Hydrogen peroxide (H2O2): Human health tier II assessment

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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

Chemical Identity

Synonyms	Hydrogen dioxide Dihydrogen dioxide Peroxide Hydroperoxide Hioxyl
Structural Formula	
Molecular Formula	H2O2
Molecular Weight (g/mol)	34
Appearance and Odour (where available)	Colourless liquid with slight sharp odour
SMILES	OO

Import, Manufacture and Use

Australian

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

The chemical has reported cosmetic use, particularly for hair bleaching and dyeing.

The chemical has reported domestic use including:

- as a bleaching agent; and
- in cleaning/washing agents and additives.

The chemical has reported commercial use including:

- as an oxidising agent; and
- in photochemicals.

The chemical has reported site-limited use in hydraulic fracturing.

The total volume introduced into Australia, reported under previous mandatory and/or voluntary calls for information, was between 10,000 and 100,000 tonnes.

International

The following international uses have been identified through European Union Registration, Evaluation, Authorisation and Restriction of Chemicals (EU REACH) dossiers; Galleria Chemica; Substances and Preparations in the Nordic countries (SPIN) database and the European Commission Cosmetic Ingredients and Substances (CosIng) database.

The chemical has reported cosmetic use.

The chemical has reported domestic uses, including in:

- bleaching agents;
- cleaning/washing agents and additives;
- drug/antiseptics, disinfectants;
- adhesives, binding agents;
- corrosion inhibitors;
- odour agents;
- paints, lacquers and varnishes;
- surface treatment; and
- surface-active agents.

The chemical has reported commercial uses including in:

- conductive agents;
- flux agents for casting or joining material;

- oxidising agents; and
- process regulators.

The chemical has reported site-limited uses, including as a product intermediate and in hydraulic fracturing.

The chemical has reported non-industrial uses, including in:

- food/feedstuff flavouring and nutrients;
- non-agricultural pesticides and preservatives;
- pesticides, agricultural; and
- pharmaceuticals.

Restrictions

Australian

Hydrogen peroxide is listed in the *Poisons Standard* (Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP, 2014)) in Schedule 5 with the following entry:

'HYDROGEN PEROXIDE (excluding its salts and derivatives):

(a) in hair dye preparations containing 12 per cent or less of hydrogen peroxide except in hair dyes containing 6 per cent or less of hydrogen peroxide; or

(b) in other preparations containing 6 per cent (20 volume) or less of hydrogen peroxide except in preparations containing 3 per cent (10 volume) or less of hydrogen peroxide'.

Hydrogen peroxide is also included in Schedule 6 with the following entry:

'HYDROGEN PEROXIDE (excluding its salts and derivatives) except:

(a) when included in Schedule 5;

(b) in hair dye preparations containing 6 per cent (20 volume) or less of hydrogen peroxide; or

(c) in other preparations containing 3 per cent (10 volume) or less of hydrogen peroxide'.

Hydrogen peroxide is listed in the Australia New Zealand Food Standards Code—Standard 1.3.3—Processing Aids—Permitted processing aids used in packaged water and in water used as an ingredient in other foods, as a bleaching, washing and peeling agent to treat all foods, and other miscellaneous uses. The maximum permissible limit (MPL) of residual hydrogen peroxide in the final food for the above permitted uses is 5 mg/kg (Food Standards Australia New Zealand, 2012).

The chemical is endorsed as a drinking water treatment chemical as listed in the Australian Drinking Water Guidelines (National Health and Medical Research Council, 2011).

International

Hydrogen peroxide is listed on the Health Canada List of prohibited and restricted cosmetic ingredients (The Cosmetic Ingredient "Hotlist").

It is listed by the United States Food and Drug Administration (US FDA) as a direct food substance affirmed as Generally Recognised as Safe (GRAS) (21 CFR 184.1366) and as acceptable to treat food as an antimicrobial agent, bleaching agent,

oxidising agent or for removing sulfur dioxide (US FDA, 2013).

Currently regulated in the European Union under Regulation (EC) No 1223/2009 in Annex III, part 1, with a limit of 0.1 % of hydrogen peroxide (or equivalent for substances that release hydrogen peroxide) in oral hygiene products, 12 % in hair products, 4 % in skin products and 2 % in nail-hardening products.

The chemical is classified as a hazardous substance under the *Hazardous Substances and New Organisms (HSNO) Act* of the Environmental Protection Authority, New Zealand.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia, 2014):

- Xn; R20/22 (acute toxicity)
- C; R35 (corrosivity)

Exposure Standards

Australian

The chemical has an exposure standard of 1.4 mg/m^3 (1 ppm) time weighted average (TWA).

International

The following exposure standards are identified (Galleria Chemica, 2014):

- TWA: 1.4 mg/m^3 (1 ppm) (Austria, Belgium, Denmark, Finland, France, Iceland, Korea, New Zealand, Norway, Peru, the United Kingdom and the USA).
- Short-Term Exposure Limit (STEL): 2–3 ppm (2.8–4.2 mg/m^3) (Finland, Sweden, the United Kingdom).

Health Hazard Information

Toxicokinetics

Hydrogen peroxide is an endogenous metabolite in aerobic cells. It is generated during cell respiration, and by oxidative stress and patho-physiological reaction, such as those involving activated phagocytes (Chance et al., 1979).

Limited data are available for oral, dermal and inhalation absorption of hydrogen peroxide in humans and animals. The small molecular weight and lack of charge facilitate rapid movement of hydrogen peroxide across biological membranes.

In cats, sublingual application of 9 % or 19 % ^{18}O-labelled hydrogen peroxide resulted in its rapid absorption and transport of the decomposition product ($^{18}O_2$) through arterial blood to the lungs. Within 34 minutes, one third of the labelled oxygen administered was detected in expired air with no increase in ^{18}O-carbon dioxide detected (Ludewig, 1965). Administering

hydrogen peroxide solutions to mucous membrane-lined body cavities resulted in increased oxygen in the venous blood and, if the amounts of hydrogen peroxide were sufficiently high, oxygen bubble formation occurred (ECB, 2003).

Hydrogen peroxide is also rapidly absorbed through the skin. In a dermal absorption study, following the application of 5–30 % solutions of hydrogen peroxide to rat skin, the chemical was localised in the epidermis within a few minutes. (Ludewig, 1964 as cited in ECB, 2003).

Topically applied hydrogen peroxide can penetrate the epidermis (or mucous membranes) followed by rapid spontaneous or enzyme-catalysed decomposition to oxygen and water in the underlying tissue (Hauschild et al., 1958).

In inhalation exposure studies, rabbits exposed to 1–6% hydrogen peroxide aerosol by inhalation showed oxygen-supersaturated arterial blood levels equivalent to oxygen administration at three atmospheres. When this dose was increased, small bubbles began to appear in the blood samples (Urschel, 1967 as cited in ECB, 2003).

No data were available on the distribution of hydrogen peroxide in body tissues. Both animal studies and human case reports indicate that hydrogen peroxide passes through the absorption surface, rapidly entering the adjacent tissues and blood vessels where it is degraded, liberating oxygen bubbles as it hydrolyses. While the bubbles are distributed in the circulation and cause lethal pulmonary and systemic embolic effects (ECB, 2003), at high concentrations of the chemical, the bubbles obstruct blood flow and prevent some hydrogen peroxide from entering the general circulation and exerting systemic effects (Dieter, 1988).

Hydrogen peroxide concentration in various tissues is regulated by the two main hydrogen peroxide-metabolising enzymes: catalase and glutathione peroxidase. Catalase decomposes hydrogen peroxide to form water and molecular oxygen. Glutathione peroxidase (more efficient at lower hydrogen peroxide concentrations) reduces hydrogen peroxide to water, consequently forming oxidised glutathione.

In the body, hydrogen peroxide can also undergo copper and iron-catalysed reactions (the Haber-Weiss- and Fenton reactions) to produce highly reactive hydroxyl radicals, which are capable of oxidising biomolecules in close proximity. Hydroxyl radical formation therefore mediates the cellular toxicity of hydrogen peroxide through lipid peroxidation, enzyme inactivation and DNA damage (ECB, 2003).

Acute Toxicity

Oral

Hydrogen peroxide has moderate acute toxicity from oral exposure. The acute oral median lethal dose (LD50) values in rats ranged from 805 mg/kg for 70 % hydrogen peroxide (Du Pont, 1996) to more than 5000 mg/kg for 10 % hydrogen peroxide solution (FMC, 1990a). The concentration dependence of the LD50 values, together with the local symptoms in the stomach, are consistent with acute toxicity and local corrosive effects.

In an acute oral toxicity study in rats using 70 % hydrogen peroxide, conducted in accordance with the Organisation for Economic Cooperation and Development (OECD) Test Guideline (TG) 401, clinical signs of toxicity were observed in all dose groups and included lethargy, immobility, irregular respiration and hunched posture. Gross changes of the tongue, oesophagus, stomach and duodenum, and adhesions in the peritoneal cavity were noted in decedent rats. At all dose levels, degenerative ulceration and regenerative hyperplasia of the pyloric antrum of the stomach were found. The LD50 in this study was 805 mg/kg bodyweight (Du Pont, 1996).

Dermal

Hydrogen peroxide has low acute toxicity from dermal exposure. The available acute dermal toxicity studies are generally poorly described. Dermal LD50 values for concentrated hydrogen peroxide solutions (90 %) ranged widely (700–5,000 mg/kg bw) depending on the species—rabbits being more sensitive to hydrogen peroxide than rats (Hrubetz et al., 1951).

For a 70 % solution, the dermal LD50 in rabbits was reported to be 9,200 mg/kg bw (FMC, 1979b). In a reliable study in rabbits, a 35 % hydrogen peroxide solution (dose 2000 mg/kg bw) under occlusive dressing for 24 hours did not result in any animal deaths. All animals displayed significant dermal effects, with a small number reported to show lacrimation and nasal discharge

(FMC, 1983a). An LD50 of 4060 mg/kg bw in rats was calculated in a poorly-reported study that probably tested a concentrated hydrogen peroxide solution (Kondrashov, 1977).

Inhalation

Hydrogen peroxide is moderately toxic to animals from inhalation exposure. In two aerosol exposure studies, mice were exposed to 12000–13000 mg/m^3 of aerosol generated from 90 % hydrogen peroxide for up to two hours (Punte et al., 1953). Half of the mice died after a 10–15 minute exposure. In a two-hour nose-only exposure study, doses of 920–2000 mg/m^3 (generated from a 70 % solution) were lethal to some mice (Solvay Duphar, 1995a). In the latter study, clinical signs in the decedents, such as discoloured skin on the head and tongue, subcutaneous emphysema and haemorrhages, red lymph nodes and diffuse red lungs were attributed to the bleaching and corrosive nature of the test substance.

In an acute inhalation toxicity study, conducted by a method equivalent to OECD TG 403, rats were exposed (whole body) for four hours to 170 mg/m^3 of hydrogen peroxide, which was the maximum attainable vapour concentration from a 50 % solution. There were no deaths and signs of toxicity were limited to nasal discharge and a transient decrease in body weight (FMC, 1990b).

In two more inhalation studies, rats were exposed (whole-body) to hydrogen peroxide vapour at 338–427 mg/m^3 concentrations ranging for four or eight hours. No deaths were reported, but pathological examination revealed congestion in the trachea and lungs. Localised areas of pulmonary oedema and alveolar emphysema were present in the lungs in addition to severe congestion (Comstock et al., 1954).

Observation in humans

Mortality has been observed in humans following accidental ingestion of hydrogen peroxide. A 2-year-old boy ingested 113–170 g of 35 % hydrogen peroxide (dose estimated at approximately 3800 mg/kg bw). Investigation showed gas in the heart and in the portal venous system, together with severe haemorrhagic gastritis without perforation. After death on day four, autopsy showed marked diffused cerebral oedema (Christensen et al., 1992). In a second case, a 16-month-old boy died 10 hours after ingesting approximately 230 g of 3 % hydrogen peroxide solution (dose estimated at 600 mg/kg bw). On postmortem examination there was frothy blood in the right ventricle and in the portal venous system. The gastric mucosa was red and the brain was oedematous. Histopathology showed oedema in the lungs, diffuse interstitial emphysema and gas emboli within the pulmonary vasculature and gastrointestinal lymphatics. Clear vacuoles were also found within the spleen, kidneys and myocardium (Cina et al., 1994).

Non-lethal poisoning has been reported in adults. Cerebral infarction, attributed to gas embolisation of the cerebral vasculature, was reported in an 84-year-old man who ingested 30 mL of 35 % hydrogen peroxide (dose estimated at approximately 150 mg/kg bw) (Sherman et al., 1994) and multiple brain embolisms occurred in a 63-year-old man who ingested 120 mL of a 35 % solution (dose estimated at approximately 600 mg/kg bw) (Ijichi et al., 1997).

Corrosion / Irritation

Respiratory Irritation

The respiratory irritation potential of hydrogen peroxide has been assessed in the mouse. Animals were exposed to aerosols generated from 70 % hydrogen peroxide at atmospheric concentrations of 300, 616, 1135, or 1856 mg/m^3. The RD50 value (the concentration causing a 50 % reduction in the respiratory rate) was estimated to be 665 mg/m^3, indicating that the aerosol was a respiratory irritant (Solvay Duphar, 1995b).

Skin Irritation

Hydrogen peroxide is corrosive to rabbit skin at 50 %, is moderately irritating at 35 % and only slightly irritating at 10 % concentrations.

Application of 3–8% hydrogen peroxide solutions to rabbit skin elicited mild reactions after a 24-hour occluded exposure (Du Pont, 1974). In studies conducted in accordance with OECD TG 404, a 10 % hydrogen peroxide solution was only slightly irritating (FMC, 1990a), while solutions at 50 % and higher concentrations were severely irritating and corrosive (FMC, 1990b).

In a rabbit study, conducted according to US EPA Guideline PB82-232984, 35 % hydrogen peroxide was applied under occlusive conditions for four hours on the dorsal skin. Slight to moderate erythema and/or oedema was observed in all rabbits at four and 24 hours post application; at 48 and 72 hours there were slight erythema and brown areas that developed into desquamation on day six. These effects persisted in 2/6 animals until at least day 14. The chemical was found to be a moderate skin irritant under the conditions of the test (FMC, 1983b).

In Draize tests in rabbits, 50 % hydrogen peroxide caused delayed corrosive effects after a one- or four-hour exposure, while similar effects were observed after a three-minute exposure to a 70 % solution (Du Pont, 1994).

Eye Irritation

Hydrogen peroxide is corrosive to rabbit eyes. Three Draize tests in rabbits, conducted in accordance with OECD TG 405, showed that solutions containing 5 %, 8 % and 10 % hydrogen peroxide exhibited the chemical's mild to highly irritating potential (FMC, 1987a, b and 1985).

In an ocular irritation study in rabbits, conducted in accordance with OECD TG 405, a 6 % hydrogen peroxide solution produced moderate corneal irritation. All animals developed slight corneal opacity, moderate iritis, mild or severe conjuctival redness and chemosis, with most exhibiting copious blood-tinged discharge (Sarver et al., 1996). Blanched conjuctiva and conjuctival haemorrhage with corneal vascularisation were observed in one rabbit. The eyes of 2/3 rabbits were clinically normal by 48 to 72 hours post application.

In a series of eye irritancy studies, conducted in accordance with the method described in the US Federal Hazardous Substances Act using an 8 %, 10 % or 12 % hydrogen peroxide solution, both 10 % and 12 % solutions produced generalised, severe injury in rabbit eyes. Penetrating corneal injury, iritis and conjunctivitis were observed (Du Pont, 1972b).

Observation in humans

Numerous accidental dermal and ocular exposures to hydrogen peroxide have been reported. The most common clinical findings for dermal exposures were abnormal tingling or prickling sensation, whitening and blistering (Dickson and Caravati, 1994). Ocular exposure caused burning, redness and blurry vision, generally as mild and transient effects (Dickson and Caravati, 1994).

In 10 volunteers, the threshold of detection for irritation was approximately 0.1 %, and less than 0.03 % when hydrogen peroxide was administered as drops directly to the eye or via contact lenses, respectively (McNally, 1990). In another ocular study in eight volunteers, the threshold of irritation (as measured by subjective discomfort and conjunctival hyperaemia) was 0.02 % when hydrogen peroxide was administered in a hydrogel contact lens (Paugh et al., 1988). A woman who had inadvertently stored a contact lens in a 3 % hydrogen peroxide disinfectant solution experienced hyperaemia, tearing, and eyelid spasm (Knopf, 1984).

In two occupational exposure cases, seven dairy workers exposed to approximately 12 mg/m^3 of hydrogen peroxide vapour (and possibly briefly to 41 mg/m^3), experienced eye and throat irritation (Kaelin et al., 1988) while slight nasal irritation was observed in factory workers involved in filling a vessel at a hydrogen peroxide production facility after a one-hour exposure to a maximum concentration of 3.5 mg/m^3 (CEFIC, 1996).

In 32 volunteers, the threshold of detection for irritation through inhalation exposure was 10 mg/m^3 (independent of the exposure time, which was from 5 minutes to four hours) when hydrogen peroxide vapour was inhaled through the nose using a face mask (Kondrashov, 1977).

Sensitisation

Skin Sensitisation

Hydrogen peroxide is not considered to be a skin sensitiser. There was no evidence of delayed contact hypersensitivity to 0.1 % or 3 % hydrogen peroxide in 10 guinea pigs tested using a modified Magnusson–Kligman procedure (Du Pont, 1953). Test solutions were re-applied six times over a two-week period before a challenge to evaluate sensitisation.

Repeated Dose Toxicity

Oral

Several rodent studies have been conducted to characterise the repeated dose toxicity of hydrogen peroxide by oral exposure. Decreased body weight gain was a common finding in all studies, as were decrements in the erythrocyte count, haematocrit, plasma protein concentration and plasma catalase. Localised effects, including changes to the gastric and duodenal mucosa, were considered to be irritant effects of the chemical.

In a reliable 90-day drinking water study, C57BL/6N mice (catalase deficient) were given 0, 100, 300, 1000, or 3000 ppm hydrogen peroxide in drinking water (male: 26, 76, 239, or 547 mg/kg bw/day; female: 37, 103, 328, or 785 mg/kg bw/day), for 90 days, followed by 42 recovery days. Reduced bodyweight gain, food and water consumption (males), decreased blood protein and globulin (males) were observed in the highest dose animals. Duodenal mucosal hyperplasia observed during the feeding period was resolved during recovery period. At the 300 and 1000 ppm doses, reduced food and water consumption (females) and duodenal mucosal hyperplasia that resolved during recovery, were observed. A no observed adverse effect level (NOAEL) of 100 ppm (corresponding to 26 and 37 mg/kg bw/day for males and females, respectively) was found, based on dose-related reductions in food and water consumption, and on the observed duodenal mucosal hyperplasia (Weiner et al. (1998).

In a 100-day gavage study, male Wistar rats were given 0, 6, 10, 20, 30, or 60 mg/kg bw/day hydrogen peroxide by gavage. Decreased body weight gain and transient increase in spleen weight, altered haematological and clinical chemistry values, including decreased plasma catalase, were observed in the highest dose group. At 30 mg/kg bw/day, decreased plasma catalase was noted. A NOAEL of 20 mg/kg bw/day was established, based on the decrease in plasma catalase (Kawasaki et al., 1969).

Dermal

There are no reliable studies on repeated dose dermal effect of hydrogen peroxide available. In a poorly-reported and unconventional study, rats with shaved skin were exposed (whole body) to hydrogen peroxide vapour at 0.1–10.1 mg/m^3 for five hours/day over four months (Kondrashov, 1977). The lowest observed effect concentration (LOEC) for vapours on the rat skin was reported to be 1 mg/m^3, with a no observed effect concentration (NOEC) of 0.1 mg/m^3, based on histo-enzymological staining of the epidermis sections that showed an increase in the activity of four tissue enzyme levels.

Inhalation

Hydrogen peroxide causes adverse health effects from repeated inhalation exposure. In a range-finding study, conducted in accordance with OECD TG 412, Alpk:APfSD rats were exposed to hydrogen peroxide vapour at 2.9, 14.6, or 33 mg/m^3 for five days per week over a period of 28 days (CEFIC, 2002). Clinical signs demonstrating respiratory tract irritation seen at the mid and high doses included necrosis and inflammation of the epithelium in the anterior regions of the nasal cavity. Mononuclear cell infiltration in the larynx was also seen at the highest dose. Perivascular neutrophil infiltration and haemorrhage in the lungs of

some animals was observed, although this was not dose related. A no observed adverse effect concentation (NOAEC) of 2.9 mg/m^3 was derived, based on local irritation effects at 14.6 mg/m^3.

Observation in humans

Adverse health effects have been reported in some workers repeatedly exposed to hydrogen peroxide. Progressive dyspnoea and nodular infiltrates of the lungs were described in a milk packaging machine operator after exposure to hydrogen peroxide vapour over a three-year period for 2–5 days per week. Air measurements of peroxide were approximately 12 mg/m^3, with transient elevations up to 41 mg/m^3. At work he (and six others) had noticed eye and throat irritation and gradual bleaching of the hair. Pulmonary function testing was consistent with interstitial lung disease and subsequent biopsy revealed alveolar collapse, thickening of the alveolar walls and interstitial infiltration by mononuclear cells. Upon withdrawal from the occupational exposure, the patient improved progressively with treatment. The authors attributed the clinical condition to the high hydrogen peroxide exposure, although heavy smoking could have been a contributing factor (Kaelin et al., 1988).

Six workers exposed to hydrogen peroxide vapours for up to three years in fruit juice packaging operations complained of irritation in the eyes and airways, headaches, temporary loss of olfaction, skin symptoms, and blanching of hair. Peak exposures up to 11 mg/m^3 (eight-hour TWA 2–3 mg/m^3) of peroxide in the air were measured in the breathing zone of the individuals, with those who handled peroxide-treated cartons reporting burning and prickling of the fingers, drying hands and face, and decreased skin elasticity. Three machine operators exhibited recurring bronchitis-sinusitis, coincidently with a 10-month period of high vapour concentrations, with two other patients presenting with bronchoconstriction and asthma symptoms. As the study did not include specific lung examinations, possible chronic lung changes caused by peroxide could not be evaluated; however, all patients monitored regained good health after the exposures were reduced (Riihimaki et al., 2002).

Genotoxicity

Hydrogen peroxide is not considered to be genotoxic. Although it gave a positive response in some in vitro tests without metabolic activation, in vivo genotoxicity studies employing modern methodologies were all negative.

In many gene mutation assays conducted in bacteria, hydrogen peroxide caused an increased number of revertants, which were primarily observed in strains sensitive to oxygen radicals. In mammalian cells, positive results were generally recorded in numerous assays validated to detect gene mutations, DNA damage and repair, unscheduled DNA synthesis (UDS), sister chromatid exchange, and chromosomal aberrations. The responses observed were modified by the presence of peroxide-degrading enzymes (including catalase), the extent of formation of hydroxyl radicals (via the Fenton reaction), and the ability of the cell to repair (ECB, 2003).

In contrast to the in vitro assays, negative results for the chemical were obtained in four erythrocyte micronucleus tests when administered to mice (via oral and intraperitonial routes) at doses up to 1000 mg/kg bw (Liarskii et al., 1983; Du Pont, 1995; CEFIC, 1995). The absence of chromosomal abnormalities in the bone marrow of these mice might be explained by the hydrogen peroxide decomposing in the gut or peritoneum before absorption and/or the high catalase activity of red blood cells, which can decompose the chemical after absorption.

A UDS study in rats, conducted in accordance with OECD TG 486, with concentrations up to 50 mg/kg bw, showed that the chemical was unable to induce UDS (CEFIC, 1997).

As a pre-screen for carcinogenicity, 0.2–3.2% hydrogen peroxide solutions were applied to the skin of Sencar mice twice weekly for four weeks (Society for Plastic Industry, 1997). There were no indication of induced DNA damage, mutations, epidermal hyperplasia or dermal cellularity changes.

A single dose of 3 % hydrogen peroxide did not induce germ cell damage in male *Drosophila* larvae in a sex-linked recessive lethal test (Di Paolo, 1952).

Overall, hydrogen peroxide is capable of acting as a genotoxicant in vitro through the reaction of hydroxyl radicals in direct contact with the target DNA. In general, adding exogenous metabolic activators (including catalase) reduces or abolishes the

mutagenicity. Most available in vivo studies do not support a significant mutagenicity of hydrogen peroxide, which could, in part, be due to the reduced systemic bioavailability of the chemical.

Carcinogenicity

Hydrogen peroxide is not considered to be carcinogenic, although it showed a weak potential to induce local carcinogenic effects in the duodenum of sensitive mouse strains. The lesions caused by exposure to hydrogen peroxide showed a marked tendency to regress or disappear after treatment ceased.

In a chronic exposure study, catalase deficient C57BL/6J mice were given 0, 0.1, or 0.4% hydrogen peroxide in drinking water (estimated doses of 300 and 1200 mg/kg bw/day) for 100 weeks (Ito et al., 1981). There was a dose-dependent incidence of erosion and ulceration in the glandular stomach, as well as single or multiple duodenal nodules, which were classified as hyperplasia, adenoma or carcinoma by their histopathological appearance. Localised duodenal carcinomas were found only in treated mice (5 % in the high dose, 1 % in the low dose and none among the controls) with these carcinomas invading the muscular layer and small vessels, but no metastatic tumours were evident.

In a limited follow up to the previous study, the effect of hydrogen peroxide on the stomach and duodenum was studied in three mouse strains (Ito et al., 1981). The C57BL/6N, DBA/2N, BALB/cAnN mice were treated with 0, 0.1, or 0.4 % hydrogen peroxide in drinking water for variable periods up to 740 days. After 140 days of treatment, the chemical was replaced with distilled water for 10-30 days. In C57BL mice, gastric lesions seen in the forestomach of mice exposed for at least 60 days mostly regressed and even disappeared after treatment ceased. Among the same strain of mice given 0, 0.1 and 0.4 % hydrogen peroxide for 420–740 days, 0 %, 1 % and 5 %, respectively, developed duodenal cancer, though they did not show any distant metastases.

In an oral tumour promotion study, rats given 1 % hydrogen peroxide in drinking water for 32 weeks did not show carcinogenic or tumour promotion activity, but the incidence of squamous cell papillomas in the forestomach was significantly increased (Takahashi et al., 1986). Rats given near lethal doses (1.5 %) of hydrogen peroxide in drinking water for 21 weeks did not develop any carcinomas in the gastrointestinal tract (Hirota & Yokoyama, 1981).

In an oral cavity tumour promotion study, a 30 % hydrogen peroxide solution was painted onto one buccal pouch of hamsters twice weekly for 22 weeks. Although chronic inflammation, hyperchromatic cells and dysplasia were noted, there were no tumours found (Weitzman et al., 1986).

In a skin tumour promotion study, female Sencar mice were used to test the complete carcinogenic activity of hydrogen peroxide. Mice received twice weekly topical applications of hydrogen peroxide (15 %) for 25 weeks. No squamous-cell carcinoma was found when these animals were observed for up to 50 weeks (Klein-Szanto & Slaga, 1982).

Overall, although hydrogen peroxide has a weak potential to induce a local carcinogenic effect in the duodenum of sensitive mouse strains, it is notable that the lesions showed a marked tendency to regress or disappear after treatment ceased. Based on these studies, the International Agency for Research on Cancer (IARC) concluded that there is limited evidence in laboratory animals for the carcinogenicity of hydrogen peroxide. It also concluded that there is inadequate evidence in humans for carcinogenicity of the chemical, and as such hydrogen peroxide is not classifiable regarding its carcinogenicity to humans (Group 3) (IARC, 1999).

Reproductive and Developmental Toxicity

Fertility

There are no reliable data on the reproductive toxicity of hydrogen peroxide. Some non-guideline studies were considered to be poorly designed and/or inadequately reported; therefore, it was difficult to evaluate the effects of hydrogen peroxide on reproductive system.

In a 1959 reproductive toxicity study, male rats were given 0.33 or 1 % hydrogen peroxide in drinking water. There were no controls (Wales et al., 1959). All female mice mated to treated males became pregnant and in each case, healthy young rats were born in litters of normal size. The concentration, morphology and motility of the spermatozoa after three weeks of treatment appeared normal. There were also no detectable abnormalities in the sperm of albino rabbits given 0.33, 1, or 3 % hydrogen peroxide in drinking water for six weeks.

Three weanling female rats were given 0.45 % hydrogen peroxide in drinking water for five months before being mated with untreated males. Normal litters were produced, suggesting that long-term treatment with the chemical did not appear to affect reproduction in female rats (Hankin, 1958).

Male and female rats were treated by gavage with 0.005, 0.05, 0.5, 5, and 50 mg of hydrogen peroxide/kg bw/day for six months before mating. Variations seen in the oestrous cycle in females were not dose dependent. Reduced mobility of spermatozoa in males was observed at the top dose, with no changes in the morphology and weight of the testes. Among the high-dose females, only 3/9 produced litters, compared with 7/9 in the control group, and both litter size and body weight gain of the offspring was reduced in the treated group (Antonova, 1974).

Overall, the data available are insufficient to allow evaluation of reproductive toxicity.

Developmental toxicity

Foetotoxic effects (including decreased bodyweight, skeletal hypoplasias, organs haemorrhages and increased mortality) were seen in the only developmental toxicity study available, in which pregnant Wistar rats were fed on a powdered feed mixed with up to 10 % hydrogen peroxide (Moriyama et al., 1982). There are major deficiencies in the study design, including test substance stability, diet palatability, dose uncertainty and small group sizes. The investigators proposed that the deleterious effect was due to the breakdown of essential nutrients in food by hydrogen peroxide. The poor study design and reporting limit the significance of these findings.

Overall, the only developmental toxicity study available for the chemical was judged as inadequate for evaluation.

Risk Characterisation

Critical Health Effects

Hydrogen peroxide has moderate acute toxicity from oral and inhalation exposure, and low acute toxicity from dermal exposure. The chemical is corrosive to the skin and eyes and is a respiratory irritant.

Public Risk Characterisation

Hydrogen peroxide has uses in domestic and cosmetic products. The main route of public exposure is expected to be through the skin and eyes. The labelling of hydrogen peroxide formulations is controlled by the *Poisons Schedule*. Provided that the appropriate precautions are taken to avoid skin and eye contact and inhaling chemical vapours, the risk from the use of domestic and cosmetic products is not considered to be unreasonable.

Occupational Risk Characterisation

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

Given the critical health effects, the chemical 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

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 chemical should be labelled in accordance with state and territory legislation (SUSMP).

Work Health and Safety

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

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Acute Toxicity	Harmful if swallowed (Xn; R22)* Harmful by inhalation (Xn; R20)*	Harmful if swallowed - Cat. 4 (H302) Harmful if inhaled - Cat. 4 (H332)
Irritation / Corrosivity	Causes severe burns (C; R35)*	Causes severe skin burns and eye damage - Cat. 1A (H314) May cause respiratory irritation - Specific target organ tox, single exp Cat. 3 (H335)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for consumers

Products containing the chemical 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 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 storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures which could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;

- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- 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 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 chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

References

Antonova VI, Salmina ZA, Latkina LL, Bukina AP and Mishina NE (1974) Argumentation hygienique de la concentration limite admisible en peroxyde dehydrogene dans les reservoirs d'eau. [Russian, French translation]. Gig Sanit 10: 20-22.

CEFIC (1995) Micronucleus Test by Intraperitoneal Route in Mice. Hydrogen Peroxide. CEFIC Peroxygen Sector Group, CIT/Study No. 12240 MAS/HYDROGEN PEROXIDE/CEFIC. Centre International de Toxicologie (CIT),Miserey.

CEFIC (1996) Determination of Hydrogen Peroxide Concentration in the Expired Air of Healthy Human Volunteers. Solvay Duphar B.V. Environmental Research Department, Weesp, CEFIC Peroxygen Sector Group.

CEFIC (1997) Hydrogen Peroxide: Measurement of Unscheduled DNA Synthesis in Rat Liver Using in vitro and in vivo/in vitro Procedures. Final Report No. 514/24-1052. Covance Laboratories Limited, Harrogate, CEFIC Peroxygen Sector Group.

CEFIC (2002) Hydrogen Peroxide: 28-day Inhalation Study in Rats. CTL/MR0211/Technical Toxicology/Report.

Chance B, Sies H and Boveris A (1979) Hydroperoxide metabolism in mammalian organs. Physiological Reviews 59: 527-605.

Christensen DW, Faught WE, Black RE, Woodward GA and Timmons OD (1992) Fatal oxygen embolization after hydrogen peroxide ingestion. Crit Care Med 20: 543-544.

Cina SJ, Downs JCU and Conradi SE (1994) Hydrogen peroxide: a source of lethal oxygen embolism. Am J Forensic Med Pathol 15: 44-50.

Comstock CC, Hackley EB and Oberst FW (1954). The Inhalation Toxicity of 90% Hydrogen Peroxide Vapor for Acute, Subacute, and Chronic Exposures to Laboratory Animals. Chemical Corps Medical Laboratories Research Report No. 243. Army Chemical Center, Edgewood, MD.

CosIng. Cosmetic Ingredients and Substances. Accessed November 2014 at http://ec.europa.eu/consumers/cosmetics/cosing/

Di Paolo JA (1952) Studies on chemical mutagenesis utilizing nucleic acid components, urethane and hydrogen peroxide. The American Naturalist 826: 49-56.

Dickson KF and Caravati EM (1994) Hydrogen peroxide exposure - 325 exposures reported to a regional poison control center. Clinical Toxicology 32: 705-714.

Dieter HH (1988) Problems of the Toxicological Compatibility of Hydrogen Peroxide in Drinking and Swimming Pool Water for Humans from the Pharmacokinetic and Biochemical Points of View [in German] Z Wasser Abwasser Forsch 21: 143-140.

Du Pont (1953) Primary Irritancy and Skin Sensitization Tests. Memphis Hydrogen Peroxide 3%. Medical Research Project. E.I. Du Pont de Nemours and Company, Wilmington, DE.

Du Pont (1974) Skin Irritation Test on Rabbits. Haskell Laboratory Report August 13, 1974. E.I. du Pont de Nemours and Company, Wilmington, DE.

Du Pont (1994) Skin Corrosion Test with Hydrogen Peroxide in Rabbits. Haskell Laboratory Report No. 6-94. E.I.du Pont de Nemours and Company, Newark, DE.

Du Pont (1995) An Evaluation of the Stability and Palatability of Hydrogen Peroxide in Water and its Potential Genotoxicity in Bone Marrow when Administered to Mice in Drinking Water. Haskell Laboratory Report No. 723-94 (Sponsor: CEFIC Peroxygen Toxicity Group). E. I. Du Pont de Nemours and Company, Newark, DE.

Du Pont (1996) Acute Oral Toxicity Study with Hydrogen Peroxide (70%) in Male and Female Rats. Haskell Laboratory Report No. 323-95. Du Pont Specialty Chemicals, E.I. du Pont de Nemours and Company, Wilmington, DE.

DuPont (1972) Federal Hazardous Substances Act Test - Rabbit Eye Irritation. Haskell Laboratory Report July 12, 1972. E.I.du Pont de Nemours and Company, Wilmington, DE.

ECB (European Chemicals Bureau) (2003) European Union Risk Assessment Report Hydrogen peroxide CAS No: 7722-84-1 EINECS No: 231-765-0, Final Report, 2003. European Commission – Joint Research Centre, Institute for Health and Consumer Protection. Office for Official Publications of the European Communities, Luxembourg. Accessed in December 2013 at http://esis.jrc.ec.europa.eu/doc/risk_assessment/REPORT/.pdf

FMC Corporation (1979a) Acute Oral Toxicity of Hydrogen Proxide (70%). Study No. ICG/T79027-01. FMC Corporation, Princeton, NJ.

FMC Corporation (1979b) Acute Dermal Toxicity of 70% Hydrogen Peroxide in Rabbits. Study No. ICG/T79027-02. FMC Corporation, Princeton, NJ.

FMC Corporation (1983a) Acute Dermal Toxicity of 35% Hydrogen Peroxide in Rabbits. Study No. I83-746. FMC Toxicology Laboratory, Somerville, NJ.

FMC Corporation (1983b) Primary Skin Irritation and Corrosion of 35% Hydrogen Peroxide in Rabbits. Study No.I83-747. FMC Toxicology Laboratory, Princeton, NJ.

FMC Corporation (1985) Preliminary Eye Irritation of 10% Hydrogen Peroxide in Rabbits. FMC Study No. I84-851. FMC Toxicology Laboratory, Princeton, NJ.

FMC Corporation (1987a) 5% Hydrogen Peroxide. Preliminary Eye Irritation Study in Rabbits. FMC Study No. I86-0949. FMC Toxicology Laboratory, Princeton, NJ.

FMC Corporation (1987b) Hydrogen Peroxide 8% STD. Preliminary Eye Irritation Study in Rabbits. FMC Study No. I87-0950. FMC Toxicology Laboratory, Princeton, NJ.

FMC Corporation (1990a) Hydrogen Peroxide 10% Standard Grade. Acute Oral Toxicity Study in Rats. Study No. I89-1077. FMC Corporation Toxicology Laboratory, Princeton, NJ.

FMC Corporation (1990b). An Acute Inhalaton Toxicity Study of Vapors of Hydrogen Peroxide (50%) in the Rat.Bio/Dynamics Project No. 89-8233 (FMC No.189-1080). FMC Corporation, Princeton, NJ.

Food Standards Australia and New Zealand. Accessed November 2014 at

http://www.foodstandards.gov.au/scienceandeducation/factsheets/factsheets/sulphites.cfm.

Galleria Chemica. Accessed November 2014 at http://jr.chemwatch.net/galleria/

Hankin L (1958) Hydrogen peroxide, ingestion and the growth of rats. Nature 181: 1453.

Hauschild F, Ludewig R, and Mühlberg H (1958) Über die "ätzende" Wirkung von Wasserstoffperoxyd. Naunyn-Schmiedeberg's Arch Exp Pathol Pharmak 235: 51-62.

Hirota N and Yokoyama T (1981) Enhancing effect of hydrogen peroxide upon duodenal and upper jejunal carcinogenesis in rats. Jpn J Cancer Res (Gann). 72: 811-812.

Hrubetz MC, Conn LW, Gittes HR and MacNamee JK (1951) The Cause of the Increasing Intravenous Toxicity of 90% Hydrogen Peroxide with Progressive Dilutions. Chemical Corps Medical Laboratories Research Report No. 75. Army Chemical Center, Maryland.

IARC (1999) Monograph on the Evaluation of Carcinogenic Risk Chemicals to Humans. Hydrogen peroxide. 71: 671-689 Lyon, France: World Health Organization. International Agency for Research on Cancer.

Ijichi I, Itoh T, Sakai R, Nakaji K, Miyauchi T, Takahashi R, Kadosaka S, Hirata M, Yoneda S, Kajita Y and Fujita Y (1997) Multiple brain embolism after ingestion of concentrated hydrogen peroxide. Neurology 48: 277-79.

Ito A, Watanabe H and Naito M (1981) Prevalence of Gastric Erosions and Duodenal Tumors with a Continuous Oral Administration of Hydrogen Peroxide in C57BL/6J Mice. Study Report. Research Institute for Nuclear Medicine and Biology, Department of Cancer Research, Hiroshima.

Ito R, Kawamura H, Chang HS, Toida S, Matsuura S, Hidano T, Nakai S, Inayoshi Y, Matsuura M, and Akuzawa K (1976) Oral safety on hydrogen peroxide, acute and subacute toxicity. [Japanese, English translation]. J Med Soc Toho 23: 531-537.

Kaelin RM, Kapanci Y and Tchopp JM (1988) Diffuse interstitial lung disease associated with hydrogen peroxide inhalation in a dairy worker. Ann Rev Resp Disease 137: 1233-1235.

Kawasaki C, Kondo M, Nagayama T, Takeuchi Y and Nagano H (1969) Effect of hydrogen peroxide on the growth of rats. [Japanese, translation]. J Jap Food Hygiene Soc 10: 68-72.

Klein-Szanto AJP and Slaga TJ (1982) Effects of peroxides on rodent skin: Epidermal hyperplasia and tumor promotion. J Invest Dermatol 79: 30-34.

Knopf HLS (1984) Reaction to hydrogen peroxide in a contact-lens wearer. Amer J Ophthalmol 97: 796 -800.

Kondrashov VA (1977) Evaluation of the toxicity of hydrogen peroxide vapors for inhalation and percutaneous exposures. [Russian, English translation]. Gig Tr Prof Zabol 21: 22-25.

Liarskii PP, Gleiberman SE, Pankratova GP, Iaroslavskaja LA and Iurchenko VV (1983) Toxicological and hygienic characterization of disinfectants based on hydrogen peroxide and its derivatives. [Russian, English translation]. Gig Sanit 48: 28-31.

Ludewig R (1964) Hydroperoxidase-Verteilung in der Haut und Transepidermale Pene-tration von Wasserstoffperoxid nach Epikutaner Applikation. Acta Histochem 19: 303-315.

Ludewig R (1965) Nachweis von 18O in Expirationsluft und Blut während sublingualer Einwirkung 18Omarkierten Wasserstoffperoxids. Abhandl. Deutsch. Akad Wiss Berlin, Kl Chem Geol Biol 7: 549-552.

McNally JJ (1990) Clinical aspects of topical application of dilute hydrogen peroxide solutions. The CLAO journal 16: S46-S51.

Moriyama I, Hiraoka K, Fujita M, Ichijo M and Ioka H (1982) Effects of food additive hydrogen peroxide studied in fetal development. [Japanese, English translation]. Acta Obst Gynaec Japan 34: 2149-2154.

NHMRC (2011) Australian Drinking Water Guidelines. National Health and Medical Research Council. Accessed June 2014 at http://www.nhmrc.gov.au/guidelines/publications/eh52.

Paugh JR, Brennan NA and Efron N (1988) Ocular response to hydrogen peroxide. Am J Optom and Physiol Optics 65: 91-98.

Punte CL, Saunders LZ and Krackow EH (1953) The Inhalation Toxicity of Aerosols of 90% Hydrogen Peroxide. Chemical Corps Medical Laboratories Research Report No. 189. Army Chemical Center, MD.

REACH Dossier (REACH). Hydrogen peroxide (CAS No. 7722-84-1). Accessed November 2014 at http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

Riihimäki V, Toppila A, Piirilä P, Kuosma E, Pfäffli P & Tuomela P (2002) Respiratory health in aseptic packaging with hydrogen

peroxide. Report of two cases. J Occup Health 44: 433-438.

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed November 2014 at http://hsis.safeworkaustralia.gov.au/HazardousSubstance

Sarver JW, Finlay C, Brock WJ and Malek DE (1996) Eye irritation and skin corrosion evaluations with hydrogen peroxide. J Am Coll Toxicol 15: S112-S114.

Sherman SJ, Boyer LV and Sibley WA (1994) Cerebral infarction immediately after ingestion of hydrogen peroxide solution. Stroke 25: 1065-1067.

Society for the Plastic Industry (1997) Determination of the Potential for Organic Peroxides to Induce Sustained Skin Hyperplasia and DNA Damage. Final Report SPI/SPRD Study #96-1. The University of Texas, MD Anderson Cancer Center, Smithville, TX.

Solvay Duphar (1995a) An Acute Inhalation Study of Hydrogen Peroxide Aerosols in Male Mice. Department of Drug Safety Report No. S. 9403. Solvay Duphar B.V., Weesp.

Solvay Duphar (1995b) An Evaluation of the Respiratory Irritating Properties of Hydrogen Peroxide Aerosols in Male Swiss Mice. Department of Drug Safety Report No. S. 9404. Solvay Duphar B.V., Weesp.

SPIN (Substances in Preparations in Nordic Countries) Database. Available: http://195.215.202.233/DotNetNuke/default.aspx

SUSMP (2014) The Standard for the Uniform Scheduling of Medicines and Poisons at http://www.comlaw.gov.au/Details/F2012L01200/Download

Takahashi M, Hasegawa R, Furukawa F, Toyoda K, Sato H and Hayashi Y (1986) Effects of ethanol, potassium metabisulphite, formaldehyde and hydrogen peroxide on gastric carcinogenesis in rats after initation with N-methyl- N'-nitro-N-nitrosoguanidine. Jpn J Cancer Res (Gann) 77: 118-124.

Urschel Jr. HC (1967) Progress in cardiovascular surgery. Cardiovascular effects of hydrogen peroxide: current status. Prog Cardiovasc Surg (Dis Chest) 51: 180-192.

USFDA (2013)) 21CFR184.1903 – Select Committee on GRAS Substances (SCOGS) Opinion: Sodium hydroxide. Direct food substances affirmed as Geneally Recognised As Safe (GRAS) at http://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS/ucm260919.htm

Wales RG, White IG and Lamond DR (1959) The spermicidal activity of hydrogen peroxide in vitro and in vivo. J Endocrin 18: 236-244.

Weiner ML, Feeman C, Trochimowicz H, Brock W, De Gerlache J, Malinverno G, Mayr W, Regnier JF (1998) A 13-week drinking water study with 6-week recovery period in catalase-deficient mice with hydrogen peroxide. Toxicol Letters 95 (Suppl 1): 175-182.

Weitzman SA, Weitberg AB, Stossel TP, Schwartz J and Shklar G (1986) Effects of hydrogen peroxide on oral carcinogenesis in hamsters. J Periodontol 57: 685-688.

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