Health Risk Assessment of Household Bleach

May 2015

PREPARED FOR:	**Ministry of Health**
CLIENT REPORT No:	**FW14001**
PREPARED BY:	**Matt Ashworth**
REVIEWED BY:	**Peter Cressey, Jeff Fowles**

ACKNOWLEDGEMENTS

The author would like to acknowledge and thank the following people for their technical contributions to this report: Dr. Natalia Foronda (New Zealand Ministry of Health), Mr Peter Cressey (ESR).

Manager	Peer reviewer	Author
Rob Lake	**Jeff Fowles**	**Matt Ashworth**
Manager, Risk and Response Group	Consultant Toxicologist, Tox-Logic LLC, USA	Scientist, Risk and Response Group

DISCLAIMER

CONTENTS

LIST OF TABLES

EXECUTIVE SUMMARY

This report presents a health risk assessment for household bleach sold for non-occupational use in New Zealand. The purpose of this health risk assessment is provide the Ministry of Health with the information needed for determining whether public health actions are needed to reduce or minimise the public health risk from household bleach.

Exposure to bleach is identified as a reason for enquiries to the National Poisons Centre helpline (average of 110 calls per year, 2008–2012) and hospitalisations (average of 26 per year, 2006–2011) in New Zealand, although no mortality has been attributed to accidental exposure to household bleach in the years studied. These data represent the information which is recorded in the National Minimum Dataset and by the National Poisons Centre.

Research in New Zealand and internationally has identified children as being most likely to be accidentally exposed to household bleach. These exposures are predominantly by ingestion. Dermal and inhalation exposure represent a far smaller percentage of reported accidental exposures, but have also been considered in the report.

Household bleach is a mixture of compounds formulated with two principal active ingredients, sodium hypochlorite (NaOCl) and sodium hydroxide (NaOH). Ingestion of NaOCl and NaOH was estimated for children aged 2 to 3 years and 6 to 11 years of age, with body weights at the 5th and 50th percentile. Ingestion was assumed to have been of 50 mL of either 5% or 10% sodium hypochlorite solutions (and 0.01% and 0.05% sodium hydroxide respectively) as undiluted household bleach. Hazard quotient values calculated for NaOCl exceeded 1 indicating that NaOCl may cause injury. No hazard index (HI) value was calculated for the mixture of NaOCl and NaOH which constitutes household bleach as no reference dose or suitable point of departure was found for the mixture as formulated. However case studies of accidental ingestion indicated that in cases where the mixture consumed did not exceed 5% NaOCl, injury was minor and the treatment required was not extensive or of long duration; and concentrations greater than this led to greater risk of injury.

Hazard quotient values for dermal exposure to household bleach under the scenarios proposed were less than 1, indicating that they are unlikely to cause injury. Where data from experimentation were lacking, published case studies provided indications that accidental dermal exposure to household bleach of concentrations available in New Zealand may cause injury due to local irritant or corrosive effects.

Calculations of the potential inhalation exposure shows that the uptake of NaOCl is in the range of 2.0–10.8 mg/kg BW, across both age and percentile groups. This suggests that injury may be caused by this single exposure to the two subject groups when faced with high concentration household bleach being sprayed directly into the face.

[Intentionally Blank]

1 INTRODUCTION

The purpose of this report is to develop a generic health risk assessment for household bleach.

The report is presented in sections which relate to hazard identification, dose-response, exposure assessment and risk characterisation.

Exposure to bleach is identified in the New Zealand Hazardous Substances Surveillance System[1] as a reason for enquiries to the National Poisons Centre helpline (average of 110 calls per year, 2008–2012) and hospitalisations (average of 26 per year, 2006–2011), although no mortality has been attributed to accidental exposure to bleach in recent years. These data represent the information which is recorded in the National Minimum Dataset and by the National Poisons Centre.

Research in New Zealand and internationally has identified children as being most likely to be accidentally exposed to household bleach. These exposures are predominantly by ingestion. Dermal and inhalation exposure represent a far smaller percentage of reported accidental exposures, but have also been considered in the report.

Household bleach is a mixture of compounds formulated with two principal active ingredients, sodium hypochlorite (NaOCl) and sodium hydroxide (NaOH) with the balance being made up predominantly of water. Household bleach is, in general, a solution containing 3–10% (30–100 mL/L) NaOCl and 0.01–0.05% (0.1–0.5 mL/L) NaOH. The NaOH is used to slow the breakdown of NaOCl into sodium chloride and sodium chlorate (Smith 1994). Additional compounds such as gelling agents, fragrance and detergents may be added on a product by product basis. Less commonly household bleach may contain 3% of either hydrogen peroxide (H_2O_2) (Meyer et al 2007), sodium peroxide (Na_2O_2), or sodium perborate ($NaBO_3$) (McGuigan 1999). These are not considered in this health risk assessment. Household bleach is classified as hazardous according to the Hazardous Substances (Classification) Regulations, 2001 New Zealand. The New Zealand Environmental Protection Authority (EPA) differentiates between household bleach (3% to 5% NaOCl concentration) and strong bleach (greater than 25% NaOCl concentration) the latter being subject to regulation for holdings in excess of 100 litres (EPA Bleach[2] information page). This report only considers non-occupational routine and incidental exposure to household bleach. Exposure scenarios have been developed for the most common or likely exposure events to assess the health risk for vulnerable groups. The report is a qualitative assessment of the health risk posed by exposure to household bleach.

The Pesticide Action Network (PAN) pesticide database in the USA describes household bleaches as containing between 2% and 12.5% NaOCl (PAN 2013). New Zealand's number one brand in bleach is Janola. A number of budget or 'own brand'

[1] Massey University, Centre for Public Health Research (Environmental Health Indicators - Hazardous Substances)
[2] EPA information page (http://www.epa.govt.nz/hazardous-substances/at-home/Pages/Bleach.aspx) accessed 17/01/14

bleach solutions are marketed and appear to have a similar market share to Janola as demonstrated in the information gathered by ESR from supermarket chain operators in New Zealand as shown in Table 1.

Table 1 - Volume of bleach held in a representative supermarket warehouse

Description	Total Litres
Janola Lemon 1.25 L	1554
Janola Regular 1.25 L	1516
Janola Regular 2.5 L	970
Janola Lemon 2.5 L	1770
Budget Bleach 750 mL	1233
Budget Bleach 2 L	6660
Harpic White & Shine Citrus 450 mL	402
Harpic White & Shine Eucalyptus 450 mL	312
Harpic White & Shine Original 450 mL	342

1.1 OUTLINE OF THE REPORT LIMITATIONS

This report uses information collected from peer-reviewed and grey literature, additionally a number of assumptions are made to facilitate the development of exposure scenarios and produce the risk characterisation. The limitations are detailed in the following list, their position in the list should not be considered to be indicative of their relative significance.

- The majority of dose-response related data used in this report were derived from animal studies using significantly higher doses than those expected in a household accident scenario.
- The animal studies identified were predominantly long-term exposure studies.
- The report only identifies two age groups for consideration in the risk characterisation; 2–3 year old children and 6–11 year old children.
- Exposures were calculated for the 5^{th} and 50^{th} percentile bodyweights in these groups, according to the United States Environment Protection Agency (USEPA) child-specific exposure factors handbook (USEPA 2008), these data are not New Zealand specific.
- Two main sets of data used were the HSSS and the National Minimum Dataset. These datasets cannot be reconciled to produce information pertaining specifically to injury from household bleach by age group and duration of stay in hospital.
- Only two concentration values were used for the household bleach mixtures, high and low, these may not represent the entire range of concentrations available through retail outlets.
- The assumption for ingestion exposure was that 50 mL of bleach solution was accidentally ingested in a single event and no mitigating steps were taken.
- The assumption for dermal exposure was that a 10 mL splash was received directly to uncovered skin where it was allowed to remain in place until dry; or, that the subject sat

in a spill of household bleach and 40% of the leg area was in contact with the spill, no residue was removed from the skin.

- The assumption for inhalation exposure, the subject receives a single spray directly to the face and mouth, a total of 30% of the spray is aspirated and deposited in the lungs.

[Intentionally Blank]

2. HAZARD IDENTIFICATION

For the purposes of this health risk assessment the compounds of interest in this formulated product are considered to be NaOCl and NaOH.

2.1 SODIUM HYPOCHLORITE

A NaOCl solution contains three chemical species, in equilibrium with each other: gaseous chlorine (Cl_2), hypochlorous acid (HOCl), hypochlorite ion (OCl^-). Their concentration depends on the pH of the solution. The pH of commercial solutions of sodium hypochlorite can range from pH 9 (diluted) to 13 (concentrated) and as such the dominant species are the OCl^- anion and HOCl, with the former predominating (Binetti and Attias 2007). Household bleaches usually contain about 5% NaOCl (a bleach solution of about pH11, irritant) and more concentrated bleaches contain 10–15% NaOCl (a bleach solution of about pH 13, corrosive).

2.1.1 Oral exposure

The oral toxicity of NaOCl has been studied predominantly in animal systems and human case studies.

Household bleaches usually contain about 5% NaOCl (a bleach solution of about pH 11, irritant) and more concentrated bleaches contain 10–15% NaOCl (a bleach solution of about pH 13, corrosive).

NaOCl is toxic by the oral route, the toxic effects are primarily due to the corrosive properties of the hypochlorite moiety. Hypochlorite causes tissue injury by liquefaction necrosis. Systemic toxicity is rare, but metabolic acidosis may occur after ingestion (ATSDR 2002). Andirian et al (1999) observed pneumonitis among patients after ingestion of household bleach and thus proposed possible systemic toxic effects of household bleaches.

Ingestion of sodium hypochlorite solution very commonly causes gastrointestinal irritation, with nausea and vomiting. Haematemesis may occur with concentrated solutions. Household bleaches are unlikely to cause severe irritation unless contact is prolonged or the amount ingested is large. Severe oesophageal damage may occur, but several reports have concluded that it is not common (Landau and Saunders 1964; Pike et al 1963). Corrosive injury of the stomach (Strange et al 1951; Van Rhee and Beaumont 1990) and hypernatraemia with hyperchloraemic acidosis (Ward and Routledge 1988) have all been reported usually following large intentional (Spiller et al 1994) ingestions by adults. However case studies of accidental ingestion indicated that in cases where the mixture consumed did not exceed 5% NaOCl, injury was minor and the treatment required was not extensive or of long duration.

2.1.2 Dermal and ocular exposure

Sodium hypochlorite has been studied predominantly for dermal toxicity in animal systems and human case studies.

Sodium hypochlorite solutions are classified as irritant for concentrations from 5% to 10% available chlorine (risk phrases: R31, R36/38)[3] and as corrosive for concentrations above 10% (risk phrases: R31, R34). In a study by Hostyneket al. (1990) skin irritation induced by 24 hour patch testing with 20 µL or 100 µL containing a constant NaOCl concentration (1 %)

[3] Risk phrases were a method for denoting the type of hazards or hazards represented by a particular substance; this system is being replaced with the Globally Harmonised System (GHS)

and different NaOH concentrations (0.01–1.00 %) was studied in adult human volunteers, by means of visual scores and skin colour reflectance measurements. No irritation was observed by application of 20 µL 1 % NaOCl independent of the NaOH concentration. However all solutions induced significant irritation when 100 µL was applied. Skin reactions did not show a straight pH dose response as a maximum was seen at 0.1 % NaOH. Skin surface pH increased after removal of the patch but returned to initial values 24 hours thereafter. The authors of this publication concluded that the study shows that the irritancy of alkaline aqueous chlorine is a cumulative effect resulting from the three major oxidants/irritants present there in equilibrium: OCl^- ion, hydroxide ion (OH^-) and HOCl. They suggest that a non-irritant concentration for diagnostic patch testing for allergic contact dermatitis using 20 µL test volume could be as high as 1 % NaOCl and 1 % NaOH.

Skin exposure to high concentrated solutions can result in serious corrosive burns (ICPS/INCHEM).

Eye contact with high concentrated solutions can result in serious corrosive burns (ICPS/INCHEM).

2.1.3 Inhalation exposure

Inhalation exposure data for NaOCL are primarily derived from inhalation of chlorine gas. Inhalation of chlorine gas released from sodium hypochlorite causes burning in the throat and coughing. High levels of exposure can lead to swelling and obstruction of the airway. In serious cases noncardiogenic pulmonary oedema can occur (ICPS/INCHEM).

Hypochlorite powder, solutions and vapour are irritating and corrosive to the eyes, skin and respiratory tract. Ingestion and skin contact produces injury to any exposed tissues. Exposure to gases may cause burning of the eyes, nose and throat. Cough, constriction and oedema of the lungs and airways can occur (ATSDR 2002).

The toxicological properties of NaOCl have been classified by a number of international and national agencies including the USEPA and the European Chemicals Agency (ECHA).

- USEPA Office of Prevention, Pesticides And Toxic Substances (7508W): Toxicity Category I (indicating the highest degree of toxicity) for its extremely corrosive effects on the eyes and skin (738-F-91-108, September 1991).
- European Chemical Agency: Hazard code H314, 400, EUH031 – causes severe skin burns and eye damage, very toxic to aquatic life; contact with acids liberates toxic gas (ECHA 2008).
- IARC classification – category 3 – not classifiable as to the carcinogenicity to humans.

2.2 SODIUM HYDROXIDE

Effects are considered in terms of four potential exposure routes; oral (ingestion), dermal, eye and inhalation. For NaOH, there is significant human toxicological information, in addition to animal toxicity information.

Information obtained from human case studies showed that in general intense pain and a decrease of the visual acuity due to damage to the corneal epithelium and corneal oedema occur. Depending on the severity of the case, effects range from sloughing of corneal and conjunctival epithelium to ischemic necrosis or even loss of the eye (Nelson and Kopietz 1987).

The toxicological properties of NaOH have been classified by a number of international and national agencies including World Health Organization International Programme on Chemical Safety (WHO IPCS),

- European Chemical Agency: Hazard code H314 – causes severe skin burns and eye damage (Ref ECHA, 2008)
- WHO Recommended Classification of Pesticides by Hazard (2009). IPCS Hazard/risk classification: “Corrosive” (World Health Organization 2009).
- USEPA Office of Prevention, Pesticides And Toxic Substances (7508W): Toxicity Category I (indicating the highest degree of toxicity) for its corrosive and irritating effects to skin, eyes and mucous membranes (EPA-738-F-92-008, September 1992).

Sodium hydroxide (NaOH) dissociates rapidly on contact with water or tissue to give sodium and the hydroxyl ion. Both of these ions are abundant in the human body. The harmful effects of NaOH are due to the irritant or corrosive effects of the hydroxide ion (OH^-). NaOH is not expected to be absorbed to any appreciable degree and, consequently, will not be systemically available in the body under likely exposure conditions (European Chemicals Bureau 2007). Risks to consumers will be due to local acute effects. The extent and degree of harm will be a function of the concentration of the hydroxide ion, the area affected and the contact time before removal or dilution. For example, when 50% NaOH was applied to shaved mouse skin (2 cm diameter circle), mortality was 20, 40, 80 and 71% when the skin was rinsed after 30 minutes, 1 hour, 2 hours or not at all (Bromberg et al 1965). When skin was immediately rinsed, no mortality or burns were observed.

2.2.1 Oral exposure

The physical form in which NaOH is ingested will influence the site and degree of harm caused (European Chemicals Bureau 2007). Solid NaOH is difficult to swallow and usually results in injury to the mouth and pharynx. For example, examination of 13 children who had sucked on granules of NaOH planted in a box of sweets revealed corrosive injury of the tongue and lips in two boys, but negative findings in the remaining 11 cases (Janoušek et al 2005). NaOH in solution is odourless and tasteless, and is easily swallowed resulting in damage to the oesophagus and stomach (Cello et al 1980; Ramasamy and Gumaste 2003). Acute injuries include tissue perforation and necrosis. Longer term complications include oesophageal stricture and antral stenosis.

Corrosive damage to the oesophagus substantially increased the risk of developing oesophageal carcinoma, usually with a latency period of about 40 years (Appelqvist and Salmo 1980; Contini and Scarpignato 2013; Hopkins and Postlethwait 1981; Isolauri and Markkula 1989; Ti 1983).

2.2.2 Eye exposure

In a rabbit low-volume eye test, a 2% NaOH solution was associated with significant epithelial damage, but more limited corneal damage, while an 8% solution caused extensive injury and reduced the corneal thickness by 26% after one hour (Jester et al 2000). A 0.1M (0.4% solution of NaOH produced irritation of the skin and eyes of rabbits (Morgan et al 1987). Exposure to the solid or concentrated liquid can cause severe burns in the eyes, skin, and gastrointestinal tract which may ultimately lead to death (ATSDR 2002).

A study examined the epidemiology, management and outcome of 42 cases of alkali burns of the eye admitted to the eye clinic of the RWTH Aachen, Germany from 1985 to 1992 (Kuckelkorn et al 1993). The majority (74%) of cases involved industrial accidents. Of the home injuries, the majority were due to drain cleaners. Sodium and potassium hydroxide produced more extended and deeper damage than lime (calcium hydroxide) due to their rapid penetration through the ocular tissues. A delayed surgical intervention led to a longer time of stay in hospital and to a higher number of operations. All eyes could be prevented from melting (liquefying), but an optical rehabilitation (visual acuity >0.3) was achieved only in a few cases (14.5%).

A review of case studies of NaOH ocular exposure (Nelson and Kopietz 1987) showed that in general intense pain and a decrease of the visual acuity due to damage to the corneal epithelium and corneal oedema occur. Depending on the severity of the case, effects range from sloughing of corneal and conjunctival epithelium to ischemic necrosis or even loss of the eye.

An Australian study reviewed 12 cases of alkali burns involving the cornea (Bunker et al 2014). Most injuries were due to NaOH from 'trivial domestic accidents'. Ten of the 12 cases recovered fully, due to effective acute management. One case suffered cicatrical ectropion requiring surgical correction.

An Indian study stressed the need for effective clinical management of acute ocular exposure (Sharma et al 2012). In a case series of 16 ocular burns (31 eyes) due to NaOH, approximately 50% were graded as severe (grade VI on the Dua classification). Grade VI injuries had significantly worse recovery outcomes than the lower grades. While epithelial damage healed by 14 weeks, glaucoma (n = 7) and cataracts (n = 6) were the most common long-term complication. Other complications were seen mainly in the cases with grade VI injuries, including pseudopterygium (n = 5), scleral melting (n = 4), adherent leucoma (n = 2), trichiasis (n = 2), pyogenic granuloma (n = 2), anterior staphyloma (n = 2) and phthisis bulbi (n = 2).

2.2.3 Dermal exposure

Studies in pigs (Yorkshire weanling) showed severe necrosis in all epidermal layers with application of 8 or 16% NaOH solutions for 15 minutes on the lower abdominal region (Srikrishna and Monteiro-Riviere 1991). With a 24% NaOH solution, necrosis extended further into the subcutaneous tissue.

In human patch tests, NaOH was irritant at a concentration of 0.5% in 55-61% of test subjects (Griffiths et al 1997; York et al 1996). Application of NaOH (0.5 or 1.0%) to back skin for 3, 15 or 60 minutes resulted in increased erythema with increasing exposure time (Dykes et al 1995). Erythema continued to increase up to 48 hours post-application. Twenty-four hour patch testing with 4% NaOH produced reaction in all of 34 volunteers, but a distinction was possible between normal reactors (25/34) and hyper-reactors (9/34) (Seidenari et al 1995).

2.2.4 Inhalation exposure

While NaOH is relatively non-volatile, spraying of NaOH solutions may result in inhalable mists or suspensions (European Chemicals Bureau 2007). Acute respiratory symptoms, including nose and throat irritation, chest pains and shortness of breath have been reported.

Exposure of rats to an aerosolised 40% NaOH solution (air concentration not reported) resulted in alveolar wall thickening with cell proliferation and congestion (Dluhos et al 1969). Ulceration and flattening of the bronchial epithelium and proliferation of lymph adenoid tissue were also reported. Undescribed, isolated tumours were observed in 3 of 10 animals.

A case report was described of a 63 year old man, who had worked for 20 years cleaning large industrial jam containers with boiling NaOH solution (Rubin et al 1992). Clinical findings indicated severe obstructive airway disease. It was concluded that this condition was probably the result of irritation and burns to the respiratory system due to NaOH exposure.

In another case report, a formerly healthy 25-year-old developed irreversible obstructive lung injury after working for one day with a caustic soda (5%) treatment of wood in a poorly ventilated room (Hansen and Isager 1991).

A cross sectional survey of workers (n = 2404) in an Australian alumina refinery, exposed to NaOH mist, was carried out (Fritschi et al 2001). Exposure to caustic mists was assessed for different work areas using a semi-quantitative method. Areas were classified as low

exposure (<0.05 mg/m^3), medium exposure (0.05–1.0 mg/m^3) or high exposure (>1.0 mg/m^3). Workers in the highest current caustic exposure category had significantly higher prevalence of work-related wheeze and rhinitis than unexposed workers, but did not have measurable changes in lung function. Workers in the low and medium exposure groups did not have significantly greater prevalence of these respiratory conditions than unexposed workers. Peak NaOH levels were measured in the factory were less than 2 mg/m^3.

2.3 COMBINED HAZARD FROM THE MIXTURE AS FORMULATED

To understand the combined effects of the individual compounds which affect the toxicity of household bleach when considered as a mixture, an understanding of the chemicals chemical or physiological action and target organ(s) is required. These data are presented in Table 2.

Table 2 – Chemical and physiological action and primary target organs for constituents of 'as-used' formulation of household bleach.

Compound	Chemical or physiological action	Reference
Sodium hypochlorite (NaOCl)	Toxic (corrosive) by the oral and dermal routes and can react to release chlorine or chloramine which can be inhaled. Causes tissue injury by liquefaction necrosis	(ATSDR 2002)
Sodium hydroxide (NaOH)	Very low levels can produce irritation of the skin and eyes. Exposure to the solid or concentrated liquid can cause severe burns in all tissues that come in contact with it.	(ATSDR 2002)

No specific target organs are identified as the site of action for either sodium hypochlorite or sodium hydroxide. The principal chemical or physiological action is direct tissue injury at the point of contact, either through necrosis or chemical burns, respectively. As the principal chemical or physiological actions are similar, it is assumed that the effects will be additive.

2.4 HUMAN STUDIES

Tanyel et al.(1988) evaluated the clinical effects of accidental chlorine bleach ingestion in 80 children admitted between 1976 and 1986. One patient was treated to prevent stricture formation, two patients for complicated strictures and 10 patients for pneumonia. The ingestion of chlorine bleaches containing 5.5 % sodium hypochlorite and 0.5 % sodium hydroxide resulted in caustic oesophageal burns and oesophageal strictures. Vomiting and pulmonary effects were also observed. The authors of the study suggest that routine oesophageal and pulmonary examinations should be carried out following chlorine bleach ingestion.

Zock et al (2009) studied the associations between household use of bleach and atopic sensitisation, allergic diseases, and respiratory health status in adults. In this study data from 3626 participants who were included in the European Community Respiratory Health Survey II (Jarvis 2002) in 10 countries were analysed. The authors conclude that people who clean their homes with hypochlorite bleach are less likely to be atopic but more likely to have respiratory symptoms.

Alkalis are known to increase the risk of oesophageal cancer, which can occur years after the initial injury (Hopkins and Postlethwait 1981; Isolauri and Markkula 1989; Ti 1983). The incidence of carcinoma following oesophageal injury from sodium hydroxide is 0.8–4%. In the study by Isolauri and Markkula (1989) out of 15 individuals with oesophageal cancer (age range 38–83), 12 had accidentally swallowed sodium hydroxide at the age of two or three years, one at 15 years and one at 23 years of age. The time between ingestion and the diagnosis of oesophageal cancer was 22–81 years. Similar findings were described by Appelqvist and Salmo (1980). Out of 60 patients with oesophageal cancer, for which the time of ingestion was known, 52 had ingested the sodium hydroxide at the age of ten years or younger.

2.4.1 Household non-occupational exposure studies

A study on reported exposures to household cleaning products in the UK (Williams et al 2012b) revealed that the majority of reported exposures (n = 5944) concerned children 5 years of age or less (n = 3893; 65.5%), occurred at home (n = 5795; 97.6%) and were accidental (n = 5561; 93.6%). Liquid detergent capsules were most commonly involved (n = 647), followed by bleaches (n = 481). The route of exposure was mainly ingestion (n = 4616; 75.8%), with eye contact (n =513; 8.4%), inhalation (n = 420; 6.9%) and skin contact (n = 187; 3.1%) being less common. A proportion (5.1%, n = 313) of enquiries involved multiple routes of exposure. In the 2008 Annual report of the American Association of Poison Control Centers, bleach was identified as the cleaning product involved most commonly in injury; with 14,640 reported poisonings to children aged six years and less, including two fatalities (Bronstein et al 2010). Work carried out in the USA prior to this suggested that bleach is the most commonly ingested household cleaning product (Harley and Collins 1997). Subsequently In the USA, 27,644 unintentional cases of exposure to NaOCl were reported in 2011. Of these, 12,663 (45.8%) cases occurred in children under the age of five (Bronstein et al 2012).

Evaluation of New Zealand data, collated in the Hazardous Substances Surveillance System (HSSS) by Massey University Centre for Public Health Research, identifies that household bleach/NaOCl ranks 11th on the HSSS hospitalisation list with 155 cases, during 2006 to 2011, an average of 26 admissions per year. Household bleach/NaOCl ranks fourth in the records of calls to the National Poisons Centre (NPC) telephone line with 547 cases during 2008 to 2012, an average of 110 calls per year. No incidents of mortality attributed to this compound or household bleach products were recorded.

2.4.2 Special Susceptibility of Children

Compared with adults, the ratios of lung surface area to body weight and respiratory volume to body weight are greater in children. Therefore, at any given concentration of NaOCl or NaOH in air, children will probably receive a larger dose than adults. Children also may be more sensitive to inhaled product because of the smaller diameter of their airways. If the inhaled dose is sufficient to cause swelling or spasms of the larynx, upper airway obstruction and asphyxia are more likely to occur in children.

Children also appear to be more susceptible to ingested NaOH because their gastric acid is not sufficiently strong or present in sufficient quantity to neutralize even small quantities of strongly alkaline chemicals. NaOH accounts for 75% of all caustic injury to the oesophagus in children less than five years of age; 83% of these cases are under three years of age, and 62% are male (Gossel 1994; OEHHA 1999).

3. DOSE-RESPONSE INFORMATION

The information below summarises available dose-response data for oral, dermal, ocular and inhalation exposure. Studies were considered valid if they were well documented and if they met generally accepted scientific principles, unless stated otherwise. More recent studies were only considered valid if they followed internationally agreed guidelines. The dose-response concept does not strictly apply to compounds which are assessed predominantly for their corrosive properties. For this report, traditional dose-response assessments are replaced with an examination of the physiological effect or endpoint of the corrosive materials in relation to the tissue of direct initial contact, and the concentrations used, rather than a characterisation of systemic doses resulting in specific target organ effects.

Where possible, data from studies of acute exposures has been used; this is to reflect the usual pattern of an accidental exposure such as a spill or splash. In the absence of good quality acute studies, chronic studies have been used.

Regarding mutagenicity and carcinogenicity through chronic exposure, the European Union Standing Committee on Health and Environmental Risks (SCHER) stated that additional testing for mutagenicity is not required despite an inconclusive database for mutagenicity since negative carcinogenicity studies for oral consumption of sodium hypochlorite solutions are available. SCHER also stated that carcinogenicity is not a relevant endpoint regarding oral exposures to sodium hypochlorite due to the availability of negative carcinogenicity studies in animals and inconclusive epidemiological studies on consumption of chlorinated drinking water and cancer incidence in humans. SCHER also supports the conclusion that there is no evidence for developmental or reproductive toxicity of sodium hypochlorite based on the available database on hypochlorite and chlorine (SCHER 2008). On the basis of this statement the cancer and reproductive endpoints are not considered in this report.

3.1 INGESTION

3.1.1 Sodium hypochlorite

Animal studies

Oral acute toxicity studies in rats, using solutions of sodium hypochlorite with concentrations of up to 12.5%, have shown LD_{50} values between 0.29 and 8.91 g/kg BW the range of concentrations appears to be due to the method of delivery of dose as detailed in the ECHA[4].

Human studies

Data on oral toxicity in humans are derived mainly from accidental ingestion by children or deliberate ingestion by adults attempting self-harm. In most cases the dose range is unknown or a rough estimate. Racioppi *et al*. (1994) propose that in adults, ingestions of at least 250 to 500 ml of a concentrated (12.5%) sodium hypochlorite solution can lead to death. Less than 5 mL/kg oral ingestion of a 7% solution is unlikely to cause severe effects (ICPS/INCHEM). Data presented in Table 3 show the toxicological studies which were considered to provide data for the exposure assessment and risk characterisation.

[4] sodium hypochlorite ECHA accessed 09/03/15

3.1.2 Sodium hydroxide

Animal studies

No acute oral toxicity study on sodium hydroxide with animals following national or international guidelines could be identified during the course of this project.

The local effects of sodium hydroxide exposure on epithelial tissue, either by liquefaction or necrosis, is dependent on the concentration of the sodium hydroxide. The mode of action at the dermis will be similar for internal, external and ocular dermis with the severity of the injury varying due to sensitivity of the specific tissue. Atug *et al* (2009) used rabbit oesophageal epithelium as a model of sodium hydroxide ingestion and their findings suggest that mucosal exposure to sodium hydroxide solutions at pH <11.5 have no damaging effects on the oesophagus. At pH 11.5 or higher, the damage was both time- and pH-dependent. This is also the lower pH limit identified by NIOSH for dermal effects of NaOH and is probably an appropriate no observable adverse effect level (NOAEL) for oral or dermal exposure. On this basis, the European Chemical Bureau (ECB) classification for NaOH should be appropriate for dose-response assessment (European Commission 2014):

0.5-2.0%	Irritating to skin (R38)
2.0-5.0%	Causes burns (R34)
>5.0%	Causes severe burns (R35)

Animal and *in vitro* studies have demonstrated damage to the oesophageal epithelium at NaOH concentrations of 1.8–2.5% (Baskerville et al 2002; Henry et al 2008; Malvasio et al 2012). The severity of damage increases with increasing NaOH concentration However, the information in the ECB classification indicates that concentrations less than 0.5% NaOH are not irritant.

Human studies

In general, ingestion of high concentrations of the substance rapidly causes corrosive injury of the mouth, throat, oesophagus, and stomach and may result in perforation, haemorrhage, and narrowing of the gastrointestinal tract. Case reports indicate that death results from shock, infection of the corroded tissues, lung damage, or loss of measurable pulse (INCHEM).

There are numerous human case studies of accidental or suicidal ingestion available; however no reference limits or doses could be identified. The severity and extent of damage produced to the gastrointestinal tract depends on the physical form of the NaOH. Solid NaOH produces injury to the mouth and pharynx and is difficult to swallow. Liquid NaOH is tasteless and odourless and therefore is easily swallowed and more likely to damage the oesophagus and stomach (Gumaste and Dave 1992). Data presented in Table 4 show the toxicological studies which were considered to provide data for the exposure assessment and risk characterisation. Patch testing in humans demonstrated reaction by about half of subjects at NaOH concentrations of 0.5%, with all subjects reacting to 4% NaOH (Dykes et al 1995; Griffiths et al 1997; Seidenari et al 1995; York et al 1996).

3.2 EYE CONTACT

3.2.1 Sodium hypochlorite

It has been suggested that the commonly used rabbit eye model tends to exaggerate the toxicity of agents since rabbits blink their eyes at a much lower frequency than humans (Pashley et al 1985). It also has been shown that the Federal Hazardous Substances Act (FHSA) method overestimates the severity of the human eye response and only the results of the low-volume rabbit test show a statistically significant correlation (Walker 1985). Therefore only studies using the latter method are considered to provide accurate dose-

response information for use in health risk assessment. Studies shown in Table 5 show the toxicological studies which were considered to provide data for the exposure assessment and risk characterisation.

3.2.2 Sodium hydroxide

Animal studies

It has been shown that alkaline substances produce liquefaction necrosis and hence are able to penetrate the tissue of the eye (Murphy et al 1982). The severity of induced effects is influenced by the amount of the causative agent, by concentration, duration and treatment. Animal data on eye irritation revealed eye irritation levels as follows: the non-irritant level was 0.2-0.3%, conjunctivitis and iritis were induced by 1.0%, while the corrosive concentration was 1.2%.

Human studies

No human data referencing dose ranges or other dose response data were identified. The studies which were considered most relevant to human exposure are presented in Table 6.

3.3 INHALATION

3.3.1 Sodium hypochlorite

Animal studies

The LC_{50} value by inhalation of sodium hypochlorite in rat was found to be greater than 10.5 mg/L for one hour exposure, using an unspecified commercial solution. The test was carried out at room temperature with a total air flow of 10 litres per minute. No death occurred and there was no sign of inactivity or lachrymation and no significant gross pathological changes reported in tests carried out by Industrial Bio-Test Laboratories Inc. (1970). This study is considered of limited interest since inhalation exposure of sodium hypochlorite is only possible if aerosols are formed.

Human studies

Studies in rhesus monkeys and human volunteers derived a ‘no observed adverse effects level’ (NOAEL) of 0.5 ppm for repeated exposure to chlorine gas (Morgan et al 1987; Schins et al 2000). Chlorine gas is relevant to this process as it is liberated from NaOCl solutions at varying rates depending on conditions; the chlorine is considered as a toxicant. The studies identified in Table 7 show the toxicological studies which were considered to provide data for the exposure assessment and risk characterisation

3.3.2 Sodium hydroxide

Animal studies

Two animal studies (Dluhos et al 1969; Vyskocil et al 1966) addressing repeated dose toxicity were conducted with unspecified concentrations (inhalation of aerosols from a 40% NaOH solution) and resulted in interruption due to bad tolerance or deaths of all rats, respectively (European Chemicals Bureau 2007). Due to the fact that no concentrations were specified in these studies, no N(L)OAELs could be established.

Human studies

There have been a few occupational cases in humans described in the literature. The inhalation of aerosols containing 5% NaOH by a 25 year old woman resulted in irreversible obstructive lung injury after working for one day in a poorly ventilated room (Hansen and Isager 1991). A 63 year old man who had been working daily with boiling NaOH solution for 20 years, presented with severe obstructive airway disease (Rubin et al 1992). The study of Fritschi et al. (2001) included 2404 employees in alumina refineries who were asked to

answer questions about their respiratory symptoms and the relationship of those symptoms to work, as well as having spirometry and providing a complete job history. In this study exposure to caustic mists (aerosolised NaOH) was observed to increase the likelihood of local effects to the respiratory tract. The data from Fritstchi et al (2001) are presented in Table 8

3.4 DERMAL

3.4.1 Sodium hypochlorite

The NOAEL for repeated dermal exposure to sodium hypochlorite solution is related to its cytotoxicity/ irritating properties and is dependent on the concentration of the applied solution (Binetti and Attias 2007). Therefore, irritation can be seen as a threshold for dermal toxicity. No dermal toxicity will occur at concentrations that do not cause irritation, either after single or repeated exposure. However, the potential of hypochlorite solutions to penetrate the skin is low given its reactivity with proteinaceous material. It has been assumed in the report of Binetti and Attias (2007) that a default fraction of 10% is penetrating the skin, this value is used as part of a conservative assessment which presents a worst case.

Animal studies

Slight to moderate local irritant effects have been observed following dermal exposure to a 5.25% NaOCl solution in rabbits and guinea pigs (Nixon et al 1975; Nixon et al 1990; Racioppi et al 1994). Lower concentrations of 0.125% and 0.8% did not show treatment related effects (Racioppi et al 1994), whereas higher concentrations led to severe burns and swellings. The studies presented in Table 9 show the toxicological studies which were considered to provide data for the exposure assessment and risk characterisation

Human studies

Nixon et al (1975) applied in a series of patch testing experiments, 15 familiar household materials including sodium hypochlorite and nine industrial chemicals, to intact and abraded skin of rabbits, guinea pigs and human for 4 hours. Skin responses were graded 4, 24 and 48 hours after application of the patches. Hypochlorite bleach caused severe reactions (weeping and eschars) on intact human skin, but produced considerably less reaction on both intact and abraded skin of rabbits and guinea pigs. The authors are of the opinion that neither rabbit nor guinea pig skin should be relied on exclusively to identify potentially hazardous irritants to human skin.

3.4.2 Sodium hydroxide

For NaOH no human data are available on repeated dose toxicity studies by the dermal route. No systemic effects of dermal exposure in humans or animals have been reported. Due to its corrosive nature acute toxicity studies with 50% NaOH in mice (Bromberg et al 1965) led to rapidly progressing burns and a mortality rate which correlated to the time interval between application and rinsing of the application area.

A wide range of studies in animals and humans performed skin irritation tests using low concentrations of NaOH. Based on human volunteer studies, concentrations of 0.5–4% NaOH were irritating. The data relating to human exposures are presented in Table 10 and show the toxicological studies which were considered to provide data for the exposure assessment and risk characterisation.

Table 3 - Dose response data of sodium hypochlorite for exposure by ingestion

Agency	Exposure type	Year	Species	Dose Range	Critical effect	NOAEL/ LOAEL	Reference
ECHA[5]	Oral	1986	Rat (m)	0 - 200 mg/kg bw/day over 90 days	Body weights and organ weights reduced; liver damages	NOAEL of 50 mg/kg bw/day; LOAEL of 100 mg/kg bw/day;	ECHA study report
Not cited	Oral, drinking water	1986	Rats	0.1, 0.05% (m), 0.2, 0.1% (f) for 104 weeks	Reduction in body-weight gain	NOAEL 50 mg/kg bw/d	(Hasegawa et al 1986)

Table 4 - Dose response data of sodium hydroxide for exposure by ingestion

Agency	Exposure type	Year	Species	Dose Range	Critical effect	NOAEL/ LOAEL	Reference
Not cited	Oesophageal infusion	2008	Rabbit	2%, 4% and 6% NaOH	Lesions in the oesophageal wall,	Not reported[6],	(Henry et al 2008)

[5] European Chemicals Agency study report of sodium hypochlorite
[6] however, a 2 % solution produced lowest effect, but had no lesser concentration to show lower effect at lower concentration

Table 5 - Dose response data of sodium hypochlorite for exposure by eye contact

Agency	Exposure type	Year	Species	Dose Range	Critical effect	NOAEL/ LOAEL	Reference
Not cited	Eye	2001	Rabbit	17.6 µmoles in 10 µL	Mild irritancy; corneal injury limited to the epithelium and superficial stroma	Not reported	(Maurer et al 2001)

Table 6 - Dose response data of sodium hydroxide for exposure by eye contact

Agency	Exposure type	Year	Species	Dose Range	Critical effect	NOAEL/ LOAEL	Reference
Not cited	Eye	1987	Rabbit	0.001M (0.004%), 0.01M (0.04%), 0.05M (0.2%), 0.1M (0.4%), 0.3M (1.2%) NaOH	According to EPA criteria: non-irritant (≤ 0.2%), mild irritation at 0.1 M (0.4%), corrosive at 0.3 M (1.2%)	NOAEL 0.2%	(Morgan et al 1987)
Not cited	Eye	1982	Rabbit	0.1%; 0.3%; 1.0% and 3.0%	0.1 and 0.3%: no conjunctivitis nor iritis; 1.0 and 3.0%: conjunctivitis and iritis	NOAEL 0.3%	(Murphy et al 1982)

Table 7 - Dose response data of sodium hypochlorite and chlorine gas for exposure by inhalation

Agency	Exposure type	Year	Species	Dose Range	Critical effect	NOAEL/ LOAEL	Reference
Not cited	Inhalation of chlorine gas	1987	Rhesus Monkey	0, 0.1, 0.5, or 2.3 ppm Cl_2 for 6 hr/day. 5 days/week for 1 year (0, 0.3, 1.5 or 6.8 mg/m^3)	Irritation, mild focal hyperplasia and cilia loss in nasal passages and trachea	NOAEL[7] 1.5 mg/m^3	(Morgan et al 1987)
ECHA	Inhalation of chlorine gas	2000	Human	0, 0.3, 0.9 and 1.5 mg/m^3 (0, 0.1, 0.3 and 0.5 ppm); 6 hr/day on 3 consecutive days; for 8 weeks	No inflammatory effect in the nose, no changes in the respiratory function at repeated exposure up to 0.5 ppm (1.5 mg/m^3)	NOAEL[8] 1.5 mg/m^3	(Schins et al 2000)

Table 8 - Dose response data of sodium hydroxide exposure by inhalation

Agency	Exposure type	Year	Species	Dose Range	Critical effect	NOAEL/ LOAEL	Reference
Not cited	Inhalation of caustic mist	2001	Human	<0.05 mg/m^3, 0.05-1.0 mg/m^3 or >1.0 mg/m^3	Lung function; local effects on the respiratory tract	Not cited Inferred NOAEL of 1mg/m^3	(Fritschi et al 2001)

[7] Converted from 0.5 ppm value figure provided in the paper using the formula $C_{mg/m^3} = (C_{ppm} \times mol.\ weight)/24.45$, where molecular weight is 71

[8] Converted from 0.5 ppm value figure provided in the paper using the formula $C_{mg/m^3} = (C_{ppm} \times mol.\ weight)/24.45$, where molecular weight is 71

Table 9 - Dose response data of sodium hypochlorite for exposure by dermal contact

Agency	Exposure type	Year	Species	Dose Range	Critical effect	NOAEL/ LOAEL	Reference
ECHA	Dermal	1978	Rabbit	7.5–20.0 g/kg bw	Bad burns and swellings, ataxia	LOAEL of 7500 mg/kg bw/day;	(ECHA 2013)
Not cited	Dermal	1990	Human	20 µL or 100 µL NaOCl (1 %) and different NaOH concentrations (0.01–1.00 %)	Significant skin irritation for 100 µL, No irritation for 20 µL 1 % NaOCl.	A potential NOAEL derived from 20 µL 1 % NaOCl.	(Hostynek et al 1990)

Table 10 - Dose response data of sodium hydroxide for exposure by dermal contact

Agency	Exposure type	Year	Species	Dose Range	Critical effect	NOAEL/LOAEL	Reference
Not cited	Dermal	1995	Human	1, 2 and 4%	Irritant	Not reported	(Seidenari et al 1995)
Not cited	Dermal	1997	Human	0.5% (0.2ml, 1h)	Irritant	Not reported	(Griffiths et al 1997)
Not cited	Dermal	1996	Human	0.5% (0.2ml, 15-60min)	Irritant	Not reported	(York et al 1996)
Not cited	Dermal	1995	Human	1% (four different protocols)	Irritant	Not reported	(York et al 1995)

4. EXPOSURE ASSESSMENT

Williams et al (2012a) reported calls to the UK National Poisons Information Centre for incidents relating to household cleaning products by exposure route as shown in Table 11. This study showed that ingestion was the principal exposure route for all household cleaning products. Other studies have also identified the main means of exposure as being ingestion (Arevalo-Silva et al 2006; Bateman 2012; Batistich and Shepherd 2013; Christesen 1994; Jones 2002; Kay and Wyllie 2009; McKenzie et al 2010; Meyer et al 2007; Presgrave Rde et al 2008; Riffat and Cheng 2009; Tanyel et al 1988)

Table 11 – Exposure routes of household cleaning products including bleach (Williams et al 2012b)

Exposure route	Number of reported cases (n)	Proportion attribution (%)
Ingestion	4616	75.8
Eye contact	513	8.4
Inhalation	420	6.9
Skin contact	187	3.1
Total reported	5736	94.2[9]

In the development of the exposure scenarios presented below, two concentrations of household bleach have been used to represent the range of concentrations found in undiluted household bleach in New Zealand. The 'High' concentration refers to a mixture comprising 100 mg/mL or 10% NaOCl, and 0.5 mg/mL or 0.05% NaOH; and the 'Low' concentration formulation is 50 mg/mL or 5% NaOCl and 0.1 mg/mL or 0.01% NaOH. Through the text of this report these formulations will be referred to as 'High concentration' or 'Low concentration'.

4.1 INGESTION EXPOSURE SCENARIO

Standardized equations were used to calculate uptake by the oral exposure route (Johnson-Restrepo and Kannan 2009). The ingestion exposure dose is a normalisation of the amount of a substance taken in by ingestion per unit body weight, the equation for calculation of this value is shown below:

$$Ingestion\ exposure\ dose\ = \frac{C\ \times IR\ \times EF}{BW}$$

Where:

C = contaminant concentration in µg/mL

IR = ingestion volume (50 mL)

EF = exposure factor (in this case 1.0, as calculations consider complete absorption of toxicants)

BW = body weight in kilograms

[9] 5.1% were reported as multiple exposure routes the composition of which was not stated in the reference.

The data for ingestion exposure doses are shown in Table 12.

Table 12 - Ingestion exposure dose for sodium hypochlorite and sodium hydroxide in two bleach concentrations for infants and children

			Ingestion exposure dose (mg/kg BW)			
			Bleach, low conc.		Bleach, high conc.	
Age	Body weight percentile	Subject body weight (kg)	NaOCl (5%)	NaOH (0.01%)	NaOCl (10%)	NaOH (0.05%)
2–3 years	5th	10.9	230	0.5	460	2.3
	50th	13.6	180	0.4	370	1.8
6–11 years	5th	19.7	0.1	0.3	0.3	1.3
	50th	29.3	0.1	0.2	0.2	0.9

Oral exposure to household bleach is predominantly due to accidental ingestion by infants and children. Occasions of deliberate ingestion in adults are also observed. Based on the information in section 2.4.1, accidental ingestion of household bleach by infants and children is assumed for the purposes of this report as the most significant route for exposure amongst the New Zealand population. Few data estimates of volumes of household bleach accidentally consumed by infants and children have been reported. Additionally, in the reporting of case studies and through national poison centre databases the concentration of sodium hypochlorite in an ingested solution does not appear to be routinely recorded. However, the UK Health Protection Agency compendium of chemical hazards for Sodium Hypochlorite (UK HPA 2011) identifies 50 mL at a concentration of less than 10% sodium hypochlorite, as a small volume for ingestion by a child (200 mL is cited as a small volume for ingestion by an adult). The mean age for children ingesting household bleach is assumed to be 24 months. This is consistent with a small cohort case study in the USA reported by Harley and Collins (1997). Age distribution data received from the New Zealand National Poisons Centre for household chemical exposure incidents (specifically, dishwasher powder) to children between July 2007 and June 2012 showed peaks at 12 and 24 months, although this may be partially due to variability in age-reporting formalities at the time of each enquiry. This report uses ingestion scenarios developed for infants of 2 to <3 and 6 to <11 years of age at the 5th and 50th percentile body weight (NHANES 1999–2006); each consuming 50 mL of undiluted household bleach at either 5% or 10% sodium hypochlorite and 0.01% or 0.05% sodium hydroxide. An exposure factor[10] (EF) of 1 (substance completely absorbed) will be used to provide a worst case scenario for the model.

4.2 INHALATION EXPOSURE SCENARIO

Standardised equations are available to calculate uptake by the inhalation exposure route (Johnson-Restrepo and Kannan 2009).

$$Uptake_{inhalation} = \frac{C_{air} \times VR_{lung} \times t_{exp}}{BW}$$

$Uptake_{inhalation}$ = internal dose by inhalation route (pg/kg/day)

C_{air} = vapour concentration (pg/m^3)

t_{exp} = time of exposure (min/day)

VR_{lung} = pulmonary ventilation rate (m^3/day)

BW = body weight (kg)

This formula is modified further to represent the OCl^- concentration in the inhalable fraction of NaOCl

The following inhalation exposure scenarios have used data pertaining to bleach spray systems derived for the European Union Risk Assessment Report for sodium hypochlorite (Binetti and Attias 2007).

4.2.1 Infant and child inhalation exposure scenario

Using the data derived from Binetti and Attias (2007) an inhalation exposure scenario has been developed to assess the health impact of an infant or child using a spray bleach bottle.

The scenario assumes that a single trigger squeeze of undiluted household bleach is directed toward the face of the subject, and that 30% of the entire volume of the aerosol produced is inhaled. The EU data states that the average volume of such a spray is approximately 1.18g; in the low concentration bleach this would equate to 59 mg NaOCl and 0.1 mg NaOH, and the high concentration household bleach would be 118 mg NaOCl and 0.6 mg NaOH. This is a conservative assumption as the cone of spray from the nozzle of the spray gun may distribute the aerosol considerably wider than the mouth and the droplet size may prevent inhalation as they will fall out of the aerosol due to gravity or be taken onto cilia or mucous membranes before reaching the lung (Binetti and Attias 2007). With the simplified approach shown below, the uptake can be calculated.

$$Uptake_{inhalation} = \frac{C_{air}}{BW}$$

$Uptake_{inhalation}$ = internal dose by inhalation route (mg/kg BW/ event)

C_{air} = vapour concentration (mg)

BW = body weight (kg)

Using this scenario the uptake for infants and children in the 5th and 50th percentile of physiological parameters are shown in Table 13.

Table 13 - inhalation exposure values assuming inhalation of entire spray volume

	Age			
	2 – 3 years		6 – 11 years	
	5th Percentile	50 th Percentile	5 th Percentile	50 th Percentile
Body weight (kg)	10.9	13.8	19.7	29.3
Low conc. NaOCl mass (mg)	59	59	59	59
Low conc. NaOH mass (mg	0.1	0.1	0.1	0.1
High conc. NaOCl mass (mg)	118	118	118	118
High conc. NaOH mass (mg)	0.6	0.6	0.6	0.6
Low conc. NaOCl exposure (mg/kg BW)	5.4	4.3	3.0	2.0
Low conc. NaOH exposure (mg/kg BW)	0.01	0.01	0.01	<0.01
High conc. NaOCl exposure (mg/kg BW)	10.8	8.6	6.0	4.0
High conc. NaOH exposure (mg/kg BW)	0.06	0.04	0.03	0.02

4.3 DERMAL EXPOSURE SCENARIO

Dermal exposure has been taken from the exposure parameters and scenarios derived for the European Union Risk Assessment Report for NaOCl, 23/11/2007.

$$A_{der} = C_{der} \times T_{der} \times Area_{der}$$

$$U_{derm\,pot} = \frac{A_{der}}{BW}$$

Where:

(OCl^-) in the product [$mg.cm^{-3}$]	C_{der}
External exposure to skin [mg/day]	A_{der}
Potential dermal uptake rate [mg.kg BW-1 day -1]	$U_{derm\ pot}$
Thickness of the film layer on skin [default = 0.01cm]	T_{derm}
Surface area of skin exposed [cm^2]	$AREA_{derm}$
Bioavailability for dermal exposure (default = 1)	BIO_{derm}
Number of events per period (usually, $events.day^{-1}$)	N_{events}
Average female bodyweight [default = 60kg]	BW
Default factor to quantify absorption [10%]	F_{absorp}

4.3.1 Infant and child dermal exposure scenarios

Using the model developed for the European Union Risk Assessment Report for sodium hypochlorite (Binetti and Attias 2007); which is detailed in section 4.3, two exposure scenarios have been developed for accidental exposure of children. The scenarios represent a dermal exposure by splashing and a dermal exposure via sitting in a spill on a surface.

Scenario 1 – Bleach splash from a bottle

The scenario assumes that an infant or child of 1–<2 years of age or 3–<6 years of age is exposed to a splash directly from an undiluted bottle of bleach. The splash is 10 mL in volume and the whole volume is deposited on bare skin with a deposit depth of 0.01cm, and remains in contact with the skin until dried. Calculations are carried out on the basis of infants or children representing the 5th or 50th percentile for physiological parameters according to the USEPA child specific exposure factors handbook table 8-3 (USEPA 2008). Two different concentrations of bleach were used to represent the range of concentrations which might typically be found in New Zealand household bleaches; these were a lower concentration solution (NaOCl, 5% or 50 mg/cm^3 and NaOH, 0.1% or 1 mg/cm^3); and a high concentration (NaOCl, 10% or 100 mg/cm^3 and NaOH, 0.5% or 5 mg/cm^3).

Calculations were made according to those set out in the EU Risk assessment report and as shown in section 4.3. The data presented in Table 14 shows the exposure for low concentration bleach, and Table 15 shows the exposure to the high concentration bleach.

Table 14 - Dermal exposure values for splashing with low concentration undiluted bleach

	Age (years)			
	2 – <3		6 – <11	
	5th Percentile	50 th Percentile	5 th Percentile	50 th Percentile
C_{der} NaOCl (mg/cm^3)	50	50	50	50
C_{der} NaOH (mg/cm^3)	0.1	0.1	0.1	0.1
T_{der} (cm)	0.01	0.01	0.01	0.01
$Area_{der}$ (cm^2)	100	100	100	100
A_{der} NaOCl (mg/event)	50	50	50	50
A_{der} NaOH (mg/event)	0.1	0.1	0.1	0.1
BW (kg)	10.9	13.6	19.7	29.3
$U_{derm\ pot}$ NaOCl (mg/kgBW/event)	4.6	3.7	2.5	1.7
$U_{derm\ pot}$ NaOH (mg/kgBW/event)	0.01	0.01	0.01	<0.01

Table 15 - Dermal exposure values for splashing with high concentration undiluted bleach

	Age (years)			
	2 – <3		6 – <11	
	5th Percentile	50 th Percentile	5 th Percentile	50 th Percentile
C_{der} NaOCl (mg/cm^3)	100	100	100	100
C_{der} NaOH (mg/cm^3)	0.5	0.5	0.5	0.5
T_{der} (cm)	0.01	0.01	0.01	0.01
$Area_{der}$ (cm^2)	100	100	100	100
A_{der} NaOCl (mg/event)	100	100	100	100
A_{der} NaOH (mg/event)	5	5	5	5
BW (kg)	10.9	13.6	19.7	29.3
$U_{derm\ pot}$ NaOCl (mg/kgBW/event)	9.2	7.4	5.1	3.4
$U_{derm\ pot}$ NaOH (mg/kgBW/event)	0.05	0.04	0.03	0.02

Scenario 2 – Exposure via sitting in a bleach spill on a surface

The scenario assumes that an infant or child of 1–<2 years of age or 3–<6 years of age is exposed to a spill from an undiluted bottle of bleach, the exposure is from the infant or child being seated in the spill with legs flat on the ground. The volume of spilled bleach in contact with skin is proportionate to the area of the subject's leg, and the entire volume is assumed to be in contact with bare skin, with a deposit depth of 0.01 cm, and remains in contact with the skin until dried. Calculations are carried out on the basis of infants or children representing the 5th or 50th percentile for physiological parameters according to the USEPA child specific exposure factors handbook, table 7-2 and 8-3 (USEPA 2008).

Calculations were made according to those set out in the EU Risk assessment report and as shown in section 4.3. A modification was made to allow for the fraction of the surface are of the leg in contact with the spill to be calculated, in this model it was estimated for the purposes of this calculation that 40% of the leg area was in contact with the spill whilst in the sitting position, this is referred to as the 'area exposure factor'. The data presented in Table 16 shows the exposure for low concentration bleach, and Table 17 shows the exposure to the high concentration bleach.

Table 16 - Dermal exposure values for sitting in low concentration undiluted bleach

	Age (years)			
	2 – <3		**6 – <11**	
	5th Percentile	**50 th Percentile**	**5 th Percentile**	**50 th Percentile**
C_{der} NaOCl (mg/cm^3)	50	50	50	50
C_{der} NaOH (mg/cm^3)	0.1	0.1	0.1	0.1
T_{der} (cm)	0.01	0.01	0.01	0.01
Total leg area (cm^2)	1220	1410	2070	2590
Area exposure factor	0.4	0.4	0.4	0.4
$Area_{der}$ (cm^2)	488	564	828	1036
A_{der} NaOCl (mg/event)	244	282	414	518
A_{der} NaOH (mg/event)	0.5	0.6	0.8	1.0
BW (kg)	10.9	13.6	19.7	29.3
$U_{derm\ pot}$ NaOCl (mg/kgBW/event)	22.4	20.7	21.0	17.7
$U_{derm\ pot}$ NaOH (mg/kgBW/event)	0.04	0.04	0.04	0.04

Table 17 - Dermal exposure values for sitting in high concentration undiluted bleach

	Age (years)			
	2 – <3		6 – <11	
	5th Percentile	50 th Percentile	5 th Percentile	50 th Percentile
C_{der} NaOCl (mg/cm^3)	100	100	100	100
C_{der} NaOH (mg/cm^3)	0.5	0.5	0.5	0.5
T_{der} (cm)	0.01	0.01	0.01	0.01
Total leg area (cm^2)	1220	1410	2070	2590
Area exposure factor	0.4	0.4	0.4	0.4
$Area_{der}$ (cm^2)	488	564	828	1036
A_{der} NaOCl (mg/event)	488	564	828	1036
A_{der} NaOH (mg/event)	24.4	28.2	41.4	51.8
BW (kg)	10.9	13.6	19.7	29.3
$U_{derm\ pot}$ NaOCl (mg/kgBW/event)	44.77	41.47	42.03	35.36
$U_{derm\ pot}$ NaOH (mg/kgBW/event)	0.2	0.2	0.2	0.2

[Intentionally Blank]

5. RISK CHARACTERISATION

The assessment for household bleach was carried out in the context of incidental non-occupational exposures, although data for routine non-occupational exposures was also presented for the inhalation and dermal route of exposure. The most commonly reported route for household bleach exposure was by ingestion, followed by dermal contact at a considerably lower frequency.

5.1 RISK CHARACTERISATION FOR INGESTION

5.1.1 Sodium hypochlorite risk characterisation

The provision of a NOAEL (50 mg/kg BW) for ingestion in a rat model, in a chronic exposure study cited by the European Chemical Agency (ECHA), allows a hazard quotient (HQ) to be derived. The HQ uses a reference value for a given point of departure to normalise an exposure dose; additionally the value derived from this calculation is multiplied by an uncertainty factor, if appropriate, to account for uncertainties such as methodology and inter-species variation. If the value of the HQ is less than 1, the postulated exposure is deemed to be acceptable and not to exceed the point of departure from which it was derived. In the exposure calculations performed for this assessment an uncertainty factor of 10 for interspecies differences was used for development of HQ from the NOAEL. For the exposure scenarios described in section 4.1 the HQ for the key groups are given in Table 18.

Table 18 - Values for hazard quotient for NaOCl exposure as described

Age	Body weight percentile	Ingestion exposure dose (mg/kgBW) Bleach – low concentration	NaOCL ingestion		
			NOAEL ingestion (mg/kgBW)	Reference value[11] (mg/kgBW)	HQ NOAEL[12]
2–3 years	5th	229.4	50	5	46
	50th	183.8	50	5	37
6–11 years	5th	126.9	50	5	25
	50th	85.3	50	5	17
Age	Body weight percentile	Ingestion exposure dose (mg/kgBW) Bleach - high concentration	NaOCL ingestion		
			NOAEL ingestion (mg/kgBW)	Reference value (mg/kgBW)	HQ NOAEL
2–3 years	5th	458.7	50	5	92
	50th	367.6	50	5	74
6–11 years	5th	253.8	50	5	51
	50th	170.6	50	5	34

[11] $Reference\ value = \frac{NOAEL_{ingestion}}{uncertainty\ factor}$

[12] Hazard quotient, $HQ = (\frac{ingetsion\ exposure\ dose}{Reference\ value})$

The values in Table 18 are inherently conservative, as the NOAEL used was taken from data pertaining to chronic exposures, whereas the exposure scenario is developed as an acute exposure. All of the values are in excess of 1; this would indicate that exposures consistent with the scenarios suggested in this health risk assessment are may cause adverse effects by ingestion. It should also be noted that even if the uncertainty factor were not included in the calculation, the HQ value would still exceed unity.

5.1.2 Sodium hydroxide risk characterisation

During the course of researching this health risk assessment, no acute or chronic reference dose or suitable point of departure reference (NOAEL or LOAEL) was discovered for NaOH. The majority of papers reported on the effects from exposure to considerably greater concentrations of NaOH than are present in the typical household bleach formulation which this assessment addresses. However, the ingestion exposure for NaOH is shown alongside the NaOCl data in Table 12.

5.1.3 Household bleach

It was not possible to produce a HI for household bleach as formulated for use in non-occupational settings. This was due to the lack of consistency between points of departure and the large uncertainties which would be introduced by comparing these data. However, the body of evidence which is present as case studies would appear to indicate that the risk of injury from accidental ingestion of household bleach is present, but is unlikely to have fatal or long-term consequences. In New Zealand, there were 547 calls to the National Poisons Centre between 2008 and 2012; and 155 hospitalisations (HSSS) between 2006 and 2011, relating to household bleach exposure, with no fatalities recorded.

5.2 RISK CHARACTERISATION FOR DERMAL CONTACT

No reference dose was found for the dermal exposure route. However, we may infer an HQ using the acute LOAEL of 7500 mg/kg BW as shown in Table 19. The two scenarios which have been developed have been related to the ECHA LOAEL for NaOCl (ECHA 2013), multiplying by an uncertainty factor of 100 to account for inter-species (x10) and intra-species (x 10) variation. The use of a factor of 10 for inter-species variation allows for a relatively conservative transferral of data relating to point of departure from non-human to human subjects. The data cited in the ECHA study was derived from rabbits where the exposure scenario differed from those used in the exposure scenario developed for this study, hence an extra uncertainty factor or 10 was preferred. A similarly conservative uncertainty factor was applied for the intra-species variation; this was as a protective measure to account for the increased risk in the infant and child age groups as opposed to the entire age range of the human cohort.

Table 19 – Hazard quotient for NaOCl dermal exposure by splashing to low concentration of undiluted bleach

	Age (years)			
	2 - <3		6 - <11	
	5th percentile	50th percentile	5 th percentile	50 th percentile
LOAEL $_{NaOCl}$ (mg/kg BW/day)	7500	7500	7500	7500
Uncertainty factor	100	100	100	100
Reference value[13] (mg/kg BW/day)	75	75	75	75
$U_{derm\ pot}$ NaOCl (mg/kg BW/event)	4.6	3.7	2.5	1.7
HQ_{NaOCl}[14]	0.06	0.05	0.03	0.02

Table 20 – Hazard quotient for NaOCl dermal exposure by splashing to high concentration of undiluted bleach

	Age (years)			
	2 - <3		6 - <11	
	5th percentile	50th percentile	5 th percentile	50 th percentile
$LOAEL_{NaOCl}$ (mg/kg BW/day)	7500	7500	7500	7500
Uncertainty factor	100	100	100	100
Reference value (mg/kg BW/day)	75	75	75	75
$U_{derm\ pot}$ NaOCl (mg/kgBW/event)	9.2	7.4	5.1	3.4
HQ_{NaOCl}	0.1	0.1	0.1	0.1

The point of departure used for the determination of the reference point data for NaOCl in Table 19,

Table 20, Table 21 and Table 22 is the LOAEL, it has not been possible to identify equivalent data for NaOH exposure. The derivation of the HQ values was undertaken with several conservative assumptions in place, these being:

- An entire 10 mL volume of bleach was in contact with the skin and was allowed to remain in contact until dry
- A 100-fold uncertainty factor applied in the HQ calculation

None of the calculated HQ values in the scenario was near to 1.0; this indicates that under these conditions, there is unlikely to be harm caused.

[13] $Reference\ value = \frac{NOAEL_{ingestion}}{uncertainty\ factor}$

[14] Hazard quotient, $HQ = (\frac{ingetsion\ exposure\ dose}{Reference\ value})$

Table 21 – Hazard quotient for NaOCl dermal exposure from sitting in a low concentration of undiluted bleach

	Age (years)			
	2 - <3		6 - <11	
	5th percentile	50th percentile	5 th percentile	50 th percentile
$LOAEL_{NaOCl}$ (mg/kg BW/day)	7500	7500	7500	7500
Uncertainty factor	100	100	100	100
Reference value[15] (mg/kg BW/day)	75	75	75	75
$U_{derm\ pot}$ NaOCl (mg/kgBW/event)	22.4	20.7	21.0	17.7
HQ_{NaOCl}[16]	0.3	0.3	0.3	0.2

Table 22 – Hazard quotient for NaOCl dermal exposure from sitting in a high concentration of undiluted bleach

	Age (years)			
	2 - <3		6 - <11	
	5th percentile	50th percentile	5 th percentile	50 th percentile
$LOAEL_{NaOCl}$ (mg/kg BW/day)	7500	7500	7500	7500
Uncertainty factor	100	100	100	100
Reference value (mg/kg BW/day)	75	75	75	75
$U_{derm\ pot}$ NaOCl (mg/kg BW/event)	44.8	41.5	42.0	35.4
HQ_{NaOCl}	0.6	0.6	0.6	0.5

In the second scenario developed, the subjects were deemed to have sat in a spilled volume of household bleach. Again, a conservative assumption was that the volume of bleach which was in contact with the subjects legs was allowed to dry in place, and was not removed by rinsing or wiping. The calculated HQ values for this exposure route show that it might be expected for an observable effect to manifest. This exposure scenario was developed to represent a worst-case, and it might be considered that a more likely scenario would be that in the event of a spill of this size it would be quickly detected and cleared up and any exposure to infants or children would be identified and mitigated, hence reducing the contact time and received dose significantly.

5.3 RISK CHARACTERISATION FOR INHALATION EXPOSURE

No reference data were available for the inhalation exposure route. However, a qualitative comparison may be tentatively drawn to the NOAEL of 1.5 mg/m^3 (Schins et al 2000). The NOAEL is based on a human exposure of six hours per day, on three consecutive days per week for eight weeks; and the criteria were that no inflammatory effects were observed in the nose, and there were no changes in the respiratory function at repeated exposure up to

[15] $Reference\ value = \frac{NOAEL_{ingestion}}{uncertainty\ factor}$

[16] Hazard quotient, $HQ = (\frac{ingetsion\ exposure\ dose}{Reference\ value})$

0.5 ppm (1.5 mg/m^3). The scenario developed for this exposure shows that the uptake of NaOCl is in the range of 2.0–10.8 mg/kg BW, across both age and percentile groups. To provide context for these data, the exposure rates indicated in the paper of Schins et al. (2000) are 0.33 mg/kg BW/day for the 2–<3 year, 50th percentile group; and 0.46 mg/kg BW/day for the 6–<11 years of age, 50th percentile group. The comparison might be seen to suggest that there is opportunity that injury may be caused by this single exposure to the two subject groups when faced with high concentration household bleach being sprayed directly into the face. A mitigating factor that may be taken into account is that commercially formulated household spray bleaches are usually formulated to contain less than 5% NaOCl, so the exposure to higher concentrations would be via 'homemade' spray solutions.

5.4 RISK CHARACTERISATION FOR LOCAL EFFECTS

Local effects of household bleach exposure are from irritant or corrosive effects at susceptible dermal sites or in the eyes. NaOH is considered to be an irritant at concentrations lower than or equal to 1%. NaOCl at concentrations ≤10% is a mild to moderate irritant with symptoms including skin burns and oral burns. In the absence of empirical data to support an assessment of local effects it may be considered that NaOCl is corrosive and may irritate skin or cause burning pain, inflammation and blisters at concentrations ≤10% (ATSDR 2002).

Ocular and dermal exposure to household bleach with NaOCl concentration ≤10% may cause irritation and on-going discomfort if eyes are washed immediately (Racioppi et al 1994); irritation may become more severe if eyes are not washed. At concentrations of <5%, where exposure is of short duration and the exposed area is not occluded, dermal irritation is not reported (Eun et al 1984).

5.5 LIMITATIONS OF THE REPORT

The majority of dose-response-related data, which were found in the preparation of this report, were derived from studies carried out on animals at doses significantly higher than those identified as likely to be found in a non-occupational accident scenario. For many of these high dose rate studies, the point of departure selected was an LD_{50} or an LC_{50}; in the context of this report such data are of limited use due to the extreme severity of the endpoint they represent. Additional studies were long-term exposure studies, which introduce uncertainties when comparing the outcomes with the short-term or acute events which occur in an accident.

The report identifies two age groups as being at risk of accidental exposure to household bleach. These groups are infants aged 2 years to 3 years old and children aged 6 years to 11 years old; from these subject groups exposures were calculated for individuals representing the 5th and 50th percentile body weight according to the USEPA, child-specific exposure factors handbook (USEPA 2008). These data are not New Zealand specific, but represent a distribution of physiological parameters which can be used as a reference in the absence of country specific data. Slight differences in country-specific body weights would not be expected to exert significant influence on the risks characterised in this report.

Data on hospitalisation due to household bleach exposure were gathered from the Hazardous Substances Surveillance System which is collated by the Centre for Public Health Research at Massey University. These data provide valuable information on the number of hospitalisations due to exposure to bleach, but the records do not show the numbers of subjects in specific age groups, or the duration of the hospitalisation. The New Zealand National Minimum Dataset holds data regarding the number of subjects per age group who were hospitalised due to poisoning and the duration of their stay, it does not contain data regarding the nature of the poison consumed. Currently, the two data sets cannot be reconciled to produce a data set which would show the number of subjects

hospitalised due to an accident involving household bleach, with their age group and duration of hospitalisation.

[Intentionally Blank]

6. CONCLUSION

Ingestion of NaOCl and NaOH was estimated for children aged 2 to 3 years and 6 to 11 years of age, with body weights at the 5th and 50th percentile. Ingestion was assumed to have been of 50 mL of either 5% or 10% sodium hypochlorite solutions as undiluted household bleach. The exposure factor was set conservatively at 1 (a 100% uptake or activity in the GI tract). For both groups HQ values calculated for NaOCl exceeded 1, so it is considered possible that injury may occur given the assumptions which were made in the exposure assessment. No hazard index (HI) value was calculated for the mixture of NaOCl and NaOH which constitutes household bleach solution as no reference dose or suitable point of departure was found for the mixture as formulated. However case studies of accidental ingestion indicated that, in cases where the mixture consumed did not exceed 10% NaOCl, injuries sustained would be due to local irritant or corrosive effects.

Hazard quotient values for dermal exposure to household bleach components, under the scenarios proposed were less than 1, indicating that, individually, they are unlikely to cause injury. Where data from experimentation were lacking, case studies provided indications that accidental dermal exposure to household bleach of concentrations available in New Zealand cause injuries due to local irritant or corrosive effects. Case studies indicate that the eyes present a more sensitive area or dermal exposure and as such the likelihood that adverse effects may be observed is greater.

Calculations of the potential inhalation exposure show that the uptake of NaOCl is estimated to fall in the range of 2.0–10.8 mg/kg BW, across both age and percentile groups. To provide context for these data, the exposure rates indicated in the paper of Schins et al. (2000) are 0.33 mg/kg BW/day for the 2–<3 year, 50th percentile group; and 0.46 mg/kg BW/day for the 6–<11 years of age, 50th percentile group and presented minor, reversible effects to nasal epithelium and lung function from the exposure. The comparison might be seen to suggest that there is opportunity that injury may be caused by this single exposure to the two subject groups when faced with high concentration household bleach being sprayed directly into the face. Mitigating factors for consideration include the stated conservative assumptions used in the development of the inhalation exposure scenario, and that commercially formulated household spray bleaches are usually formulated to contain less than 5% NaOCl, so the exposure to higher concentrations would be via ‘homemade’ spray solutions.

The assessment of the exposure scenarios indicates that opportunity for injury to be sustained by exposed individuals may be considered significant. The exposure scenarios applied in this report identified that both ingestion and inhalation exposures may lead to acute injury and these types of unintentional exposures are more likely to occur to infants and children less than five years old. Case study data indicates that there is an opportunity for injury from dermal exposure to solutions containing higher concentrations of NaOCl (5–10% solution); and that for accidental ingestion, where the mixture consumed did not exceed 5% NaOCl, injury was minor and the treatment required was not extensive or of long duration; and concentrations greater than this led to greater risk of injury. Child-proof measures on containers of these products may mitigate the risk of injury. Other exposures and injury may occur but not be recorded by the current systems, this report cannot comment on the extent or severity of such exposures.

[Intentionally Blank]

GLOSSARY

Acuity	Sharpness of perception
Acute toxicity	1. *Adverse effects* of finite duration occurring within a short time (up to 14 d) after administration of a single *dose* (or *exposure* to a given *concentration*) of a test substance or after multiple doses (exposures), usually within 24 hrs of a starting point (which may be exposure to the *toxicant*, or loss of reserve capacity, or developmental change, etc.) 2. Ability of a substance to cause *adverse effects* within a short time of dosing or *exposure*
Adverse effect	A change in biochemistry, physiology, growth, development morphology, behaviour, or lifespan of an organism which results in impairment of functional capacity or impairment of capacity to compensate for additional stress or increase in susceptibility to other environmental influences
Alkaline	The property of having a pH of greater than seven (pH 7)
Alkalis	Inorganic compounds, which are water soluble hydroxides of the group 1 metals; or ammonium hydroxide.
Ataxia	Unsteadiness or loss of coordination of movement
Atopic sensitisation	Hypersensitivity, often related to allergies
Bench mark dose	A dose or concentration which causes a predetermined change in response rate of an adverse effect compared to background
Bleach solution	An aqueous solution of commercially produced bleach, containing both hypochlorite and hydroxide ions as well as other ions and compounds included in the bleach formulation by manufacturers
Cilia	A hair-like appendage which is found in numbers on the surface of a cell
Conjunctivitis	Inflammation of the conjunctiva, the membrane which covers the front of the eye
Critical effect	For deterministic effects, the first adverse effect that appears when the threshold (critical) concentration or dose is reached in the critical organ. Adverse effects with no defined threshold concentration are regarded as critical
Critical organ	Organ that first attains the critical concentration of a substance and exhibits the critical effect under specified circumstances of exposure and for a given population
Cytotoxicity	The property of causing damage to cell structure or function
Dermal	Cutaneous, pertaining to the skin
Deterministic effect	Phenomenon committed to a particular outcome determined by fundamental physical principles.

Dose	Total amount of a substance administered to, taken up, or absorbed by an organism, organ, or tissue
Dose response	Association between dose and the incidence of a defined biological effect in an exposed population
Dose response assessment	Analysis of the relationship between the total amount of an agent administered to, taken up by, or absorbed by an organism, system, or (sub)population and the changes developed in that organism, system, or (sub)population in reaction to that agent, and inferences derived from such an analysis with respect to the entire population. Dose–response assessment is the second of four steps in risk assessment
Epithelium	Sheet of one or more layers of cells covering the internal and external surfaces of the body and hollow organs
Eschars	Slough or dry scab on an area of skin that has been burnt
Exposure assessment	Evaluation of the exposure of an organism, system, or (sub)population to an agent (and its derivatives). Exposure assessment is the third step in the process of risk assessment.
Haematemesis	The vomiting of blood
Harm	An adverse effect. Damage or adverse effect to a population, species, individual organism, organ, tissue, or cell
Hazard identification	The identification of the type and nature of adverse effects that an agent has an inherent capacity to cause in an organism, system, or (sub)population. Hazard identification is the first stage in hazard assessment and the first of four steps in risk assessment.
Hazard index (HI)	The sum of more than one hazard quotient for multiple substances and/or multiple exposure pathways. The HI is calculated separately for chronic, sub-chronic and shorter-duration exposures
Hazard quotient (HQ)	The ratio of a single substance exposure level over a specified time period (eg sub-chronic) to a reference dose for that substance derived from a similar exposure period. If the hazard quotient exceeds unity, the toxicant may produce an adverse effect, but normally this will require a hazard quotient of several times unity; a hazard quotient of less than 1.0 indicates that no adverse effects are likely over a lifetime of exposure.
Household bleach	An aqueous solution of commercially produced bleach, containing both hypochlorite and hydroxide ions as well as other ions and compounds included in the bleach formulation by manufacturers
Hydroxide solution(s)	An aqueous solution containing the hydroxide (OH^-) ion as the ion of interest. The solution does not contain hypochlorite ion derived from added sodium hypochlorite
Hyperchloraemic acidosis	Acidosis defined by decrease in plasma bicarbonate increase in plasma chloride concentrations
Hypernatraemia	Excessive concentration of sodium in the blood
Hyperplasia	Abnormal multiplication or increase in the number of normal cells in a tissue or organ

Hypochlorite solution(s)	An aqueous solution containing the hypochlorite (OCl^-) ion as the ion of interest. The solution does not contain hydroxide ion derived from added sodium hydroxide
Incidence	Number of occurrences of illness commencing, injury, or of persons falling ill, during a given period in a specific population usually expressed as a rate
Injury	Any physical harm or damage serious enough to warrant medical treatment by a health professional either at the scene or in a hospital or primary care practice.
Iritis	Inflammation of the iris
Ischemic necrosis	Cell or tissue death due to reduced blood supply
Lachrymation	Secretion and discharge of tears
LC_{50}	Concentration of a substance in an environmental medium that causes death of 50% of test subjects following a certain period of exposure.
LD_{50}	Amount of a substance or physical agent that causes death of 50% of test subjects when taken into the body
Liquefaction necrosis	Tissue death from liquefying effect of a substance
Lowest observed adverse effect level (LOAEL)	Lowest concentration or amount of a substance (dose), found by experiment or observation, that causes an adverse effect on morphology, functional capacity, growth, development, or life span of a target organism distinguishable from normal (control) organisms of the same species and strain under defined conditions of exposure.
Margin of exposure (MOE)	Ratio of the no-observed-adverse-effect level (NOAEL) for the critical effect to the theoretical, predicted, or estimated exposure dose or concentration
Metabolic acidosis	An over production of acid by the metabolism, leading to lowered blood pH.
Mode of action (MOA)	The understanding of how chemicals perturb normal biological function; the key steps in the toxic response after chemical interaction at the target site that are responsible for the physiological outcome or pathology of the chemical
Moiety	A part of a molecule which may include whole functional groups or parts of functional groups as substructures
Mucosal exposure	A dose received via a mucus membrane
NaOCl	Sodium hypochlorite
NaOH	Sodium hydroxide, caustic soda, lye
New Zealand EPA	New Zealand Environment Protection Authority
Noncardiogenic pulmonary oedema	Oedema caused by changes in permeability of the pulmonary capillaries due to pathologic (in this case, chemical) insult
No observed adverse effects level	Greatest concentration or amount of a substance, found by experiment or observation, that causes no alterations of morphology, functional capacity, growth, development, or life span

(NOAEL)	of target organisms distinguishable from those observed in normal (control) organisms of the same species and strain under the same defined conditions of exposure
Ocular	Pertaining to the eye
Oedema	A fluid build-up in tissue
Oesophageal	Of or relating to the oesophagus
Oral	Pertaining to or via the mouth
Permanent harm	An adverse effect from which the subject does not recover
Pneumonitis	Inflammation of pulmonary (lung) tissue
Point of departure (POD)	A NOAEL or LOAEL for an observed incidence or change in level of response to a chemical toxicant.
Polarity	Pertaining to the separation of positive and negative charge between parts of a molecule
Proteinaceous	Consisting of protein
Qualitative	Relating to the presence
Quantitative	Relating to the amount
Reference dose	An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used
Reference value	Quantity value, generally accepted as having a suitably small measurement uncertainty, to be used as a basis for comparison with values of quantities of the same kind.
Risk characterisation	The qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of occurrence of known and potential adverse effects of an agent in a given organism, system, or (sub)population, under defined exposure conditions. Risk characterization is the fourth step in the risk assessment process.
Spirometry	Measurement of inhaled or exhaled air volume
Stricture	Abnormal narrowing of a duct or passage such as blood vessels or urethra
Stroma	Supportive tissue of an epithelial organ or tumour, consisting of connective tissue, blood vessels and other tissue
Threshold concentration	Dose or exposure concentration below which a defined effect will not occur
Toxicological endpoints	An observable or measurable biological event or chemical concentration (e.g., metabolite concentration in a target tissue) used as an index of an effect of a chemical exposure

REFERENCES

Andiran F, Tanyel FC, Ayhan A et al. 1999. Systemic harmful effects of ingestion of household bleaches. *Drug Chem Toxicol* 22 (3): 545-53

Appelqvist P,Salmo M. 1980. Lye corrosion carcinoma of the esophagus: A review of 63 cases. *Cancer* 45 (10): 2655-8

Arevalo-Silva C, Eliashar R, Wohlgelernter J et al. 2006. Ingestion of caustic substances: A 15-year experience. *Laryngoscope* 116 (8): 1422-6

ATSDR. 2002. *Calcium hypochorite and sodium hypochlorite fact sheet*.

Atug O, Dobrucali A,Orlando RC. 2009. Critical ph level of lye (naoh) for esophageal injury. *Digestive Diseases and Science* 54 (5): 980-7

Baskerville JR, Nelson RE, Reynolds TL et al. 2002. Development of a standardized animal model for the study of alkali ingestion. *Vet Hum Toxicol* 44 (1): 45-7

Bateman DN. 2012. Household products. *Medicine* 40 (3): 125-6

Batistich E,Shepherd M. 2013. *Management of childhood poisoning*. Starship Foundation and Auckland District Health Board 05/02/14. http://www.adhb.govt.nz/starshipclinicalguidelines/Poisoning.htm

Binetti R,Attias L. 2007. *European union risk assessment report sodium hypochlorite*. Italy:

Bromberg BE, Song IC, Walden RH et al. 1965. Hydrotherapy of chemical burns. *Plastic and Reconstructive Surgery* 35 (1): 85-95

Bronstein AC, Spyker DA, Cantilena JR LR et al. 2010. 2009 annual report of the american association of poison control centers' national poison data system (npds): 27th annual report. *Clin Toxicol (Phila)* 48 (10): 979-1178

Bronstein AC, Spyker DA, Cantilena LR et al. 2012. 2011 annual report of the american association of poison control centers' national poison data system (npds): 29th annual report. *Clin Toxicol (Phila)* 50 911-1164

Bunker DJL, George RJ, Kumar RJ et al. 2014. Alkali-related ocular burns: A case series and review. *Journal of Burn Care & Research* Publish Ahead of Print 10.1097/BCR.0b013e31829b0037

Cello JP, Fogel RP,Boland C. 1980. Liquid caustic ingestion spectrum of injury. *Archives of Internal Medicine* 140 (4): 501-4

Christesen HB. 1994. Epidemiology and prevention of caustic ingestion in children. *Acta Paediatr* 83 (2): 212-5

Contini S,Scarpignato C. 2013. Caustic injury of the upper gastrointestinal tract: A comprehensive review. *World Journal of Gastroenterology* 19 (25): 3918-30

Dluhos M, Sklensky B,Vysckocil J. 1969. Experimental study of the effect of aerosol inhalation of a caustic soda solution on the respiratory system of rats. *Vnitirni lekarstvi* 15 38-42

Dykes PJ, Black DR, York M et al. 1995. A stepwise procedure for evaluating irritant materials in normal volunteer subjects. *Human & Experimental Toxicology* 14 (2): 204-11

ECHA. 2008. *Summary of classification and labelling - harmonised classification annex vi of regulation (ec) 1272/2008 (clp regulation)*.

ECHA. 2013. *Sodium hypochlorite - exp key acute toxicity:Dermal.001*. 10/02/14. http://apps.echa.europa.eu/registered/data/dossiers/DISS-9ebc257c-cef7-6dc4-e044-00144f67d031/AGGR-e8a19bcd-d17f-4c52-bb6c-fecbb77586cd_DISS-9ebc257c-cef7-6dc4-e044-00144f67d031.html#AGGR-e8a19bcd-d17f-4c52-bb6c-fecbb77586cd

Eun HC, Lee AY,Lee YS. 1984. Sodium hypochlorite dermatitis. *Contact Dermatitis* 11 (1): 45

European Chemicals Bureau. 2007. *European union risk assessment report - sodium hydroxide*. Luxembourg: Communities OfOPotE

European Commission. 2014. *Esis : European chemical substances information system* 27 January 2014. http://esis.jrc.ec.europa.eu/

Fritschi L, De Klerk N, Sim M et al. 2001. Respiratory morbidity and exposure to bauxite, alumina and caustic mist in alumina refineries. *Journal of Occupational Health - English Edition* 43 (5): 231-7

Gossel TA. 1994. *Principles of clinical toxicology*. CRC Press

Griffiths HA, Wilhelm KP, Robinson MK et al. 1997. Interlaboratory evaluation of a human patch test for the identification of skin irritation potential/hazard. *Food and Chemical Toxicology* 35 (2): 255-60

Gumaste VV,Dave PB. 1992. Ingestion of corrosive substances by adults. *American Journal of Gastroenterology* 87 (1): 1-5

Hansen KS,Isager H. 1991. Obstructive lung injury after treating wood with sodium hydroxide. *Journal of the Society of Occupational Medicine* 41 (1): 45-6

Harley EH,Collins MD. 1997. Liquid household bleach ingestion in children: A retrospective review. *Laryngoscope* 107 (1): 122-5

Hasegawa R, Takahashi M, Kokubo T et al. 1986. Carcinogenicity study of sodium hypochlorite in f344 rats. *Food Chem Toxicol* 24 (12): 1295-302

Henry MA, Pelissari CE,Carvalho LR. 2008. Morphological and functional evaluation of distal esophagus of rabbits submitted to esophageal infusion with caustic soda. *Acta Cirurgica Brasileira* 23 (1): 16-21

Hopkins RA,Postlethwait RW. 1981. Caustic burns and carcinoma of the esophagus. *Ann Surg* 194 (2): 146-8

Hostynek JJ, Wilhelm KP, Cua AB et al. 1990. Irritation factors of sodium hypochlorite solutions in human skin. *Contact Dermatitis* 23 (5): 316-24

Isolauri J,Markkula H. 1989. Lye ingestion and carcinoma of the esophagus. *Acta Chir Scand* 155 (4-5): 269-71

Janoušek P, Jurovčík M, Grabec P et al. 2005. Corrosive oesophagitis in children following ingestion of sodium hydroxide granules - a case report. *International Journal of Pediatric Otorhinolaryngology* 69 (9): 1257-60

Jarvis D. 2002. The european community respiratory health survey ii. *European Respiratory Journal* 20 (5): 1071-9

Jester JV, Molai A, Petroll WM et al. 2000. Quantitative characterization of acid- and alkali-induced corneal injury in the low-volume eye test. *Toxicologic Pathology* 28 (5): 668-78

Johnson-Restrepo B,Kannan K. 2009. An assessment of sources and pathways of human exposure to polybrominated diphenyl ethers in the united states. *Chemosphere* 76 (4): 542-8

Jones AB. 2002. Caustic ingestions. *Techniques in Gastrointestinal Endoscopy* 4 (4): 196-200

Kay M,Wyllie R. 2009. Caustic ingestions in children. *Current Opinion in Pediatrics* 21 651 - 4

Kuckelkorn R, Makropoulos W, Kottek A et al. 1993. [retrospective study of severe alkali burns of the eye]. *Klinische Monatsblätter für Augenheilkunde* 203 (6): 397-402

Landau GD,Saunders WH. 1964. The effect of chlorine bleach on the esophagus. *Archives of Otolaryngology—Head & Neck Surgery* 80 (2): 174

Malvasio V, Ainoedhofer H, Ackbar R et al. 2012. Effects of sodium hydroxide exposure on esophageal epithelial cells in an in vitro ovine model: Implications for esophagus tissue engineering. *Journal of Pediatric Surgery* 47 (5): 874-80

Maurer JK, Molai A, Parker RD et al. 2001. Pathology of ocular irritation with bleaching agents in the rabbit low-volume eye test. *Toxicol Pathol* 29 (3): 308-19

McGuigan M. 1999. Common culprits in childhood poisoning. *Pediatric Drugs* 1 (4): 313-24

McKenzie LB, Ahir N, Stolz U et al. 2010. Household cleaning product-related injuries treated in us emergency departments in 1990-2006. *Pediatrics* 126 (3): 509-16

Meyer S, Eddleston M, Bailey B et al. 2007. Unintentional household poisoning in children. *Klin Padiatr* 219 (5): 254-70

Morgan RL, Sorenson SS,Castles TR. 1987. Prediction of ocular irritation by corneal pachymetry. *Food and Chemical Toxicology* 25 (8): 609-13

Murphy JC, Osterberg RE, Seabaugh VM et al. 1982. Ocular irritancy responses to various phs of acids and bases with and without irrigation. *Toxicology* 23 (4): 281-91

Nelson JD,Kopietz LA. 1987. Chemical injuries to the eyes. Emergency, intermediate, and long-term care. *Postgrad Med* 81 (4): 62-6, 9-71, 5

Nixon G, Tyson C,Wertz W. 1975. Interspecies comparisons of skin irritancy. *Toxicol Appl Pharmacol* 31 (3): 481-90

Nixon G, Bannan E, Gaynor T et al. 1990. Evaluation of modified methods for determining skin irritation. *Regulatory Toxicology and Pharmacology* 12 (2): 127-36

OEHHA. 1999. *Determination of acute reference exposure levels for airborne toxicants. Acute toxicity summary: Sodium hydroxide*.

PAN. 2013. *Sodium hypochlorite - identification, toxicity, use, water pollution potential, ecological toxicity and regulatory information*. PAN pesticide database http://www.pesticideinfo.org/Detail_Chemical.jsp?Rec_Id=PC34390

Pashley EL, Birdsong NL, Bowman K et al. 1985. Cytotoxic effects of naocl on vital tissue. *Journal of Endodontics* 11 (12): 525-8

Pike DG, Peabody Jr JW, Davis EW et al. 1963. A re-evaluation of the dangers of clorox ingestion. *The Journal of Pediatrics* 63 (2): 303-5

Presgrave Rde F, Camacho LA,Villas Boas MH. 2008. A profile of unintentional poisoning caused by household cleaning products, disinfectants and pesticides. *Cad Saude Publica* 24 (12): 2901-8

Racioppi F, Daskaleros PA, Besbelli N et al. 1994. Household bleaches based on sodium hypochlorite: Review of acute toxicology and poison control center experience. *Food and Chemical Toxicology* 32 (9): 845-61

Ramasamy K,Gumaste VV. 2003. Corrosive ingestion in adults. *Journal of Clinical Gastroenterology* 37 (2): 119-24

Riffat F,Cheng A. 2009. Pediatric caustic ingestion: 50 consecutive cases and review of the literature. *Diseases of the Esophagus* 22 89-94

Rubin AE, Bentur L,Bentur Y. 1992. Obstructive airway disease associated with occupational sodium hydroxide inhalation. *Br J Ind Med* 49 (3): 213-4

SCHER. 2008. *Risk assessment report on sodium hypochlorite human health part*.

Schins RP, Emmen H, Hoogendijk L et al. 2000. Nasal inflammatory and respiratory parameters in human volunteers during and after repeated exposure to chlorine. *European Respiratroy Journal* 16 (4): 626-32

Seidenari S, Pepe P,Di Nardo A. 1995. Sodium hydroxide-induced irritant dermatitis as assessed by computerized elaboration of 20 mhz b-scan images and by tewl measurement: A method for investigating skin barrier function. *Acta Derm Venereol* 75 (2): 97-101

Sharma N, Singh D, Sobti A et al. 2012. Course and outcome of accidental sodium hydroxide ocular injury. *American Journal of Ophthalmology* 154 (4): 740-9.e2

Smith WT. 1994. *Human and environmental safety of hypochlorite.*

Spiller H, Ross M,Nichols G. 1994. Fatal caustic ingestion of sodium hypochlorite bleach with associated hypernatremic-hyperchloremic acidosis. *Veterinary and Human Toxicology* 36

Srikrishna V,Monteiro-Riviere NA. 1991. The effects of sodium hydroxide and hydrochloric acid on isolated perfused skin. *In Vitro Toxicology* 4 207-15

Strange DC, Finneran JC, Shumacker HB et al. 1951. Corrosive injury of the stomach: Report of a case caused by ingestion of clorox® and experimental study of injurious effects. *AMA archives of surgery* 62 (3): 350-7

Tanyel FC, Büyükpamukçu N,Hiçsönmez A. 1988. Chlorine bleach ingestion in children: A review of 80 cases. *The Turkish journal of pediatrics* 30 (2): 105

Ti TK. 1983. Oesophageal carcinoma associated with corrosive injury--prevention and treatment by oesophageal resection. *British Journal of Surgery* 70 (4): 223-5

UK HPA. 2011. *Hpa compendium of chemical hazards - sodium hypochlorite*. United Kingdom Health Protection Agency

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/318241/HPA_Compendium_of_Chemical_Hazards_SODIUM_HYPOCHLORITE_v3-1.pdf

USEPA. 2008. Child-specific exposure factors handbook. (September 2008):

Van Rhee F,Beaumont D. 1990. Gastric stricture complicating oral ingestion of bleach. *Br J Clin Pract* 44 (12): 681

Vyskocil J, Tuma J,Dluhos M. 1966. The effect of aerosol inhalations of sodium hydroxide on the elimination of quartz dust from lungs of rats. *Sca Med Fac Nat Univ Brun Purkynianae* 40 25-9

Walker AP. 1985. A more realistic animal technique for predicting human eye response. *Food and Chemical Toxicolology* 23 (2): 175-8

Ward MJ,Routledge PA. 1988. Hypernatraemia and hyperchloraemic acidosis after bleach ingestion. *Hum Exp Toxicol* 7 (1): 37-8

Williams AL, Watson RE,DeSesso JM. 2012a. Developmental and reproductive outcomes in humans and animals after glyphosate exposure: A critical analysis. *Journal of Toxicology and Environmental Health, Part B Critical Review* 15 (1): 39-96

Williams H, Moyns E, Bateman DN et al. 2012b. Hazard of household cleaning products: A study undertaken by the uk national poisons information service. *Clinical toxicology (Philadelphia, Pa.)* 50 (8): 770-5

World Health Organization. 2009. *The who recommended classifcation of pesticides by hazard and guidelines to classification: 2009*.

York M, Basketter DA, Cuthbert JA et al. 1995. Skin irritation testing in man for hazard assessment--evaluation of four patch systems. *Human Experimental Toxicology* 14 (9): 729-34

York M, Griffiths HA, Whittle E et al. 1996. Evaluation of a human patch test for the identification and classification of skin irritation potential. *Contact Dermatitis* 34 (3): 204-12

Zock JP, Plana E, Anto JM et al. 2009. Domestic use of hypochlorite bleach, atopic sensitization, and respiratory symptoms in adults. *Journal of Allergy and Clinical Immunology* 124 (4): 731-8.e1

INSTITUTE OF ENVIRONMENTAL SCIENCE AND RESEARCH LIMITED

Kenepuru Science Centre
34 Kenepuru Drive, Kenepuru, Porirua 5022
PO Box 50348, Porirua 5240
New Zealand
T: +64 4 914 0700 **F:** +64 4 914 0770

Mt Albert Science Centre
120 Mt Albert Road, Sandringham, Auckland 1025
Private Bag 92021, Auckland 1142
New Zealand
T: +64 9 815 3670 **F:** +64 9 849 6046

NCBID – Wallaceville
66 Ward Street, Wallaceville, Upper Hutt 5018
PO Box 40158, Upper Hutt 5140
New Zealand
T: +64 4 529 0600 **F:** +64 4 529 0601

Christchurch Science Centre
27 Creyke Road, Ilam, Christchurch 8041
PO Box 29181, Christchurch 8540
New Zealand
T: +64 3 351 6019 **F:** +64 3 351 0010

www.esr.cri.nz