin complaints indicative of sensitisation in occupationally-exposed human subjects. In general, persulfates are associated with immediate and delayed contact hypersensitivity, contact urticaria, eczema, dermatoses and rashes (White et al., 1982).

Occupational asthma, rhinitis, bronchitis and decreased lung function has been widely reported in hairdressers from bleaching powders and industrial workers exposed to persulfate salts. Several occupational studies have been reviewed in CIR (2001). The persulfates caused both delayed-type and immediate skin reactions. These reactions include irritant dermatitis, allergic eczematous dermatitis, localised contact urticaria, generalised urticaria, rhinitis, asthma, and syncope. The most common causes of allergic dermatitis in hairdressers are the active ingredients in hair dyes, and ammonium persulfate has been identified as a frequent allergen. A number of occupational case studies document these types of reactions, but no incidence data were available (CIR, 2001).

Repeated Dose Toxicity

Oral

The persulfates have low repeat dose toxicity. Twenty-eight-day repeated dose oral (dietary) toxicity studies were conducted in rats with all three persulfate salts. The oral doses for the three salts were 0, 100, 316, 1000 ppm (equivalent to 0, 12.6, 41.2, 131.5 mg/kg bw/day for the potasium salt). Tests were performed in male rats only. The no observed adverse effect levels (NOAEL) for sodium and potassium salts were 137 and 131.5 mg/kg bw/day, respectively (the highest doses tested), while the NOAEL for ammonium persulfate was 41 mg/kg bw/day, based on decreased relative adrenal weight at the highest dose (FMC, 1979a; FMC, 1979b; FMC1979c).

Another oral (dietary) subchronic toxicity study using sodium persulfate was conducted in rats. Rats (20/sex/group; strain not provided) were fed rodent chow containing 0, 300, 1000 or 3000 ppm sodium persulfate (0, 23, 100 or 225 mg/kg bw/day) for 90 days. On day 48 of the study, the concentration of the group receiving 1000 ppm was increased to 5000 ppm for the remainder of the study. At the two high dose levels body weight was decreased during the last 6 weeks of treatment (FMC 1979e).

There were no treatment-related effects on urinalysis, clinical chemistry or haematology parameters. Pathological findings were limited to the 3000 ppm group only and consisted of necrosis and atrophy of the gastrointestinal tract epithelial lining. The absence of the gastrointestinal lesions in the group receiving 1000 ppm for 8 weeks, followed by 5000 ppm for 5 weeks, indicates that the lesions are related both to concentration in diet (dose) and length of exposure. There were no treatment-related pathological findings in reproductive organs or any other organ system or tissue. A lowest observed adverse effect level (LOAEL) of 3000 ppm (200-250 mg/kg bw/day) was established in this study (CIR, 2001).

| ח | er | m | al |
|---|-----|---|----|
| ப | CI. | | а |

No data are available.

Inhalation

The persulfates have low repeat dose inhalation toxicity.

A well conducted 90-day inhalation study using ammonium persulfate gave evidence of inflammation of the airways, reduced body weight gain, rales, increased respiratory rate and increased lung weights (FMC 1998). In the study, rats (10/sex/group, rat strain not specified) were exposed in whole body chambers to dust aerosol concentrations of 0, 5, 10 or 25 mg/m³ ammonium persulfate, 6 hours/day, 5 days/week for 13 weeks. Additional groups of 5 animals/sex/group were exposed for 13 weeks followed by a 6-week or 13-week recovery periods. Rales and increased respiratory rates were noted in high dose males and females during the study, and sporadically in the mid-dose group. At 25 mg/m³, inflammation of the trachea and bronchi/bronchioles, decreased body weights and increased lung weights were found after 13 weeks. These lesions had reversed to normal by the end of the 6-week recovery period. The no observed adverse effect concentration (NOAEC) in this study was determined to be 10.3 mg/m³.

Observation in humans

Pulmonary function tests conducted on employees of a persulfate production facility indicated no adverse effects on pulmonary function at workplace exposure levels, measured at 0.5 mg/m³ (FMC, 1992). Follow-up of these same employees indicated that exposure at 0.5 mg/m³ had no long-term effects on pulmonary function (Greaves, 1997).

Genotoxicity

Based on the limited available data, ammonium, sodium and potassium persulfates were not mutagenic.

Negative results were obtained in the Ames tests, with or without metabolic activation in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA 1538 for the sodium salt (FMC, 1990a) and *S. typhimurium* strains TA92, TA94, TA98, TA100, TA1535, TA1537 and *Escherichia coli* strain WP2 uvrA (Shimizu, 1985) or *S. typhimurium* strains TA97 or TA102 (Ishidate, 1984) for the ammonium salt. *S. typhimurium* strain TA97 was incubated in triplicate at either 25 °C or 37 °C with ammonium persulfate (concentration not specified) for 30 minutes at pH 5.0 (Pagano, Zeiger, and Stark 1990). Following incubation, the mean number of *his* C revertants was determined. Ammonium persulfate was not mutagenic at both temperatures.

An in vitro unscheduled DNA synthesis test was also negative for sodium persulfate (FMC, 1990d). The ammonium salt was not clastogenic in Chinese hamster fibroblasts in the absence of metabolic activation in a chromosome aberration test (Ishidate et al., 1988).

Sodium persulfate was negative in two *in vivo* genotoxicity studies. Doses of sodium persulfate up to 338 mg/kg injected into mice intraperitoneally did not increase the incidence of micronuclei in bone marrow polychromatic erythrocytes (FMC, 1990c). Sodium persulfate was found to be non-genotoxic when tested up to 820 mg/kg in an in vivo unscheduled DNA synthesis test in rats (FMC, 1991c).

Carcinogenicity

Based on the limited data available, there is no eveidence of carcinogenicity of any of the persulfate salt.

In a non-guideline study, female SENCAR mice were exposed dermally twice weekly to 0.2 mL of a 200 mg/mL solution of ammonium persulfate for 51 weeks. The investigators concluded that ammonium persulfate is neither a tumour promoter nor a complete carcinogen when applied to the skin (Kurokawa et al., 1984).

Reproductive and Developmental Toxicity

Based on the limited data available for ammonium persulfate, the three chemicals are not toxic to reproduction or development.

In a well conducted fertility/developmental study (OECD 421), groups of rats (CrI:CD (SD)IGS BR, 12/sex/group) were administered ammonium persulfate in the diet at doses of 0, 40, 100 and 250 mg/kg bw/day (Weaver, 2004). Animals (both sexes) were dosed two weeks prior to and during mating. Females were administered the substance following mating, throughout gestation and until lactation day 4. In the parental generation group, there were no treatment related clinical signs, effects on body and organ weights or gross lesions. There were no significant adverse effects on the gonads and progression of spermatogenesis, although a non-significant decrease in pregnancy rates was reported at = 100 mg /kg bw/day. On this basis, it was concluded that the NOAEL for fertility indices and reproductive performance was the top dose of 250 mg /kg bw/day. There were no treatment-related clinical signs, mortality or necropsy findings among pups (live birth and viability indices were similar across all groups). There was a slight transient depression in mean pup body weight; however it was not considered adverse. The developmental toxicity NOAEL determined was the highest dose of 250 mg /kg bw/day (Weaver, 2004).

Risk Characterisation

Critical Health Effects

Ammonium, sodium and potassium persulfates have very similar physical/chemical properties and available animal and human data indicate that they also have similar toxicological properties.

Although the persulfate salts are harmful by the oral route, potential for acute toxicity was generally not demonstrated via the dermal or inhalation routes. The persulfate salts were irritating to eyes and respiratory system but not skin irritants in animal studies, while studies in humans indicate that persulfates can cause skin irritation.

The persulfates are capable of inducing skin and respiratory sensitisation in animals and these are also the major chronic effects observed in humans. Mouse LLNA results for ammonium and sodium persulfate suggest that persulfates are moderate to strong sensitisers.

Overall, the main critical effects to human health are skin and respiratory sensitisation and irritation.

Public Risk Characterisation

The public could be exposed to these chemicals if they are used in hair bleaches and hair colouring preparations in Australia. The extent of current usage in Australia is unknown.

The directions for use in hair bleach and hair dye preparations normally include instructions for pre-testing for skin irritation and skin sensitisation. Therefore, the local effects, including skin irritation and skin sensitisation, are not a high priority for assessment. The risk to public health is not considered to be unreasonable and further risk management is not considered necessary for public safety.

The chemicals are currently listed on Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) in hair preparations and in products for the treatment of water for swimming pools and spa. A number of warning statements, first aid instructions and safety directions relating to the use of these chemicals apply.

Occupational Risk Characterisation

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

Given the critical health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise 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.

NICNAS Recommendation

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

Regulatory Control

Public Health

Products containing the chemicals should be labelled in accordance with state and territory legislation (SUSMP, 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)* | Harmful if swallowed - Cat. 4 (H302) |
| Irritation / Corrosivity | Irritating to eyes (Xi; R36)* Irritating to skin (Xi; R38)* Irritating to respiratory system (Xi; R37)* | Causes serious eye irritation - Cat. 2A (H319) Causes skin irritation - Cat. 2 (H315) May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335) |
| Sensitisation | May cause sensitisation by skin contact (Xi; R43)* May cause sensitisation by inhalation (Xn, R42)* | May cause an allergic skin reaction - Cat. 1 (H317) May cause allergy or asthma symptoms or breathing difficulties if inhaled - Cat. 1 (H334) |

^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.

References

BG Chemie 1996. Toxicological evaluations 10: Potential health hazards of existing chemicals: ammonium persulfate. Berlin, Springer Verlag.

BIBRA International 1997. Toxicity profile: ammonium, potassium and sodium persulphates. Surrey, UK, BIBRA.

Calnan CD, Shuster S 1963. Reactions to Ammonium Persulfate. Archives of Dermatology 46: 812–815

Castell DO and Moore EW 1971. Ammonium absorption from the human colon. The role of non-ionic diffusion. Gastroentorology, 60:33-42.

Cosmetic Ingredient Review (CIR) (2001). Final report on the safety assessment of ammonium, potassium, and sodium persulfate. Int J Toxicol, 20 (Suppl. 3), 7–21.

Cronin E 1980. Contact dermatitis. Edinburgh, Churchill Livingstone Inc.

Cruz MJ, De Vooght V, Munoz X, Hoet PHM, Morell F, Nemery B& Vanoirbeek JAJ 2009. Assessment of the sensitization potential of persulfate salts used for bleaching hair. Contact Dermatitis 60(2): 85–90.

de Wit-Bos L, Salverda-Nijhof JGW, Kooi MW, Bourgeois FC, van Gorcum TF, van Engelen JGM& Donker GA 2012. Cosmetovigilance in The Netherlands: Trend report 2011 – 2012 RIVM Report 320113005

Degussa AG 1979. Unpublished report: Degussa AG - US-IT-Nr 79-0017-DKT (cited in IUCLID 1996b)

Fisher AA, Dooms-Goossens A 1976. Persulfate hair bleach reactions. Cutaneous and respiratory manifestations. Arch Dermatol 112: 1407–1409.

FMC 1979a. FMC Corporation, Acute and 28-day subacute toxicity of ammonium persulfate, unpublished study ICG/T-79-025.

FMC 1979b. FMC Corporation, Acute and 28-day subacute toxicity of potassium persulfate, unpublished study ICG/T-79-024 (Summary).

FMC 1979c. FMC Corporation, Acute and 28-day subacute toxicity of sodium persulfate, unpublished study ICG/T-79-029.

FMC 1979d FMC Corporation, Sodium Persulfate: skin irritation and corrosion study in rabbits, Study no. 179-326.

FMC 1979e. FMC Corporation, Safety evaluation of sodium persulfate: a 90-day dietary feeding study in rats, Study no. 190-1151.

FMC 1980. FMC Corporation, Sodium Persulfate: skin corrosion study in rabbits, Study no. I80-403.

FMC 1988. FMC Corporation, Ammonium persulfate: primary skin irritation study in rabbits, Study no. 187- 0970.

FMC 1990a. FMC Corporation, Sodium persulfate: Salmonella/mammalian-microsome plate incorporation mutagenicity assay (Ames test) Study no. I90-1119.

FMC 1990b. FMC Corporation, FMC shock treatment: Skin sensitization study in guinea pigs, Study no. 190-1113.

FMC 1990c. FMC Corporation, Micronucleus cytogenetic assay in mice (sodium persulfate), Study no.190-1120.

FMC 1990d. FMC Corporation, Unscheduled DNA synthesis in rat primary hepatocytes, Study no. I90- 1121.

FMC 1991a. FMC Corporation, unpublished study I91-1201 (Summary).

FMC 1991b. FMC Corporation, Ammonium persulfate: acute dermal toxicity study in rats, unpublished study I91-1200 (Summary).

FMC 1991c. FMC Corporation, In vivo – in vitro rat hepatocyte unscheduled DNA synthesis assay(sodium persulfate), Study no. 190-1173.

FMC 1992. FMC Corporation, Report of persulfate worker study of the FMC plant in Buffalo, New York. Unpublished report. FMC study I1992-1712.

FMC 1994. FMC Corporation, Sodium persulfate: sensory irritation study in Swiss Webster mice, unpublished report. Study no. 193-1803.

FMC 1995. FMC Corporation, Sodium persulfate: acute inhalation toxicity study in rats, unpublished study 195-2017 (Summary).

FMC 1996. FMC Corporation, Repeated insult patch study, unpublished report. Study no. I95-2037.

FMC 1998. FMC Corporation, A 13-week inhalation toxicity study (with recovery) of ammonium persulfate in albino rats, unpublished report. Study no. 197-2205.

FMC 2001. FMC Corporation. Acute oral toxicity of ammonium persulfate in rats. Study no. I2001-2331.

Food and Drug Administration (FDA). 1984. Cosmetic product formulation and frequency of use data. FDA database. Washington, DC: FDA.

Food Standards Australia New Zealand (FSANZ) 2012. Australian and New Zealand Food Standards Code - Standard 1.3.1 - Food additives list. Accessed December 2015 at http://archive.foodstandards.gov.au/_srcfiles/Additives%20-

Forck G 1968. Frequency and persistence of persulfate allergies. Berufsdermatosen, 16: 84-92.

Greaves W 1997. Preliminary Report: Lung Function Assessment of Persulfate Workers: 1990-1996. Unpublished report.

Ishidate MJ, Harnois MC, Sofuni T 1984. Primary mutagenicity screening of food additives currently wsed in Japan. Food Chem Toxicol 22: 623–636.

Ishidate MJ, Harnois MC, Sofuni T 1988. A comparative analysis of data on the clastogenicity of 951 chemical substances tested in mammalian cell cultures. Mutat Res 195: 151–213.

Kurokawa Y, Takamura N, Matsushima Y, Imazawa T&Hayashi Y 1984. Studies on the promoting and complete carcinogenic activities of some oxidizing chemicals in skin carcinogenesis. Cancer Letters, 24, 299–304.

Mensing T, Marek W, Raulf-Heimsoth M& Baur X 1995. [Components of hair bleaches as triggers of bronchial hypersensitivity-studies using a model for occupationally-induced lung damage]. Pneumologie 49: 418–427.

National Industrial Chemicals Notification and Assessment (NICNAS) 2001. Priority Existing Chemical Assessment Report No. 18: Ammonium, Potassium and Sodium Persulfates. Accessed December 2015 at www.nicnas.gov.au.

National Occupational Health and Safety Commission (NOHSC) 2004. Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)]. National Occupational Health and Safety Commission.

Organisation for Economic Development and Cooperation (OECD) 2005. OECD Screening Information Data Set (SIDS), Screening Initial Assessment Report (SIAR), for Persulfates, CAS # 7727-54-0, 7727-21-1, 7775-27-1. OECD, Paris. Accessed in December 2015 at http://www.chem.unep.ch/irptc/sids/OECDSIDS/Persulfates.pdf

Pagano DA, Zeiger E and Stark AA 1990. Autoxidation and mutagenicity of sodium bisulfite. Mutat. Res. 228:89–96.

Pepys J, Hutchcroft BJ, Breslin AB 1976. Asthma due to inhaled chemical agents--persulphate salts and henna in hairdressers. Clin Allergy 6: 399–404.

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed December 2015 at http://hsis.safeworkaustralia.gov.au/HazardousSubstance

Shimizu H 1985. The results of microbial mutation test for forty-three industrial chemicals, Jpn. J. Ind. Health, 27, 400-419.

Smyth HF Jr., Carpenter CP, Weil CS, Pozzani UC, Striegel JA, Nycum JS 1969. Range-finding toxicity data: List VII. Am Ind Hyg Assoc J 30: 470–476.

Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) 2015. Accessed November 2015 at http://www.comlaw.gov.au/Details/F2012L01200/Download.

Vandenplas O, Delwiche JP, Jamart J, Van de Weyer R 1996. Increase in non-specific bronchial hyperresponsiveness as an early marker of bronchial response to occupational agents during specific inhalation challenges. Thorax 51: 472-478.

Wass U and Belin L 1990. An in vitro method for predicting sensitizing properties of inhaled chemicals. Scand. J. Work Environ. Health 16:208–214.

Weaver E 2004. Oral Reproductive/Developmental Toxicity Screening Test in Rats with Ammonium Persulfate in Feed. Covance Laboratories, Inc. Vienna, VA, USA. Covance Study Number 7463-101, FMC Study Number I2003-2337.

Wenninger JA, Canterbery RC and McEwen GN., eds. 2000. International cosmetic ingredient dictionary and handbook, 8th ed., Vol. 1–2, 80, 1168, 1387. Washington, DC: CTFA.

White IR, Catchpole HE, Rycroft RJ 1982. Rashes amongst persulphate workers. Contact Dermatitis 8: 168-172.

Last Update 05 February 2016

Chemical Identities

| Chemical Name in the Inventory and Synonyms | Peroxydisulfuric acid (((HO)S(O)2)2O2), dipotassium salt potassium persulfate (K2S2O8) peroxydisulfuric acid, dipotassium salt potassium peroxydisulfate |
|---|--|
| CAS Number | 7727-21-1 |
| Structural Formula | 0 |

| Molecular Formula | H2O8S2.2K |
|-------------------|-----------|
| Molecular Weight | 270 |

| Chemical Name in the Inventory and Synonyms | Peroxydisulfuric acid (((HO)S(O)2)2O2), diammonium salt ammonium persulfate ((NH4)2S2O8) peroxydisulfuric acid diammonium salt ammonium peroxydisulfate |
|---|---|
| CAS Number | 7727-54-0 |
| Structural Formula | 0 = S = 0 $0 = S = 0$ $0 =$ |
| Molecular Formula | H3N.1/2H2O8S2 |
| Molecular Weight | 228 |

| Chemical Name in the Inventory and Synonyms Peroxydisulfuric acid (((HO)S(O)2)2O2), disodium salt sodium persulfate (Na2S2O8) peroxydisulfuric acid disodium salt sodium peroxydisulfate | |
|---|--|
|---|--|

| 04/2020 | IMAP Group Assessment Report |
|--------------------|------------------------------|
| CAS Number | 7775-27-1 |
| Structural Formula | 0==s-00-s=0 |
| | |
| Molecular Formula | H2O8S2.2Na |
| Molecular Weight | 238 |

Share this page