HYPOCHLORITE SALTS

1. Chemical and Physical Data

1.1 Synonyms and molecular formulae

Table 1. Synonyms (Chemical Abstracts Service names are given in bold) and molecular formulae of hypochlorite salts

Chemical name	Chem. Abstr. Services Reg. No.[a]	Synonyms	Formula	Molecular weight
Calcium hypochlorite	7778-54-3	Calcium oxychloride; chlorinated lime; chlorolime chemical; **hypochlorous acid, calcium salt**; lime chloride	$Ca(OCl)_2$	142.98
Dibasic calcium hypochlorite	12394-14-8	**Calcium hydroxide hypochlorite**; lime chloride	$Ca(OCl)_2 \cdot 2Ca(OH)_2$	291.14
Calcium hypochlorite dihydrate	22464-76-2	**Hypochlorous acid, calcium salt, dihydrate**	$Ca(OCl)_2 \cdot 2H_2O$	174.98
Lithium hypochlorite	13840-33-0	**Hypochlorous acid, lithium salt**; lithium chloride oxide; lithium oxychloride	LiOCl	58.39
Potassium hypochlorite	7778-66-7	**Hypochlorous acid, potassium salt**; potassium chloride oxide	KOCl	90.55
Sodium hypochlorite	7681-52-9	**Hypochlorous acid, sodium salt**; sodium chloride oxide; sodium oxychloride	NaOCl	74.44
Sodium hypochlorite heptahydrate	64131-03-9	**Hypochlorous acid, sodium salt, heptahydrate**	$NaOCl \cdot 7H_2O$	200.44
Sodium hypochlorite hydrate (2:5)	55248-17-4	**Hypochlorous acid, sodium salt, hydrate (2:5)**	$NaOCl \cdot 2{\cdot}5H_2O$	119.48
Sodium hypochlorite pentahydrate	10022-70-5	**Hypochlorous acid, sodium salt, pentahydrate**	$NaOCl \cdot 5H_2O$	164.52
Calcium sodium hypochlorite	53053-57-9	**Hypochlorous acid, calcium sodium salt (3:1:1)**	$Ca(OCl)_2 \cdot NaOCl$	217.42

1.2 Chemical and physical properties of the pure substances

From Weast (1989) unless otherwise specified

Calcium hypochlorite

(*a*) *Description:* White powder or flat plates
(*b*) *Melting-point*: Decomposes at 100°C
(*c*) *Density*: Specific gravity = 2.35
(*d*) *Solubility*: Soluble in cold water, 21.4% soluble at 25°C (Wojtowicz, 1979); insoluble in ethanol
(*e*) *Stability*: Solid form decomposes exothermically when heated to 175°C, releasing oxygen (Mannsville Chemical Products Corp., 1987). Can react vigorously, and sometimes explosively, with organic and inorganic materials; aqueous solutions subject to decomposition which is influenced by concentration, ionic strength, pH, temperature, light and impurities (Wojtowicz, 1979).
(*f*) *Reactivity*: Strong oxidizer of organic and inorganic materials; also acts as a chlorinating agent toward some classes of organic compounds (Wojtowicz, 1979)

Sodium hypochlorite pentahydrate

(*a*) *Description:* Colourless crystals
(*b*) *Melting-point*: 18°C
(*c*) *Solubility*: In water (g/l): 293 at 0°C, 942 at 23°C
(*d*) *Stability*: Highly unstable (Budavari, 1989)
(*e*) *Reactivity*: Strong oxidizer of organic and inorganic compounds (Wojtowicz, 1979)

Sodium hypochlorite solution (aqueous)

(*a*) *Description:* Clear or slightly yellow solution
(*b*) *Stability*: Anhydrous hypochlorite is highly explosive; the solution is subject to decomposition, which is influenced by its concentration, ionic strength, pH, temperature, light and impurities; also susceptible to catalysis by trace metal impurities (Wojtowicz, 1979)
(*c*) *Reactivity*: Strong oxidizer of many organic and inorganic substances and chlorinates some classes of organic compounds. Contact with acid releases chlorine gas (Jones Chemical, 1989). Reacts violently with ammonium salts, aziridine, methanol and phenylacetonitrile, sometimes resulting in explosion. Reacts with primary aliphatic and aromatic amines to form explosively unstable *N*-chloramines. Reaction with formic acid becomes explosive at 55°C (Sigma-Aldrich Company, 1989).

Sodium hypochlorite dihydrate

(*a*) *Description*: Colourless hygroscopic crystals
(*b*) *Melting-point*: 57.5°C
(*c*) *Solubility*: Very soluble in cold water

The chemistry of hypochlorite ion in aqueous solutions is discussed in the monograph on chlorinated drinking-water (p. 50). All hypochlorite salts, as well as chlorine itself, in aqueous solution produce equilibrium mixtures of hypochlorous acid, hypochlorite ion and chlorine. In concentrated solutions, hypochlorite ion tends to disproportionate to form chlorate and chloride ions. The reaction is slow at room temperature, but in hot solutions (e.g., 80°C) the reaction is rapid and produces high yields of chlorate ions (Aieta & Roberts, 1986).

1.3 Technical products and impurities

Calcium hypochlorite

Trade names: B-K Powder; Camporit; Chemichlor G; Chloride of lime; Eusol BPC; HTH; HTH (bleaching agent); Lime chloride; Losantin; Pittchlor; Solvox KS; T-Eusol

Calcium hypochlorite (bleach liquor) is produced commercially as a solution of calcium hypochlorite and calcium chloride containing some dissolved lime. Commercial products usually contain 50% or more calcium hypochlorite. The available chlorine content varies but is usually about 30-35 g/l (Wojtowicz, 1979; Budavari, 1989).

Calcium hypochlorite is one of the few metal hypochlorites that is stable enough to be produced as a solid salt. It is produced on a large scale as a 65-70% pure product (dihydrate salt) containing sodium chloride and water as the main impurities. It is also manufactured, to a smaller extent, in the form of bleaching powder (Wojtowicz, 1979), which contains approximately 37% available chlorine in a complex mixture of calcium hydroxide, calcium chloride and various calcium hypochlorite species. Calcium oxide is often blended with bleach powder as a desiccant in order to avoid deliquescence of the powder in hot and humid conditions; this blended product, tropical bleach, contains about 15-30% available chlorine (Baum *et al.*, 1978).

Sodium hypochlorite (liquid bleach)

Trade names: Antiformin; B-K Liquid; Carrel-Dakin solution; Chloros; Clorox; Dakin's solution; Deosan; Hyclorite; Javex; Klorocin; Milton; Neo-cleaner; Neoseptal CL; Parozone; Purin B; Surchlor

Commercial strength sodium hypochlorite is available as a solution that contains 12-15% available chlorine; a weaker solution that is marketed contains

approximately 5% available chlorine. The main impurities in these solutions include sodium chlorate, sodium carbonate, sodium chloride and sodium hydroxide. Sodium hypochlorite solution produced on-site for industrial processes generally contains 30-40 g/l of available chlorine (Wojtowicz, 1979).

Lithium hypochlorite

Commercial lithium hypochlorite is a solid product usually containing 35% lithium hypochlorite, 34% sodium chloride and various additional salts (Baum *et al.*, 1978; Wojtowicz, 1979).

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(*a*) *Production*

Berthollet first used chlorine in a commercial textile bleaching process in the 1790s; he later discovered that chlorine could be absorbed by caustic potash to form potassium hypochlorite solution (Javel water). Labarraque replaced the expensive potash with caustic soda, and by the early 1800s Labarraque's solution had replaced potassium hypochlorite in the bleaching of textiles. Tennant experimented with a solution of chlorine and milk of lime in 1798 and later discovered that when slaked lime was treated with chlorine a solid bleaching powder (calcium hypochlorite and other salts) was formed, representing the first solid form of chlorine bleach that could be easily transported. Bleaching powder remained the principal textile bleach throughout the 1800s. Tropical bleach, stable in high tropical temperatures, was produced by the addition of quicklime to bleaching powder. After the First World War, technology for shipping liquid chlorine and caustic economically was developed, allowing bleach solutions to be made at the point of use. In 1928, the first dry calcium hypochlorite with 70% available chlorine was produced in the USA and was used widely in the bleaching of textiles and pulp (Baum *et al.*, 1978; Wojtowicz, 1979).

At the inception of the commercial laundry industry in about 1900, sodium hypochlorite solution made with bleaching powder and soda ash was used. When chlorine became more readily available, sodium hypochlorite was produced directly at the point of use. Dry calcium hypochlorite bleaches were introduced in the 1930s. Home bleaching became more common when sodium hypochlorite solutions began to displace bleaching powders in the 1930s; they came into extensive use in the 1940s (Baum *et al.*, 1978). Other hypochlorites, such as lithium

hypochlorite, first introduced in 1964, have had limited commercial use (Wojtowicz, 1979).

Calcium hypochlorite solution (bleach liquor) is prepared by adding chlorine to a diluted high quality lime slurry. Solid calcium hypochlorite is generally made by drying a filter cake of neutral calcium hypochlorite dihydrate prepared from hydrated lime, caustic and chlorine. Several industrial processes were developed to eliminate or minimize calcium chloride in the hypochlorite product (Wojtowicz, 1979).

Sodium hypochlorite is usually prepared by chlorinating aqueous sodium hydroxide solution at reduced temperatures to prevent excessive chlorate formation, which can contribute to lower stability. Conversion of sodium hydroxide to hypochlorite is usually limited to 92-94% to prevent overchlorination and to improve stability. Sodium hypochlorite is also prepared electrolytically using small diaphragm-less or membrane cells with a capacity of 1-150 kg per day of equivalent chlorine; these produce dilute hypochlorite solutions of 1-3 and 5-6 g/l from seawater and brine, respectively (Wojtowicz, 1979).

Solid lithium hypochlorite is produced by combining concentrated solutions of sodium hypochlorite and lithium chloride (Baum *et al.*, 1978).

Production capacity of calcium hypochlorite in 1989-90 in countries for which data were available are presented in Table 2. Japanese production of sodium hypochlorite (12% solution) was 947 thousand tonnes in 1984, 954 in 1985, 996 in 1986, 972 in 1987 and 989 in 1988 (Anon., 1985; Ministry of International Trade and Industry, 1989).

Table 2. Production capacity of calcium hypochlorite in selected countries (in thousands of tonnes)[a]

Country	Active chlorine (%)	
	65-70	60
Canada	5.9	None
China	0.5	10.8
India	None	1.0
Italy	0.9	4.1
Japan	34.7	11.0
Republic of Korea	1.0	None
South Africa	12.0	None
USA	105.3	None
Total	160.3	26.9

[a]From PPG Industries (1990)

Sodium hypochlorite is produced by two companies in Africa, three in the Middle East, five in Oceania, 13 in North America, 18 in South America, 30 in Asia and 48 companies in Europe (Chemical Information Services Ltd., 1988). Calcium hypochlorite is produced by 21 companies and potassium chlorite by three companies throughout the world (Anon., 1989).

(*b*) *Use*

Calcium hypochlorite is widely used as a sanitizer, oxidizer and bleaching agent. Calcium hypochlorite solutions are used primarily in pulp and textile bleaching, while the solid form is used in less developed countries for textile bleaching and commercial laundering (Baum *et al.*, 1978). The largest use of calcium hypochlorite within the USA is in swimming pools to kill bacteria, control algae and oxidize organic contaminants. It is also used to destroy cyanides in industrial wastes, in disinfection and deodourizing of wastes generated from canneries, dairy plants, beet sugar plants and tanneries, as a biocide in controlling contamination in public, private and industrial water supplies, in sanitizing beverage plants and food processing operations and equipment, in disinfecting sewage disposal plants, in sanitizing fruits and vegetables during growth and following harvest, as a toilet tank sanitizer and in multistage pulp bleaching processes. It can also be reacted with acetone to produce USP chloroform (Mannsville Chemical Products Corp., 1987).

Consumption of calcium hypochlorite in 1989-90 was estimated to be 7.0 thousand tonnes in Japan, 80.1 thousand tonnes in the USA and 40 thousand tonnes in the rest of the world. Use distribution figures for 1989-90 were estimated to be 85% for swimming pools and 15% for other uses in the USA, and 55% for swimming pools and 45% for other uses in the rest of the world (PPG Industries, 1990).

The largest use for sodium hypochlorite solutions (5% concentration) is as a household bleach. More concentrated solutions are used in swimming pool sanitation, in commercial laundry bleaching, in paper and pulp production, in disinfecting municipal water (particularly in small water supplies) and sewage, in the sanitation of dairy plants and food processing operations, to control fungal plugging of oil production equipment, as a desulfurizing agent in oil refineries, and as a disinfectant and sanitizer in health care industries. Large quantities of sodium hypochlorite are used in the chemical industry, primarily in the production of hydrazine (see IARC, 1987) as well as in the synthesis of organic chemicals and the manufacture of chlorinated trisodium phosphate. Sodium hypochlorite solutions produced directly by electrolysis of seawater or brine are used primarily in sewage and wastewater treatment, commercial laundries, large swimming pools and aboard ships (Baum *et al.*, 1978; Wojtowicz, 1979; White, 1986; Mannsville Chemical Products Corp., 1987).

Small quantities of lithium hypochlorite are produced for use in swimming pool sanitation (Mannsville Chemical Products Corp., 1987) and in household laundry detergents (Baum *et al.*, 1978).

2.2 Occurrence

(*a*) *Natural occurrence*

Hypochlorous acid is generated in mammalian neutrophils by myeloperoxidase (MP) by the following reaction:

$$MP + H_2O_2 \rightarrow MP{\cdot}H_2O_2$$

$$MP{\cdot}H_2O_2 + Cl^- \rightarrow MP + HOCl + OH^-$$

(Winterbourn, 1985).

(*b*) *Occupational exposure*

Due to the wide range of uses of hypochlorite salts, many workers may be exposed to them by dermal (and ocular) contact or inhalation. During routine monitoring in a US calcium hypochlorite manufacturing facility, personal samples contained an 8-h time-weighted average of 0.31 mg/m^3 (geometric mean) and a 15-min short-term exposure level of 0.38 mg/m^3 (geometric mean); work area samples contained an 8-h time-weighted average of 0.13 mg/m^3 and a mean 15-min short-term exposure level of 0.88 mg/m^3 (PPG Industries, 1990). No published data were available on occupational exposures to or the environmental occurrence of hypochlorites. No regulatory standards or guidelines have been established for exposures to hypochlorite.

(*c*) *Water*

The chemistry of hypochlorous acid and hypochlorite ion in aqueous solutions is discussed in the monograph on chlorinated drinking-water (p. 50). Residual chlorine in drinking-water is present in part as hypochlorite, indicating widespread exposure of the general population to low levels of hypochlorite in solution.

(*d*) *Other*

Another significant potential route of exposure to hypochlorite derives from its widespread use as a household sanitizer and bleach and in swimming pools. No data were found which directly characterize these exposures.

2.3 Analysis

The analysis of hypochlorite and related chlorine species in aqueous media is well documented (White, 1986) and involves a variety of colorimetric and

iodometric procedures. No specific method is available for the analysis of occupational exposures to hypochlorite salts in air. General methods for dusts (e.g., NIOSH Method 500; Eller, 1984a) and the appropriate metal (e.g., NIOSH Method 7020; Eller, 1984b) are used.

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals

(a) *Oral administration*

Mouse: Groups of 50 male and 50 female B6C3F$_1$ mice, four to six weeks old, were given 500 or 1000 mg/l sodium hypochlorite (14% effective chlorine [purity unspecified]) in the drinking-water for 103 weeks. Groups of 73 male and 72 female mice served as controls. Survival at 106 weeks was: males—control, 48/73, low-dose, 39/50; high-dose, 37/50; females—control, 56/72; low-dose, 40/50; high-dose, 39/50. There was no effect upon tumour incidence in either male or female mice (Kurokawa *et al.*, 1986).

Rat: A group of 60 male and female BDII (cPah albino) rats, 100 days old [sex ratio unspecified], was given tap water [organic content not analysed] containing 100 mg/l chlorine prepared with chlorine gas. The animals were mated and the treatment was continued for life through six generations, with the exception of F_3 and F_4 animals, which were treated during the weaning period only. Altogether, 236 animals in five generations were exposed. Two groups of 20 and 36 rats [sex and age unspecified] from two previous experiments served as controls. There was no difference in survival or in tumour incidence in any generation group as compared to untreated controls (Druckrey, 1968).

Groups of 50 male and 50 female Fischer 344 rats, seven weeks old, were given 0, 500 or 1000 (males) and 0, 1000 or 2000 (females) mg/l sodium hypochlorite (14% effective chlorine [purity unspecified]) in the drinking-water for 104 weeks. Survival at 112 weeks was: males—control, 30/50; low-dose, 26/50; high-dose, 31/50; females—control, 31/50; low-dose, 36/50; high-dose, 35/50. The occurrence of tumours at any site was not significantly greater in rats receiving sodium hypochlorite than in controls. The proportions of low- and high-dose female rats with fibroadenomas of the mammary gland were significantly lower than among controls (control, 8/50; low-dose, 0/50; $p < 0.01$, chi-square test; high-dose, 1/50; $p < 0.01$). Similarly, the proportion of high-dose male rats with nodular hyperplasia of the liver was decreased (control, 23/49; low-dose, 17/50; high-dose, 10/50; $p < 0.01$) (Hasegawa *et al.*, 1986).

(*b*) *Skin application*

Mouse: A group of 40 strain ddN female mice, five weeks old, was given 60 topical applications of sodium hypochlorite (10% effective chlorine solution) [purity, vehicle and frequency of application unspecified]. Another group of 40 female mice was given 20 applications of 4-nitroquinoline 1-oxide [dose, purity and frequency unspecified]; and a third group of 40 mice was given 45 applications of sodium hypochlorite following applications of 4-nitroquinoline 1-oxide [number and frequency of applications and dose unspecified]. No skin tumour occurred in mice given applications of sodium hypochlorite alone, whereas skin tumours occurred in 9/32 mice given applications of sodium hypochlorite following initiating doses of 4-nitroquinoline 1-oxide. The skin tumours included one fibrosarcoma, three squamous-cell carcinomas and five papillomas. No skin tumour occurred in mice given applications of 4-nitroquinoline 1-oxide only (Hayatsu *et al.*, 1971). [The Working Group noted the lack of details on dose, frequency of applications, age at termination of the study, and survival.]

A group of 20 female Sencar mice, six weeks old, was given topical applications of 0.2 ml of a solution of 10 g/l sodium hypochlorite [purity unspecified] in acetone twice a week for 51 weeks at which time the study was terminated. A group of 15 female mice given applications of acetone served as controls. All mice survived to the end of the study and no skin tumour was observed in the treated or control groups (Kurokawa *et al.*, 1984). [The Working Group noted the small number of animals used.]

In an initiation/promotion study, a group 20 female Sencar mice, six weeks old, was given a single topical application of 20 nmol [5 μg] 7,12-dimethylbenz[*a*]-anthracene in acetone followed by applications of 0.2 ml of a 10 g/l sodium hypochlorite solution [purity unspecified] in acetone twice a week for 51 weeks. A group of 15 female mice given a single application of 7,12-dimethylbenz[*a*]-anthracene followed by applications of acetone served as controls. The effective number of mice was 20; the number of survivors was not given. A squamous-cell carcinoma of the skin occurred in 1/20 mice treated with 7,12-dimethylbenz[*a*]-anthracene and sodium hypochlorite; none occurred in the initiated controls (Kurokawa *et al.*, 1984).

3.2 Other relevant data

(*a*) *Experimental systems*

(i) *Absorption, distribution, excretion and metabolism.*

Radiolabel (^{36}Cl) derived from hypochlorous acid given to male rats was absorbed and appeared in serum at a rate constant of 0.3/h compared to 0.04/h for

sodium chloride. The radiolabel was eliminated from plasma with a half-time of 44 h, compared to 52 h for sodium chloride. The distribution of radiolabel from hypochlorous acid and from sodium chloride in tissues was similar (Abdel-Rahman, 1985).

(ii) *Toxic effects*

Blabaum and Nichols (1956) provided mice with concentrations of 100 and 200 mg/l chlorine in the drinking-water (pH 5.9-6.5) for up to 50 days. They reported no effect on body weight or gross morphology.

Chronic treatment of male and female BDII albino rats with drinking-water containing 100 mg/l chlorine [pH unspecified] had no significant toxic effect over seven generations (Druckrey, 1968).

Cunningham (1980) gave sodium hypochlorite in drinking-water at levels of 0, 20, 40 and 80 mg/l as chlorine to male Wistar rats for up to six weeks. In a separate experiment, female rats were administered sodium hypochlorite at doses equivalent to 0, 8, 40 and 200 mg/kg bw available chlorine in milk by gavage twice daily for 14 days. Guinea-pigs were administered sodium hypochlorite at 0 and 50 mg/l as chlorine in drinking-water for five weeks. There were small but significant increases in body weights in rats given drinking-water, and increased kidney weights in rats treated with 200 mg/kg bw by gavage. No significant increase in body weight was seen in guinea-pigs.

Administration of sodium hypochlorite in drinking-water to mice at levels of 25-30 mg/l reduced the number of peritoneal exudate cells recovered by lavage after one to four weeks of treatment (Fidler, 1977). The phagocytic activity of macrophages recovered from treated animals was decreased by approximately 50% relative to control animals during the first two weeks of treatment and was completely absent by the third week. Subsequent experiments demonstrated that the in-vivo phagocytic activity of macrophages recovered from the liver and spleen was also decreased. The treatment also prevented the destruction by injection of macrophage activating factors of spontaneous metastases arising from B16-BL6 melanoma cells implanted subcutaneously (Fidler *et al.*, 1982). Exon *et al.* (1987) observed no decrement in the in-vitro phagocytic activity of peritoneal macrophages recovered by lavage from rats given 5, 15, 30 mg/l sodium hypochlorite; however, decreases in spleen weights, delayed-type hypersensitivity reactions and macrophage oxidative metabolism were observed at the high dose.

In rats, concentrations of sodium hypochlorite of 625 mg/l and above given in drinking-water for 14 days progressively depressed water consumption. In a 92-day study, no significant effect on body weight, organ weights or serum chemistry was observed until concentrations reached 4000 mg/l (Furukawa *et al.*, 1980). In chronic studies in mice and rats (see section 3.1), there was no significant effect on survival

of either mice or rats treated with 500-2000 mg/l drinking-water, but dose-related decreases in body weight gain occurred (Hasegawa *et al.*, 1986; Kurokawa *et al.*, 1986).

Robinson *et al.* (1986) examined the effects of hypochlorous acid and hypochlorite on mouse skin. With 10 min of contact per day for four days, hypochlorous acid (pH 6.5) markedly increased skin thickness at concentrations of 300 mg/l and above; a similar but less marked effect was observed with hypochlorite (pH 8.5) at 1000 mg/l.

Cotter *et al.* (1985) applied gauze soaked in 0.1 and 0.5% solutions of sodium hypochlorite (pH 7.49) to the skin of guinea-pigs for two weeks. The 0.1% solution produced no effect on isolated epidermal basal-cell viability, but the 0.5% solution was reported to reduce it.

Male white Carneau pigeons and New Zealand rabbits administered 15 mg/l chlorine in drinking-water (pH 6.5 or 8.5) for three months had increased plasma low-density lipid cholesterol levels and decreased plasma thyroxine levels. The effects were more pronounced in animals fed high-cholesterol diets (Revis *et al.*, 1986). Subsequent experiments by the same authors failed to confirm these observations (Holdsworth *et al.*, 1990).

In a neutrophil migration assay *in vitro*, sodium hypochlorite (0.00025% solution buffered with sodium carbonate) suppressed migration of stimulated and nonstimulated neutrophils (Kozol *et al.*, 1988).

(iii) *Effects on reproduction and prenatal toxicity*

In BDII rats given water containing free chlorine at 100 mg/l in drinking-water daily during seven generations, there was no toxic effect on fertility, growth or survival (Druckrey, 1968).

(iv) *Genetic and related effects* (Table 3)

In one differential toxicity test involving DNA repair-deficient bacteria, a positive result was obtained with sodium hypochlorite. Mutations were induced in *Salmonella typhimurium*.

In a single study, sodium hypochlorite caused chromosomal aberrations in Chinese hamster CHL cells but not in human fibroblasts. [The Working Group noted that lower doses were used in the latter tests.] It was reported in an abstract that sodium hypochlorite did not induce transformation in C3H 10T½ cells (Abernethy *et al.*, 1983). The number of micronuclei was increased in erythrocytes of newt larvae reared in hypochlorite-containing water for 12 days. Neither micronuclei, chromosomal aberrations nor aneuploidy were observed in mice after repeated oral dosing; but abnormal sperm morphology was seen.

Table 3. Genetic and related effects of sodium hypochlorite

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
ECD, *Escherichia coli pol A*/W3110–P3478, differential toxicity	+	0	0.4000	Rosenkranz (1973)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	+	2500.0000	Ishidate *et al.* (1984)
SA3, *Salmonella typhimurium* TA1530, reverse mutation	+	0	0.0100	Wlodkowski & Rosenkranz (1975)
SA3, *Salmonella typhimurium* TA1530, reverse mutation	+	0	5.0000	Wlodkowski & Rosenkranz (1975)[a]
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	0	0.0100	Wlodkowski & Rosenkranz (1975)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	0	5.0000	Wlodkowski & Rosenkranz (1975)
???, Micronucleus test, newt larvae	+	0	0.0000	Gauthier *et al.* (1989)[b]
CIC, Chromosomal aberrations, Chinese hamster CHL cells	+	(+)	500.0000	Ishidate (1987)
SHF, Sister chromatid exchange, human diploid fibr. lung cell line	+	0	74.0000	Sasaki *et al.* (1980)
CHF, Chromosomal aberrations, human diploid fibr. lung cell line	–	0	149.0000	Sasaki *et al.* (1980)
MVM, Micronucleus test, bone-marrow cells of CD-1 mice *in vivo*	–	0	6.0000	Meier *et al.* (1985)
MVM, Micronucleus test, bone-marrow cells of ddY mice *in vivo*	–	0	1250.0000	Hayashi *et al.* (1988)
MVM, Micronucleus test, bone-marrow cells of ddY mice *in vivo*	–	0	300.0000	Hayashi *et al.* (1988)
CBA, Chromosomal aberrations, bone-marrow cells of CD-1 mice *in vivo*	–	0	6.0000	Meier *et al.* (1985)
AVA, Aneuploidy, bone-marrow cells of CD-1 mice *in vivo*	–	0	6.0000	Meier *et al.* (1985)
SPM, Sperm morphology, B6C3F$_1$ mice *in vivo*	+	0	3.0000	Meier *et al.* (1985)

[a]Treatment in liquid medium

[b]Larvae reared in hypochlorite-containing water

In a report lacking details, negative findings were reported in a *Bacillus subtilis* $rec^{+/-}$ assay, in a mutation assay in silkworms and in a test for chromosomal aberrations in rat bone marrow *in vivo* (Kawachi *et al.*, 1980).

(*b*) *Humans*

(i) *Absorption, distribution, excretion and metabolism*

No data were available to the Working Group.

(ii) *Toxic effects*

Release of chlorine during acidification of sodium hypochlorite solutions (below pH 7.5) is an occasional cause of poisoning (Phillip *et al.*, 1985). The effects are reversible if the exposure is low enough to permit survival from the acute respiratory distress that results (Jones *et al.*, 1986).

The use of hypochlorite solutions to disinfect haemodialysis machines has led to accidental introduction of sodium hypochlorite into the blood. If such exposures are high, they can lead to massive haemolysis (Hoy, 1981).

Skin hypersensitivity to concentrations of 400-600 mg/l sodium hypochlorite was reported in one patient (Eun *et al.*, 1984).

No clinical sign of general or local toxicity was observed following the use of sodium hypochlorite for bladder irrigation in urological patients (Eisen *et al.*, 1976).

In a clinical trial, Wones *et al.* (1990) examined the biochemical effects in 17 healthy men given a daily amount of 1.5 l distilled drinking-water fortified with chlorine at concentrations increasing from 2 to 10 mg/l during 12 weeks. Each person served as his own control. There was a small but significant increase in serum cholesterol levels and total thyroxine concentrations during the exposure period.

(iii) *Effects on reproduction and prenatal toxicity*

No data were available to the Working Group.

(iv) *Genetic and related effects*

No data were available to the Working Group.

3.3 Case reports and epidemiological studies of carcinogenicity to humans

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Exposure data

The principal hypochlorite salts produced commercially are calcium, sodium and lithium hypochlorites. Calcium hypochlorite (solid or aqueous solution) is

widely used for disinfection in swimming pools and in industrial applications and for pulp and textile bleaching. Sodium hypochlorite (aqueous solution) is used as a household laundry bleach, in commercial laundering, in pulp and paper manufacture, in industrial chemical synthesis and in the disinfection of drinking-water. Lithium hypochlorite (solid) is used in swimming pools for disinfection and in household detergents.

Hypochlorite salts (principally sodium hypochlorite) are used to disinfect drinking-water at many small treatment works. In the disinfection of drinking-water and wastewater, addition of hypochlorite salts and of chlorine gas gives the same chlorine species in solution—i.e., an equilibrium mixture of mainly hypochlorous acid and hypochlorite anion. In this way, much of the general population is exposed to hypochlorite *via* chlorinated drinking-water (see the monograph on Chlorinated drinking-water).

4.2 Experimental carcinogenicity data

Sodium hypochlorite was tested for carcinogenicity in a two-year study in male and female B6C3F$_1$ mice and Fischer 344 rats by oral administration in drinking-water, in limited studies in female Sencar mice and in female ddN mice by skin application. Sodium hypochlorite was also tested for promoting effects in female Sencar mice following initiation with 7,12-dimethylbenz[*a*]anthracene and in female ddN mice following initiation with 4-nitroquinoline 1-oxide. Sodium hypochlorite administered in the drinking-water did not increase the proportion of rats or mice with tumours. Sodium hypochlorite applied to the skin of Sencar mice or ddN mice did not produce skin tumours. No skin promoting effect was observed in the study with 7,12-dimethylbenz[*a*]anthracene, whereas some effect was seen in the study with 4-nitroquinoline 1-oxide.

Drinking-water containing 100 mg/l chlorine was tested for carcinogenicity in a multigeneration study in male and female BDII rats. No increase in the incidence of tumours was seen in treated animals relative to controls through six generations.

4.3 Human carcinogenicity data

No data were available to the Working Group.

4.4 Other relevant data

Sodium hypochlorite induced genotoxic effects in bacteria. In single studies, chromosomal aberrations were observed in cultured mammalian cells, whereas sister chromatid exchange but no chromosomal aberration was seen in cultured human cells. In a single study, micronuclei were induced in newt larvae. In mice, no

induction of micronuclei, aneuploidy or chromosomal aberrations was observed in bone marrow, but abnormal sperm morphology was seen after administration of sodium hypochlorite.

4.5 Evaluation[1]

There is *inadequate evidence* for the carcinogenicity of hypochlorite salts in experimental animals.

No data were available from studies in humans on the carcinogenicity of hypochlorite salts.

Overall evaluation

Hypochlorite salts *are not classifiable as to their carcinogenicity to humans (Group 3).*

5. References

Abdel-Rahman, M.S. (1985) Pharmacokinetics of chlorine obtained from chlorine dioxide, chlorine, chloramine, and chloride. In: Jolley, R.L., Bull, R.J., Davis, W.P., Katz, S., Roberts, M.H., Jr & Jacobs, V.A., eds, *Water Chlorination: Chemistry, Environmental Impact and Health Effects*, Vol. 5, Ann Arbor, MI, Lewis Publishers, pp. 281-293

Abernethy, D.J., Frazelle, J.H. & Boreiko, C.J. (1983) Relative cytotoxic and transforming potential of respiratory irritants in the C3H/1OT1/2 cell transformation system (Abstract No. Cd-20). *Environ. Mutagenesis, 5*, 419

Aieta, E.M. & Roberts, P.V. (1985) The chemistry of oxo-chlorine compounds relevant to chlorine dioxide generation. In: Jolley, R.L., Bull, R.J., Davis, W.P., Katz, S., Roberts, M.H., Jr & Jacobs, V.A., eds, *Water Chlorination: Chemistry, Environmental Impact and Health Effects*, Vol. 5, Ann Arbor, MI, Lewis Publishers, pp. 783-794

Anon. (1985) Chemical industry trends in 1984. In: Japan Chemical Week, ed., *Japan Chemical Annual 1985*, Tokyo, The Chemical Daily Co., pp. 14-18

Anon. (1989) *OPD Chemical Buyers Directory*, 76th annual ed., New York, Schnell Publishing Company, pp. 125, 150, 505, 576

Baum, B.M., Finley, J.H., Blumbergs, J.H., Elliott, E.J., Scholer, F. & Wooten, H.L. (1978) Bleaching agents. In: Mark, H.F., Othmer, D.F., Overberger, C.G., Seaborg, G.T. & Grayson, M., eds, *Kirk-Othmer Encyclopedia of Chemical Technology*, 3rd ed., Vol. 3, New York, John Wiley & Sons, pp. 938-958

[1]For description of the italicized terms, see Preamble, pp. 30-33.

Bercz, J.P., Jones, L., Garner, L., Murray, D., Ludwig, D.A. & Boston, J. (1982) Subchronic toxicity of chlorine dioxide and related compounds in drinking water in the nonhuman primate. *Environ. Health Perspect.*, *46*, 47-55

Blabaum, C.J. & Nichols, M.S. (1956) Effect of highly chlorinated drinking water on white mice. *J. Am. Water Works Assoc.*, *48*, 1503-1506

Budavari, S., ed. (1989) *The Merck Index*, 11th ed., Rahway, NJ, Merck & Co., pp. 254, 1363

Chemical Information Services Ltd (1988) *Directory of World Chemical Producers 1989/90*, Oceanside, NY, p. 522

Cotter, J.L., Fader, R.C., Lilley, C. & Herndon, D.N. (1985) Chemical parameters, antimicrobial activities, and tissue toxicity of 0.1 and 0.5% sodium hypochlorite solutions. *Antimicrob. Agents Chemother.*, *28*, 118-122

Cunningham, H.M. (1980) Effect of sodium hypochlorite on the growth of rats and guinea pigs. *Am. J. vet. Res.*, *41*, 295-297

Druckrey, H. (1968) Chlorinated drinking water, toxicity tests, involving seven generations of rats (Ger.). *Food Cosmet. Toxicol.*, *6*, 147-154

Eisen, M., Jurcovic, K., Pfeiffer, E., Skoluda, D. & Busse, K. (1976) Clinical use of sodium hypochlorite for local treatment and prevention of urinary tract infections and treatment of retracted bladders (Ger.). *Urologe A*, *15*, 39-43

Eller, P.M. (1984a) *NIOSH Manual of Analytical Methods*, 3rd ed., Vol. 2, *Nuisance Dust, Total, Method 500*, Cincinnati, OH, National Institute for Occupational Safety and Health, pp. 500-1—500-3

Eller, P.M. (1984b) *NIOSH Manual of Analytical Methods*, 3rd ed., Vol. 1, *Calcium and Compounds, as Ca, Method 7020*, Cincinnati, OH, National Institute for Occupational Safety and Health, pp. 7020-1—7020-3

Eun, H.C., Lee, A.Y. & Lee, Y.S. (1984) Sodium hypochlorite dermatitis. *Contact Derm.*, *11*, 45

Exon, J.H., Koller, L.D., O'Reilly, C.A. & Bercz, J.P. (1987) Immunotoxicologic evaluation of chlorine-based drinking water disinfectants, sodium hypochlorite and monochloramine. *Toxicology*, *44*, 257-269

Fidler, I.J. (1977) Depression of macrophages in mice drinking hyperchlorinated water. *Nature*, *270*, 735-736

Fidler, I.J., Barnes, Z., Fogler, W.E., Kirsh, R., Bugelski, P. & Poste, G. (1982) Involvement of macrophages in the eradication of established metastases following intravenous injection of liposomes containing macrophage activators. *Cancer Res.*, *42*, 496-501

Furukawa, F., Kurata, Y., Kokubo, T., Takahashi, M. & Nakadate, M. (1980) Oral acute and subchronic toxicity studies for sodium hypochlorite in F-344 rat. *Bull. natl Inst. Hyg. Sci.*, *98*, 62-69

Gauthier, L., Levi, Y. & Jaylet, A. (1989) Evaluation of the clastogenicity of water treated with sodium hypochlorite or monochloramine using a micronucleus test in newt larvae (*Pleurodeles waltl*). *Mutagenesis*, *4*, 170-173

Hasegawa, R., Takahashi, M., Kokubo, T., Furukawa, F., Toyoda, K., Sato, H., Kurokawa, Y. & Hayashi, Y. (1986) Carcinogenicity study of sodium hypochlorite in F344 rats. *Food chem. Toxicol.*, *24*, 1295-1302

Hayashi, M., Kishi, M., Sofuni, T. & Ishidate, M., Jr (1988) Micronucleus tests in mice on 39 food additives and eight miscellaneous chemicals. *Food chem. Toxicol., 26*, 487-500

Hayatsu, H., Hoshino, H. & Kawazoe, Y. (1971) Potential cocarcinogenicity of sodium hypochlorite. *Nature, 233*, 495

Holdsworth, G., McCauley, P. & Revis, N.W. (1990) Long-term effects of chlorine-containing disinfectants on plasma levels of cholesterol and thyroxine, in rabbits and pigeons. In: Jolley, R.L., Condie, L.W., Johnson, J.D., Katz, S., Minear, R.A. & Mattice, J.S., eds, *Water Chlorination: Chemistry, Environmental Impact and Health Effects*, Vol. 6, Chelsea, MI, Lewis Publishers, pp. 319-328

Hoy, R.H. (1981) Accidental systemic exposure to sodium hypochlorite (Clorox) during hemodialysis. *Am. J. Hosp. Pharm., 38*, 1512-1514

IARC (1987) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Suppl. 7, *Overall Evaluations of Carcinogenicity: An Updating of* IARC Monographs *Volumes 1 to 42*, Lyon, pp. 223-224

Ishidate, M., Jr (1987) *Data Book of Chromosomal Aberration* In Vitro, rev. ed., Tokyo, Life-Science Information Center, p. 383

Ishidate, M., Jr, Sofuni, T., Yoshikawa, K., Hayashi, M., Nohmi, T., Sawada, M. & Matsuoka, A. (1984) Primary mutagenicity screening of food additives currently used in Japan. *Food chem. Toxicol., 22*, 623-636

Jones Chemical (1989) *Material Data Safety Sheet, Sodium Hypochlorite*, New York

Jones, R.N., Hughes, J.M., Glindmeyer, H. & Weill, H. (1986) Lung function after acute chlorine exposure. *Am. Rev. respir. Dis., 134*, 1190-1195

Kawachi, T., Komatsu, T., Kada, T., Ishidate, M., Sasaki, M., Sugiyama, T. & Tazima, Y. (1980) Results of recent studies on the relevance of various short-term screening tests in Japan. In: Williams, G.M., Kroes, R., Waaijers, H.W. & van de Poll, K.W., eds, *The Predictive Value of Short-term Screening Tests in Carcinogenicity Evaluation*, Amsterdam, Elsevier/North-Holland Biomedical Press, pp. 253-260

Kozol, R.A., Gillies, C. & Elgebaly, S.A. (1988) Effects of sodium hypochlorite (Dakin's solution) on cells of the wound module. *Arch. Surg., 123*, 420-423

Kurokawa, Y., Takamura, N., Matsushima, Y., Takayoshi, I. & Hayashi, Y. (1984) Studies on the promoting and complete carcinogenic activities of some oxidizing chemicals in skin carcinogenesis. *Cancer Lett., 24*, 299-304

Kurokawa, Y., Takayama, S., Konishi, Y., Hiasa, Y., Asahina, S., Takahashi, M., Maekawa, A. & Hayashi, Y. (1986) Long-term in vivo carcinogenicity tests of potassium bromate, sodium hypochlorite, and sodium chlorite conducted in Japan. *Environ. Health Perspect., 69*, 221-235

Mannsville Chemical Products Corp. (1987) *Chemical Products Synopsis: Calcium Hypochlorite*, Asbury Park, NJ

Meier, J.R., Bull, R.J., Stober, J.A. & Cimino, M.C. (1985) Evaluation of chemicals used for drinking water disinfection for production of chromosomal damage and sperm-head abnormalities in mice. *Environ. Mutagenesis, 7*, 201-211

Ministry of International Trade and Industry (1989) *Yearbook of Chemical Industries Statistics, 1988*, Tokyo, International Trade and Industry Association

Phillip, R., Shepherd, C., Fawthrop, F. & Poulsom, B. (1985) Domestic chlorine poisoning (Letter to the Editor). *Lancet, ii*, 495

PPG Industries (1990) *Report on Calcium Hypochlorite from PPG Chemicals Group*, Pittsburgh, PA

Revis, N.W., McCauley, P. & Holdsworth, G. (1986) Relationship of dietary iodide and drinking water disinfectants to thyroid function in experimental animals. *Environ. Health Perspect., 69*, 243-248

Robinson, M., Bull, R.J., Schamer, M. & Long, R.E. (1986) Epidermal hyperplasia in mouse skin following treatment with alternative drinking water disinfectants. *Environ. Health Perspect., 69*, 293-300

Rosenkranz, H.S. (1973) Sodium hypochlorite and sodium perborate: preferential inhibitors of DNA polymerase-deficient bacteria. *Mutat. Res., 21*, 171-174

Sasaki, M., Sugimura, K., Yoshida, M.A. & Abe, S. (1980) Cytogenetic effects of 60 chemicals on cultured human and Chinese hamster cells. *Kromosomo II, 20*, 574-584

Sigma-Aldrich Company (1989) *Material Safety Data Sheet, Sodium Hypochlorite*, Gillingham, Dorset

Weast, R.C., ed. (1989) *CRC Handbook of Chemistry and Physics*, 70th ed., Boca Raton, FL, CRC Press, pp. B-79, B-117, B-130

White, G.C. (1986) *The Handbook of Chlorination*, 2nd ed., New York, Van Nostrand Reinhold

Winterbourn, C.C. (1985) Comparative reactivities of various biological compounds with myeloperoxidase-hydrogen peroxide-chloride, and similarity of the oxidant to hypochlorite. *Biochim. biophys. Acta, 840*, 204-210

Wlodkowski, T.J. & Rosenkranz, H.S. (1975) Mutagenicity of sodium hypochlorite for *Salmonella typhimurium*. *Mutat. Res., 31*, 39-42

Wojtowicz, J.A. (1979) Chlorine oxygen acids and salts (chlorine monoxide, hypochlorous acid, and hypochlorites). In: Mark, H.F., Othmer, D.F., Overberger, C.G., Seaborg, G.T. & Grayson, M., eds, *Kirk-Othmer Encyclopedia of Chemical Technology*, 3rd ed., Vol. 5, New York, John Wiley & Sons, pp. 586-611

Wones, R.G, Mieczkowski, L. & Frohman, L.A. (1990) Effects of drinking water chlorine on human lipid and thyroid metabolism. In: Jolley, R.L., Condie, L.W., Johnson, J.D., Katz, S., Minear, R.A. & Mattice, J.S., eds, *Water Chlorination: Chemistry, Environmental Impact and Health Effects*, Vol. 6, Chelsea, MI, Lewis Publishers, pp. 301-308