Sodium Metasilicate, Anhydrous [6834-92-0], Sodium Metasilicate Pentahydrate [10213-79-3], and Sodium Metasilicate Nonahydrate [13517-24-3]

Review of Toxicological Literature

January 2002

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Executive Summary

Basis for Nomination

Sodium metasilicate was nominated for subchronic inhalation toxicity testing based on the large number of individuals occupationally exposed to the compound, evidence for biological activity, and the gaps in available toxicity data.

Nontoxicological Data

Sodium metasilicate, a very corrosive compound, is precipitated by acids and alkaline earth and heavy metal ions. When heated or acidified, solutions of the compound are hydrolyzed to free sodium ions and silicic acid.

Sodium metasilicate is produced by the fusion of sodium carbonate with silicon dioxide or silica sand at about 1400 °C. It is commercially available in various grades and in both the anhydrous and pentahydrate forms from several U.S. companies. Annual capacities range from 50 to 806 million pounds.

Sodium metasilicate is used in fireproofing mixtures; in laundry, dairy, metal, and floor cleaning; in deinking paper; in washing carbonated drink bottles; in insecticides, fungicides, and antimicrobial compounds; as a chemical intermediate for silica gel catalysts; as an additive in soaps and synthetic detergents; as an ingredient in adhesives; as a bleaching aid; and as a boiler compound. Combined with other salts such as sodium bicarbonate, it can be applied to aluminum as a paint stripper. In field experiments, compounds composed of sodium metasilicate, an alkali metal carbonate, and a preservative have been used as desiccants for forage crops. Sodium silicate solutions, reacted with solutions of many soluble salts to form complex gelatinous precipitates, have been used in soil stabilization. The pentahydrate form is considered generally recognized as safe (GRAS) by the Food and Drug Administration (FDA) for use in washing mixtures for fruits and vegetables, in sanitizing solutions for food-contact surfaces, in boiler water, as a denuding agent for tripe, as a hog scald agent for the removal of hair, and as a cooling and retort water agent for the prevention of staining of the outside surfaces of canned goods. Sodium metasilicate is also regulated by the Environmental Protection Agency (EPA). It has been Reregistration Eligibility Decision (RED) approved.

Little information was found on actual cases of sodium metasilicate determination in environmental media or in potential releases to the environment. Potential human exposure to sodium metasilicate may occur from its use in cleaning products, fireproofing materials, pesticides, deinking paper, etc. For the general population, exposure is possible through the use of soaps, detergents, cosmetics, and other cleaning products containing the compound, as well as from its use as an indirect GRAS food ingredient. Residues remaining in fruits, vegetables, etc., however, are "minute" and therefore exposure from food is not of great concern.

Human Data

On intact and abraded skin, sodium metasilicate (37%) in a detergent with sodium carbonate (50% w/v aqueous) was a severe irritant. In modified soap chamber tests, sodium metasilicate had no adverse effects (i.e., erythema and edema scores were low). In elbow crease tests and semi-occluded patch tests, mild and temporary irritation was observed with sodium metasilicate. Ingestion of 0.5 L of colloidal sodium metasilicate resulted in the death of an individual within one to 1.5 hours. Autopsy revealed alkali burns in the gastric mucosa and condensed waterglass in the stomach, while microscopic examination showed amorphous sodium metasilicate in the bronchioles and alveoli of the lungs.

Animal Data

Absorption, Distribution, Metabolism, and Excretion

In rats perorally given sodium metasilicate nonahydrate (average daily dose of silicon of 0.1 mg/g body weight for the first six weeks, 0.2 mg/g body weight for the next six weeks, and 0.4 mg/g body weight for the last six weeks), serum and tissue (liver, kidney, lung, and aorta) silicon levels were significantly increased compared to those of controls. When rats were dosed with sodium metasilicate (40, 200, or 1000 mg/kg body weight), urinary silicon excretion increased rapidly, and within 24 hours, the peak excretion rate occurred. The half-life was 24 hours. In another rat study, 3% of an oral dose of sodium metasilicate (100 mg) was excreted in urine within 72 hours. When the compound (2.4 g/kg/day) was provided in a semisynthetic diet, however, urine and blood measurements were within normal limits.

When guinea pigs were orally administered radiolabeled sodium [^{31}Si]metasilicate, the majority of silica was quickly absorbed and excreted in urine; but a significant amount remained in the tissues. Single oral doses of sodium metasilicate solution (80 mg as SiO_2) resulted in maximum urinary excretion after 48 hours; levels returned to baseline value after eight days. Four doses administered at 48-hour intervals to guinea pigs resulted in 96% silica excretion in the urine and feces (~18% of this value was total urinary excretion) as urinary levels returned to baseline level.

Toxicity Studies

Acute Toxicity: Acute toxicity values (LD_{50}s) (route not provided) for sodium metasilicate in male and female rats were 1152.8 and 1349.3 mg/kg (9.4438 and 11.053 mmol/kg), respectively. In mice, values of 820 and 770 mg/kg (6.72 and 6.31 mmol/kg), respectively, were reported (route not provided). The oral LD_{50} was calculated to be 1280 mg/kg (10.49 mmol/kg) for rats and 2400 mg/kg (19.66 mmol/kg) for mice. Additionally, an oral LD_{50} of 847 mg/kg (6.94 mmol/kg) was reported in rats for the pentahydrate. LD_{Lo} values for dogs, pigs, and guinea pigs have also been calculated.

Oral administration of sodium metasilicate to rats and mice (1153 and 770 mg/kg, respectively) produced ulceration or bleeding in the stomach, duodenum, and small intestine. Oral doses of a 20% solution (464, 1000, 2150, and 4640 mg/kg) produced gasping, dyspnea, acute depression, and/or nasal discharge at ≥1000 mg/kg; and the highest dose caused death. Intraperitoneal injection of the nonahydrate form (300 mg on day 1 and 200 mg on days 2 and 3) resulted in lesions in the spleen and lymph nodes and mitotic changes in nuclei of cells. Intraperitoneal (i.p.) injection of a solution of sodium metasilicate pentahydrate (15-mL dose containing 20 mg SiO_2/mL) to guinea pigs produced siliceous deposits in kidney tubules. In another study, i.p. injection of a neutralized 2.0% sodium metasilicate solution (~1200 mg/kg on day 1 and 800 mg/kg on days 2 and 3) decreased rat spleen weight by 60% and increased kidney weight. Microscopic lesions of the lymphatic tissues and cellular damage in the intestinal mucosa were also observed.

When a laundry detergent containing sodium metasilicate and sodium carbonate was applied to the eyes of rabbits, corneal damage with opacification occurred. Single oral doses of a commercially available detergent containing sodium metasilicate (percentage not provided) caused gross lesions in the oral cavity, pharynx, esophagus, stomach, larynx, and lungs in dogs and pigs. When dogs were orally given sodium metasilicate (200 mg/kg), unspecified damage to the kidneys, ureters, bladder, gastrointestinal tract, and the lungs, thorax, or respiration was observed.

Short-Term and Subchronic Toxicity:

When rats were orally given sodium metasilicate (up to 2.4 g/kg/day), increased body weights in males and decreased body weights in females, slight degenerative changes in the epithelia of renal tubules, polydipsia, polyuria, soft stools, and an increase in growth rates were observed.

Dogs given sodium metasilicate (2.4 g/kg/day) in a highly palatable diet for one month had polydipsia, polyuria, and soft stools in some animals. The incidence of renal lesions was 100% for males and 87.5% for females; renal function, however, was not affected.

Synergistic/Antagonistic Effects: Using solutions of sodium metasilicate nonahydrate (average daily dose of silicon: 0.1 mg/g body weight with a 0.05% solution for the first six weeks, 0.2 mg/g body weight with a 0.1% solution for the next six weeks, and 0.4 mg/g body weight with a 0.2% solution for the last six weeks), the effects of silicon on the mineral metabolism of rats were studied by Najda and co-workers. Serum and tissue (liver, kidney, lung, and aorta) copper levels were significantly higher in the test animals compared to those in controls, while serum and tissue zinc levels were lower in the former group compared to those of the latter group. In another study, under the same conditions, serum calcium levels were increased in test rats versus in controls, while serum magnesium levels were decreased. In contrast, calcium levels were lower and magnesium levels were higher in the liver, kidneys, and lungs of test animals versus those of controls.

Genotoxicity: In assays using *Bacillus subtilis* strains without metabolic activation, sodium metasilicate (0.005-0.5 M) was not genotoxic.

Immunotoxicity: A delayed-type hypersensitivity response was observed with sodium metasilicate in the mouse ear-swelling test but not in the local lymph node assay.

No data were available regarding chronic exposure, reproductive or teratological effects, or carcinogenicity for sodium metasilicate. However, some data were available for structurally related compounds. (See the Structure-Activity Relationships section.)

Other Data

Nutritional Requirements for Silicon: Silicon has been found to be essential to the growth and skeletal development of rats and chicks. When added to purified or chemically defined diets, a concentration of 250 mg/kg silicon has been set as a guideline.

Several studies in livestock (broilers, pigs, and lambs) have investigated nutritional requirements for silicon using sodium metasilicate. When chicks were fed a low-silicon diet, growth retardation and a disturbance in bone formation occurred. However, when the diet was supplemented with sodium metasilicate nonahydrate, the chicks exhibited normal growth and development. When broiler chickens and ducks were fed sodium metasilicate (0.5-2.5%) in feed mixtures up to 60-days-old, no adverse effects occurred. Carcass yield, feed utilization efficiency, percentage survival, and activity of digestive enzymes were greater compared to controls (diets without silicate). A level of 2 g per 100 g feed was safe to use as a growth promoter. In a similar study, chickens had increased vitamin B_{12} and niacin in the muscles and gizzard. When sodium metasilicate (providing 120 ppm sodium and 74 ppm silicon) was supplemented to the drinking water, no effects on growth rate, feed conversion, mortality, or litter conditions were observed. The compound had intermediate results on the breaking strength and ash content of humeri and tibiae.

When lambs were given the silicate in water (solution equivalent to 800 mg SiO_2/L) for a period of 75 days, a significant interaction between silica and sex was observed. The weight gain of males was increased while that of females was slightly reduced. The effect was generally greater in diets without urea.

Growing pigs fed a basal diet supplemented with sodium metasilicate (amount not provided) gained 5.06 kg more in body weight and consumed 0.36 feed units less to gain 1 kg compared to controls (fed diet alone). The average daily silicon requirements for young pigs were reported to be 39.8 and 161.3 mg/kg

body weight at the beginning and end of the experiment (slaughtered when 3 or 7.5 months old), respectively.

Other Beneficial Effects in Domestic Animals: Poultry studies observed a positive effect on bone mineralization and on metabolism. In a balance trial with steers, sodium metasilicate (solu-bilized in drinking water at 800 ppm as SiO_2) as a high-energy (HE) density diet produced the following digestibilities for plain and silicated treatments: 75.5% versus 69.2% for nitrogen, 80.0% versus 77.0% for dry matter, and 71.0% versus 65.0% for cellulose. For the low-energy (LE) density diet, digestibilities were 54.0% versus 59.0%, respectively, for nitrogen. A digestion trial, designed to compare heifers and bulls, showed that when fed the HE diet, heifers had reduced digestion coefficients for nitrogen, dry matter, and cellulose, while these were all increased in bulls. For the LE diet, heifers showed increases in digestibility of all compounds, while bulls only showed an increase in cellulose digestibility.

Hens given sodium metasilicate nonahydrate (0.5, 1.0, or 1.5 g per 100 g) in a standard mixed feed from 150- to 330-days-old had increased numbers and weights of eggs and increased egg shell quality; best results were obtained with the mid dose. In another study, laying hens were given sodium metasilicate (0.5 or 1%) in diets containing (a) 3.4% calcium and 0.34% phosphor-us or (b) 2.7% calcium and 0.27% phosphorus for 15 weeks. At 32 weeks of age, egg production was increased, and the lower dose decreased egg specific gravity more than the higher dose with diet A. At 52 weeks of age, increased egg production and feed efficiency were observed with both diets. Additionally, diet B with 1% sodium metasilicate significantly reduced egg specific gravity.

Effects of Silicon on Lipid Levels and Enzyme Activities: Rats perorally given solutions of solutions of sodium metasilicate nonahydrate (average daily dose of silicon: 0.1 mg/g body weight using a 0.05% solution for the first six weeks, 0.2 mg/g body weight using a 0.1% solution for the next six weeks, and 0.4 mg/g body weight using a 0.2% solution for the last six weeks) exhibited increases in serum HDL-cholesterol and HDL-phospholipid concentrations, as well as significant increases in serum thyrotropin levels, suggesting a role for sodium silicate in functions of the pituitary gland. In the liver and kidney, the activities of superoxide dismutase, catalase, and glutathione peroxidate were decreased in test animals, while those of alanine and aspartate aminotransferases, alkaline phosphatase, and γ-glutamyl transpeptidase in serum were not changed. There were also no statistically significant differences in hydroxyproline and hydroxylysine blood serum concentrations and elastin levels in aortic walls between both groups. The difference in all parameters between the test and control groups increased with time of experiment and dose of solution. No compound-related toxic effects or behavioral changes in the animals were observed.

Miscellaneous Studies: Sodium metasilicate destabilized liposomes with cholesterol *in vitro*. The effect, caused by the dissolution of monosilicic acid from silicate, decreased as concentration increased. Neutralized sodium metasilicate at concentrations up to 0.025 M inhibited urease and invertase *in vitro* but did not significantly affect other enzymes (e.g., pepsin, trypsin, lipase, catalase, and cholinesterase). In Skin^2 ZK 1350 cultures, sodium metasilicate was corrosive. In an *in vitro* system using pig platelets, sodium metasilicate nonahydrate was found to be a strong inducer of histamine release.

Structure-Activity Relationships

Available toxicological data for sodium silicate, sodium carbonate, and sodium hydroxide are presented in this section. For amorphous silica and simple three-element silicates (metal, silicon, oxygen) and their hydrates, focus was placed on inhalation studies in both animals and humans.

<u>Sodium Silicate</u>

Two case reports regarding human toxicity were available. One man, who had come in contact with sodium silicate in a dyeing process, experienced recurrent ulcerative lesions on his left hand for two

years, as well as contact urticaria. Another man who had drunk 200 mL of a neutralized sodium silicate solution (waterglass; ~100 g sodium silicate) experienced vomiting, diarrhea, and gastrointestinal bleeding and had albumin, casts, acetone, sugar, and blood in the urine; he recovered. In women with silicone breast implants, preincubation of sera with sodium silicate inhibited more than 90% of the binding of immunoglobulin G (IgG) and IgM antibodies with silicate.

Similar to the metasilicate, urinary silicate excretion was increased in experimental animals. In rats, oral administration of sodium silicate (600 ppm silica/L) in drinking water for six months caused a 6.0% increase in the weight of males and a 5.0% decrease in females. Additionally, the numbers of offspring and survival weights were reduced. When the animals were given sodium silicate (80 µmol/kg) for one day subcutaneously or intratesticularly, there were no effects on morphology, histology, or spermatozoa. In Sd-4 (streptomycin-dependent) *Escherichia coli* treated cells, sodium silicate (concentrations of 0.025-0.300%) failed to induce back mutations.

Amorphous Silica

Amorphous silicas, which are naturally occurring and synthetic, include diatomaceous earth, precipitated silica, silica gel, fumed silica, and silica fume (thermally generated). The limited data on the effects of inhaled amorphous silica on the respiratory tract suggest that effects following exposure may be reversible upon termination of the exposure. A review of the toxicity of amorphous silica observed that some tissue reaction occurred but no collagen formation.

Animals studies have indicated limited and mostly reversible cytotoxic and possibly fibrogenic effects with some forms, and the few carcinogenicity studies available do not suggest that amorphous silica is carcinogenic. The IARC Working Group concluded that there was inadequate evidence in experimental animals for the carcinogenicity of synthetic amorphous silica and uncalcined diatomaceous earth. A recent rat study of subchronic inhalation of amorphous silica (precipitated silica; Aerosil 200 Degussa) (50 mg/m^3 for 6 hours/day, five days/week for up to 13 weeks) found no genotoxic effects in alveolar epithelial cells.

The health effects of amorphous silicas in humans are unclear. In general, limited studies indicate minimal effects, including a negative carcinogenic effect. The IARC Working Group concluded that there was inadequate evidence in humans for the carcinogenicity of amorphous silica; the evaluation was based on inhalation exposures in the workplace. Silicosis has not been observed in individuals exposed to amorphous silica, including those experiencing chronic exposure to the product. However, several cases of pneumoconiosis or silicosis among those exposed to diatomaceous earth have been reported. An association between silica fume and the development of silicosis in exposed individuals working in silicon smelters was suggested.

Calcium, Aluminum, and Magnesium Silicates

Calcium silicate [10101-39-0], potassium silicate [1312-76-1], and sodium silicate [1344-09-8] are not U.S. EPA registered. However, all are listed as "inert" ingredients in pesticide products registered by the agency.

Inhalation of silicates causes fibrogenesis in the lungs but to a lesser extent than silica. Heavy prolonged exposure to silicates produces characteristic lesions.

Calcium Silicate

When male rats were exposed to the dust of three commercially produced calcium silicate insulation materials (10 mg/m^3 respirable dust) for seven hours/day, five days/week for a total of 224 over one year, no major pulmonary damage was observed; only small amounts of dust were recovered from the lungs. Calcium silicates had no effect on the survival or health of the animals.

Aluminum Silicate

Long-term retention of inhaled fused aluminosilicate particles (FAP) has been studied in several animal species and in humans. Fischer 344 male rats were exposed nose-only for 45 minutes to an aerosol of ^{57}Co-labeled FAP with 3.95 µm activity median aerodynamic diameter (AMAD). Clearance of FAP from the alveolar compartment of the lung (measured as thoracic retention of ^{57}Co) was 60% at 112 days after inhalation. The total amounts of ^{57}Co recovered in the washings and in the tissues of the trachea and bifurcation one day after inhalation were 98 and 87%, respectively, and decreased with time but never fell below 30% during the study period. There were no significant amounts of ^{57}Co in the gastrointestinal tract, liver, spleen, kidneys, or the remainder of the carcass. Most of the small quantities dissolving from the FAP remaining in the lung were excreted in urine and feces.

In another study, rats, mice, and dogs were "briefly exposed" to ^{134}Cs-labeled FAP (mono-disperse particles of 0.7-, 1.5-, or 2.8-µm AMAD or polydisperse particles with 1.5- to 2.0-µm AMAD). In dogs, the dominant factor in long-term (i.e., up to 850 days after exposure) lung clearance for particles was solubilization. In rats and mice, the dominant factor was mechanical clearance. In all animals, a small portion of the initial deposit was found in the upper respiratory tract. Using a model with a two-lung compartment for lung retention (half-life of 10,000 days in one, and a half-life of 50, 200, and 400 days for mice, rats, and dogs, respectively, in the other), the predicted different retention patterns for the animals at the same concentration of aerosol of FAP were attributed to interspecies differences in the anatomy of the lung.

In Syrian hamsters exposed to aerosols of ^{137}Cs-labeled FAP (a monodisperse aerosol with AMAD of 1.53 µm and a polydisperse aerosol with AMAD of 1.87 µm), an estimated relative lung deposition of 9.5% of inhaled aerosols was observed. The right apical lobe contained more activity on a per gram lung weight basis than the total lung, while the right cardiac and right diaphragmatic lobe had less activity (exposure period not provided).

In seven volunteers who inhaled monodisperse FAP (diameters of 1.2 and 3.9 µm labeled with ^{85}Sr and ^{88}Y, respectively), approximately 8% of the smaller particles and 40% of the larger particles were cleared within six days. Approximately 4% of the smaller particles and 11% of the larger particles retained at six days were cleared with a half-time of about 20 days; the rest was cleared with half-times of 330 and 420 days, respectively. For both, mechanical clearance was slow with a half-time of about 600 days.

Magnesium Silicate (Talc)

The resulting lung injury from the inhalation of talc is partly caused by its contaminants, asbestos and crystalline silica. The irritation induced can lead to inflammation at the deposition site in the lung tissue and then attraction and activation of neutrophils, which may increase the lung injury.

The National Toxicology Program (NTP) performed toxicology and carcinogenicity studies of non-asbestiform talc (CASRN 14807-96-6; also called non-fibrous talc) in F344/N rats and B6C3F$_1$ mice. The animals were exposed to aerosols containing 0, 6, or 18 mg/m^3 talc for 6 hours/day, 5 days/week for up to 113 weeks for male rats, 122 weeks for female rats, and 104 weeks for all mice. There was some evidence of carcinogenicity of talc in male rats (increased incidence of benign or malignant pheochromocytomas of the adrenal gland), clear evidence in female rats (increased incidences of alveolar/bronchiolar adenomas and carcinomas of the lung and benign or malignant pheochromocytomas of the adrenal gland), and no evidence in male or female mice.

Of five reported cases of accidental inhalation of talcum powder (consisting of 90% anhydrous magnesium silicate) in children (one to two years old), three died within one to 20 hours. Their symptoms included respiratory distress, choking, tachycardia, cyanosis, intercostal retraction, and bronchitis. Inflammatory exudate was found in the larynx, trachea, bronchi, and bronchioles, with gross

obstruction of the lower air passages, and atelectasis and compensatory emphysema were seen in the lungs. Microscopic examination revealed cellular desquamation and leucocytic infiltration.

Sodium Carbonate

The analogous compound sodium carbonate (Na_2CO_3) would not be expected to induce mineral balance changes other than those due to perturbations in physiological pH.

The effects of overexposure to dusts or vapors of sodium carbonate can range from irritation of the mucous membranes to damage of the nasal septum. Sodium carbonate is non-irritating to intact skin. However, on abraded skin, symptoms of dermal contact can range from minor irritation and redness to sensitization, dermatitis, and vesicular skin reactions. Severe irritation may also occur in the eyes; sodium carbonate can be corrosive and cause conjunctival edema and corneal destruction.

Oral administration of sodium carbonate (LD_{Lo} = 714 mg/kg) was a general anesthetic in man. It produced ulceration or bleeding from the small intestine as well as other unspecified gastrointestinal changes (e.g., severe abdominal pain, vomiting, diarrhea, collapse, and death).

In mice, the following LD_{50} values were reported: 6600 mg/kg (oral), 117 mg/kg (i.p.), and 2210 mg/kg (s.c.). In the rat, the oral LD_{50} was calculated as 4090 mg/kg. In mice, rats, and guinea pigs administered sodium silicate (1200, 2300, and 800 mg/m^3, respectively) via inhalation for two hours, dyspnea and other gastrointestinal changes occurred. In rabbits, dermal exposure to sodium carbonate (500 mg) for 24 hours produced mild irritation. A lower dose (100 mg) applied to the eyes for 24 hours caused moderate irritation. At an even lower dose (50 mg), severe irritation was observed (duration was not provided).

When mammals (species not specified) inhaled sodium carbonate (TC_{Lo} = 16.2 mg/m^3) intermittently for 17 weeks, changes in the sensation of smell, lowering of blood pressure (other than as an effect on the autonomic nervous system), and respiratory depression were observed. In mice, sodium carbonate (TD_{Lo} = 8.48 µg/kg) injected into the uterus for four days of pregnancy resulted in pre-implantation mortality (e.g., reduction in the number of implants per female and the total number of implants per corpora lutea).

Sodium Hydroxide

Sodium hydroxide is corrosive to all body tissues regardless of the route of exposure. Dermal exposure to sodium hydroxide can cause nasal irritation, pneumonitis, temporary loss of hair, intercellular edema, erythema, keratin material decomposition, and burns. Contact with the eyes can result in ulceration, perforation, opacification, and blindness. Besides burns, oral ingestion of sodium hydroxide has been indirectly "implicated in the production of esophageal cancer" (i.e., the result of scar formation and tissue destruction). Persons exposed to sodium hydroxide in the workplace have described nose and throat irritation, respiratory irritation, chest pains, and shortness of breath. Cases of irreversible obstructive lung disease have also been reported.

An i.p. LD_{50} of 40 mg/kg was reported in mice. In rabbits, the dermal LD_{50} was calculated as 1350 mg/kg and the oral LD_{Lo} as 500 mg/kg. In mice and rats, dermal application of sodium hydroxide (dose not provided) caused severe irritation, leading to necrosis and death. When applied to the skin of rabbits for 24 hours, sodium hydroxide (500 mg) produced severe irritation. When administered to the eyes (0.050-1 mg and 1 mg followed with a 30-second rinse) for 24 hours, severe irritation was observed. Other observed effects have included ulceration, perforation, corneal necrosis and opacification, vascularization, and increased intraocular pressure.

Inhalation studies in rats with sodium hydroxide from an aerosolized 40% solution (dose not provided) for one-half hour two times daily for 2.5 months produced alveolar wall thickening, accompanied with cell proliferation and congestion, ulceration and flattening of the bronchial epithelium, and proliferation

of lymphadenoid tissue. In addition, three of ten rats had tumors. In another study where exposure was two times weekly for one month, all rats died; the major cause was bronchopneumonia. Exposure to aerosol produced from lower concentrations caused dilatation and damage to the alveolar septae (20% solution) and bronchial dilatation and mucous membrane degeneration (5% solution). In Chinese hamster V79 lung and ovary cells, sodium hydroxide (10 and 16 mmol/L, respectively) presumably induced cytogenic effects.

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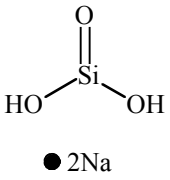
Tables

1.0 Basis For Nomination

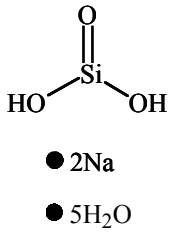
Sodium metasilicate was nominated for subchronic inhalation toxicity testing based on the large number of individuals occupationally exposed to the compound, evidence for biological activity, and gaps in the available toxicity data.

2.0 Introduction

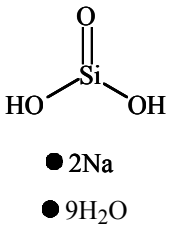
Sodium Metasilicate
[6834-92-0]



Sodium Metasilicate Pentahydrate
[10213-79-3]



Sodium Metasilicate Nonahydrate
[13517-24-3]



2.1 Chemical Identification and Analysis

Sodium metasilicate (Na_2SiO_3; mol. wt. = 122.07) is also called:

B-W	Silicon sodium oxide
Crystamet	Simet A
Disodium metasilicate	Simet AP
Disodium monosilicate	Simet G5
Disodium silicate	Simet GA 5
Metso 2048	SMS
Metso 510	Sodium metasilicate, anhydrous
Metso beads, drymet	Sodium silicate (Na_2SiO_3)
Metso Pentabead 20	Sodium silicon oxide (Na_2SiO_3)
Orthosil	SP 20
P 84	SP 20 (silicate)
P 84 (silicate)	Starso
Silicic acid (H_2SiO_3), disodium salt	Water glass

(Sources: HSDB, 2000; Registry, 2001)

The generic name "sodium silicate" has been used randomly for several silicate forms, including sodium metasilicate (Loweinheim and Moran, 1975; cited by FASEB, 1981). The series of compounds are water solutions of sodium oxide (Na_2O) and silicon dioxide (SiO_2) combined in various ratios (OxyChem, 1997). In this report, the chemical name given in each source was used. Studies were selected for inclusion if the database used the CASRN or gave the molecular formula for sodium metasilicate.

Analytical methods suitable for determination of sodium metasilicate in laundry detergent products include X-ray fluorescence spectrometry (XRF) (e.g., Kawauchi, 1999); isotachophoresis (Abe et al., 1988); differential thermogravimetry (DTG) and thermogravimetry (TG) (Medvedev et al., 1970); and spectrophotometry (e.g., as silicomolybdate in the presence of tartaric acid [Abe et al., 1966]).

2.2 Physical-Chemical Properties

Property	Information	Reference(s)
Sodium Metasilicate		
Physical States	usually obtained as a glass; orthorhombic crystals; colorless monoclinic crystals; dustless white granules	HSDB (2000)
Melting Point (^oC)	1089	
Specific gravity (g/cm^3)	2.614	
Refractive Indices (glass, α, γ)	1.520, 1.518, 1.527	
Specific Heat (20 °C)	0.217	
Heat of Formation (kcal/mol)	-371.2	
Heat of Solution (cryst.) (kcal/mol)	-7.45	
Heat of Fusion (kcal/mol)	10.3	
Soluble in:	cold water	
Insoluble in:	alcohol, acids, and salt solutions	
Sodium Metasilicate Pentahydrate		
Physical State	white, free flowing granules	OxyChem (1997); HSDB (2000)
Melting Point (^oC)	72.2	
Density (g/cm^3)	1.75	
Sodium Metasilicate Nonahydrate		
Physical State	white, free flowing granules; orthorhombic bipyramidal platelets; efflorescent	OxyChem (1997); HSDB (2000)
Melting Point (^oC)	48 in water of crystallization	
Boiling Point (^oC) (-$6H_2O$)	100	
Heat of Hydration (kcal/mol)	-24.15	
Soluble in:	cold and hot water and dilute sodium hydroxide	
Insoluble in:	alcohol and acids	

Methods for analyzing sodium metasilicate itself include acid titration of NaOH formed from sodium metasilicate hydrolysis with a methyl orange indicator (Huang et al., 1990) and potentiometric titration (Grosvenor, 1982). The SiO_2 content of sodium silicates can be determined by titration with standard hydrochloric acid to pH 4.3. For more precise determinations, a gravimetric process is used, which initially involves the dilution of a weighed sample in deionized water, followed by acidification with dilute hydrochloric acid. After evaporating to dryness, the resultant silica gel is rinsed to remove chlorides, and the residue is ignited; the residue (total solids of liquid silicates) is then calculated directly as SiO_2 (OxyChem, 1997). In air, sodium metasilicate has been determined in microgram quantities with a colorimetric method using an ammonium molybdate-sulfuric acid reagent (HSDB, 2000).

Sodium metasilicate is very corrosive. In fluorine, it ignites. The compound is precipitated by acids as a gel of hydrous SiO_2 (silica gel, sometimes called precipitated silicic acid) (Budavari, 1996). Alkaline earth and heavy metal ions are precipitated as metasilicates from sodium metasilicate solutions. When heated or acidified, solutions of sodium metasilicate are hydrolyzed to free sodium ions and silicic acid (Falcone, 1985; HSDB, 2000). As the natural pH (about 12 in 0.1% solution) decreases, sodium metasilicate exists in the dynamic equilibrium of an alkali/silica/water system. At intermediate pH, the compound is partially neutralized to give $1Na_2O:XSiO_2$, where X>1. Addition of an alkali results in reformation of the metasilicate (FASEB, 1981).

2.3 Commercial Availability

Various grades, differing in sodium silicate concentration in water, in specific gravity, and in viscosity, are available (HSDB, 2000). Those of liquid sodium silicate are produced by varying the ratio of alkali to silica and the content of the solids (OxyChem, 1997). Typical commercial soluble sodium silicates, as anhydrous glasses and hydrated amorphous powders, have a modulus ($SiO_2:Na_2O$) of 3.33, while the value in solutions ranges from 1.65 to 3.86. For crystalline solids, sodium orthosilicate and sesquisilicate have a modulus of 0.50 and 0.67, respectively, while the anhydrous sodium metasilicate and its pentahydrate both have a modulus of 1.00 (Falcone, 1985, 1997).

Sodium metasilicate is commercially available in the United States from Alfa Aesar/Johnson Matthey (Ward Hill, MA), Crosfield Company (Joliet, IL), OxyChem (aka Occidental Chemical Corporation) (Dallas, TX), PQ Corporation (Valley Forge, PA), Rhodia Phosphate Products (Cranbury, NJ), Chem One LTD. (Houston, TX), and J.T. Baker (Phillipsburg, NJ). The first five companies also supply the pentahydrate. Other companies producing the sodium metasilicate pentahydrate are KIC Chemicals, Inc. (Armonk, NY), Chemical Products Corporation (Cartersville, GA), and Schweizerhall, Inc. (Piscataway, NJ) (SRI Int., 2000b; Chemcyclopedia Online, 2001).

Among the bulk producers, OxyChem supplies anhydrous sodium metasilicate (S-25®) and its pentahydrate (Uniflo®26) in bulk bags, bulk rail cars, and bulk trucks. Their standard commercial grades of liquid sodium silicates range in weight ratio of SiO_2 to Na_2O from 1.6 to 3.3 (OxyChem, 1997). Aldrich provides the metasilicate in 25-g and 1-kg quantities (Aldrich, 1998-1999).

3.0 Production Processes

Sodium metasilicate is produced by the fusion of sodium carbonate (soda ash) with SiO_2 or silica sand (HSDB, 2000) in appropriate stoichiometric ratio. This occurs at about 1400 ^oC (Lowenheim and Moran, 1975; Mark et al., 1969; both cited by FASEB, 1981).

4.0 Production And Shipment Volumes

From 1984 to 1996, sodium metasilicate production declined an average of 1.5% annually, being replaced by liquid sodium silicates. The most recent U.S. production volumes available for anhydrous sodium metasilicate (on a 100% $Na_2O{\cdot}SiO_2$ basis) ranged from 44 to 60 thousand short tons (88 to 120 million pounds) during the years 1990 to 1997. Production volumes for the pentahydrate form (on a 100% $Na_2O{\cdot}SiO_2{\cdot}5H_2O$ basis) ranged from 42 to 48 thousand short tons

(84 to 96 million pounds) during the same period. Between 1990 and 1996, the mean U.S. total shipments (including interplant transfers) were 49,000 short tons (98 million pounds) for the anhydrous form and 45,000 short tons (90 million pounds) for the pentahydrate (SRI Int., 2000a). The annual capacity of sodium silicates, which includes sodium metasilicate pentahydrate, at Chemical Products Corporation is 25,000 short tons (50 million pounds). Crosfield Company produces 65,000 short tons (130 million pounds) of sodium silicates, which includes the anhydrous product that is used for production of the anhydrous and pentahydrate forms. Occidental Chemical Corporation's subsidiary in Dallas, TX, has an annual capacity of 48,000 short tons (96 million pounds) of anhydrous and hydrated meta- and orthosilicates, while its divisions in Jersey City, NJ, and Mobile, AL, produce 35 and 32 thousand short tons (70 and 64 million pounds), respectively. The PQ Corporation, with divisions in several states, has an annual capacity of 403,000 short tons (806 million pounds) for anhydrous and hydrated sodium metasilicates (SRI Int., 2000b).

5.0 Uses

Sodium metasilicate is used in fireproofing mixtures; in laundry, dairy, metal, and floor cleaning; in deinking recycled paper products in the pulp and paper industry; in washing carbonated drink bottles; in insecticides, fungicides, and antimicrobial compounds; and as a chemical intermediate for silica gel catalysts, an additive in soaps and synthetic detergents, an ingredient in adhesives, a bleaching aid, and a boiler compound. Combined with other salts such as sodium bicarbonate, it can be applied to aluminum as a paint stripper. In field experiments, compounds composed of sodium metasilicate, an alkali metal carbonate, and a preservative have been used as desiccants for forage crops (OxyChem, 1997; HSDB, 2000). In detergents, sodium metasilicate has been used as a precipitating builder for calcium and magnesium (Coppock et al., 1988). In cosmetic formulations, it is a chelating agent and corrosion inhibitor; 77% of 168 formulations was used in hair dyes and colors (CIR, 2001). It has also been used in flotation materials at fruit packing plants (Kupferman, 1998). Its gel-forming property has been employed in soil stabilization (OxyChem, 1997).

The pentahydrate form is considered generally recognized as safe (GRAS) for use in washing mixtures for fruits and vegetables, in sanitizing solutions for food-contact surfaces, in boiler water, as a denuding agent for tripe, as a hog scald agent for the removal of hair, and as a cooling and retort water agent for the prevention of staining of the outside surfaces of canned goods (Buckley, 1968; Cassidy, 1962; Office of the Federal Register, 1980b; Schaefer, 1975; all cited by FASEB, 1981).

6.0 Environmental Occurrence and Persistence

Little information was found on actual cases of sodium metasilicate determination in environmental media or in potential releases to the environment. Thermal analysis was used by Vennekens and Odding (1988) to analyze water treatment plant sludge from South Africa. Methods used included TG, DTG, and DSC (differential scanning calorimetry). [It is unclear from the abstract whether the water treated was an industrial or municipal wastewater or possibly a raw water to be purified for drinking.] A titrimetric method involving conversion to K_2SiF_6 and subsequent release and titration of HF was used to determine sodium metasilicate in a degreasing solution used in China (Liao, 1986). Sodium metasilicate concentrations were not given in either abstract.

Sodium silicate solutions, reacted with solutions of many soluble salts to form complex gelatinous precipitates, have been used in soil stabilization. The results are an increased load-bearing capacity, an increased prevention of settlement and lateral movement of foundations, and an increased control of the flow of water in earthwork engineering projects (e.g., dams, mines, tunnels, and excavations) (OxyChem, 1997).

7.0 Human Exposure

Potential human exposure to sodium metasilicate may occur from its use in cleaning products, fireproofing materials, pesticides, deinking paper, etc. (See Section 5.0.) For the general population, exposure is possible through the use of soaps, detergents, cosmetics, and other cleaning products containing the compound, as well as from its use as an indirect GRAS food ingredient. Residues remaining in fruits, vegetables, etc., however, are "minute;" the amounts of sodium metasilicate were estimated to be orders of magnitude less than the estimated daily consumption of 20-30 mg silica from dietary natural sources and drinking water. Therefore, there are "no reasonable grounds to suspect a hazard to the public when it is used as a food ingredient in the manner now practiced at levels that are now current or that might reasonably be expected in the future" (FASEB, 1981).

8.0 Regulatory Status

U.S. government regulations pertaining to sodium metasilicate are summarized in **Table 1**. Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Environmental Protection Agency (EPA) assigned sodium metasilicate to List D (Case No. 4081), the group consisting of pesticides of less concern in regards to human exposure potential and other factors. In September of 1991, it was Reregistration Eligibility Decision (RED) approved (U.S. EPA, 1998). Sodium metasilicate is listed as an "inert ingredient" in pesticide products registered by the EPA. It is in category 3, meaning that it may be downgraded to category 4B—"Inerts which have sufficient data to substantiate they can be used safely in pesticide products"—or removed from the List of Inert Ingredients (Orme and Kegley, 2000d; U.S. EPA, 2001b). There are no Occupational Safety and Health Administration (OSHA) permissible exposure limits (PELs) (29CFR1910) and no American Conference of Governmental Industrial Hygienists (ACGIH) or National Institute of Occupational Safety and Health (NIOSH) recommended exposure limits.

Table 1. Federal Regulations Relevant to Sodium Metasilicate

Reference		Summary of Regulation
FDA	21CFR184.1769a (04/01/93)	When added directly to human food, sodium metasilicate was affirmed as generally recognized as safe (GRAS).
EPA	40CFR180.1001(c) (07/01/92)	Residues of sodium metasilicate have been exempted from the requirement of a tolerance when used as a surfactant, emulsifier, wetting agent, suspending agent, dispersing agent, or buffer in accordance with good agricultural practices as inert, and in rare cases active, ingredients in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest.
	40CFR180.2(a) (07/01/92)	Sodium metasilicate is not to exceed 4% by weight in aqueous solutions when used in pesticide chemicals.

9.0 Toxicological Data

9.1 General Toxicology

Reviews regarding the safety of sodium metasilicate have been published, summarizing studies dating as far back as 1920 (e.g., a monograph on the compound by Weissler [1978] and more recently a 2001 tentative report by Cosmetic Ingredient Review [CIR]). Many mention a majority of the same studies. In this report, data were extracted from the 1981 document by the Federation of American Societies for Experimental Biology (FASEB) and supplemented by any new data in the CIR (2001) report.

9.1.1 Human Data

Depending on the concentration, the silica to alkali ratio, the sensitivity of the exposed tissue, and the length of exposure, soluble silicates can induce effects ranging from irritation to corrosion (Falcone, 1985). Sodium metasilicate can produce caustic burns (i.e., colliquative necrosis) and induce hypocalcemia by binding calcium. It is the most caustic builder among precipitating builders for detergents (e.g., sodium sesquicarbonate and polyphosphates) (Coppock et al., 1988). The pentahydrate form is corrosive when in contact with the skin, but is not dangerous unless in contact with wet skin, resulting in dermatitis, since alkaline solutions remove the skin's natural oils (Stokinger, 1981). When applied to the skin for 24 hours, sodium metasilicate (250 mg; 2.05 mmol) produced severe irritation (RTECS, 2000c). The metasilicates, as well as water solutions of the compounds, may also cause chemical burns to the eyes (OxyChem, 1997).

A granular detergent (50% w/v aqueous) containing sodium metasilicate (37%) and sodium carbonate applied to the intact and abraded skin of humans for four hours produced one site of tissue destruction out of eight abraded skin test sites; the compound was rated a severe irritant (Nixon et al., 1975; cited by CIR, 2001).

Using a modified soap chamber test, hair color kits were tested in 19 to 21 subjects. Patches with the following sodium metasilicate concentrations were applied to their lower backs: 13.5% (w/w) in the activator and 1.34, 1.43, or 2.58% (w/w) on the head. When observed up to 28 hours after each application, no adverse reactions occurred (i.e., no fissuring, scaling, burning, or itching [erythema and edema scores were low]) (Clairol, 2000, 2000b; cited by CIR, 2001).

Using the elbow crease test, 15 bleach formulations were studied in 20 to 40 individuals. Products containing sodium metasilicate concentrations ranging from 3.4 to 14% in the activators and from 1 to 7% in the product mixtures were applied for 50 minutes without occlusion. All products induced mild irritation—mostly mild erythema and occasionally moderate erythema at five minutes. Upon removal, changes immediately diminished; only a few volunteers had slight erythema at one hour (L'Oreal, 2000; cited by CIR, 2001).

Semi-occluded patch tests were used to assess 32 hair bleaches in 25 healthy subjects. Products contained sodium metasilicate concentrations of 3.4 to 14% in the activators and 0.75 to 6.8% in the mixed products and were applied to the back for one hour and 15 minutes. Mild and temporary irritation was observed; the scores seemed to be independent of the silicate concentrations (L'Oreal, 2000b; cited by CIR, 2001).

Oral administration of sodium metasilicate (TD_{Lo} = 1 mL/kg; 217 mg/kg) produced changes in kidney tubules and hematuria and caused nausea or vomiting (RTECS, 2000c). In one reported case study, a patient who ingested 0.5 L colloidal sodium metasilicate died within one to 1.5 hours. Autopsy showed alkali burns in the gastric mucosa and condensed waterglass in the stomach (pH 11.5). Microscopic examination revealed amorphous sodium metasilicate in numerous bronchioles and alveoli of the lungs (Sigrist and Flury, 1985; cited by CIR, 2001).

9.1.2 Chemical Disposition, Metabolism, and Toxicokinetics

When ingested, alkaline sodium metasilicate is neutralized by gastric acid, forming monomeric silicic acid, which is rapidly absorbed from the gut and distributed throughout the extracellular fluid (Baumann, 1960; cited by FASEB, 1981).

The details of the following studies are presented in **Table 2**.

In rats perorally given sodium metasilicate nonahydrate (average daily dose of silicon of 0.1 mg/g body weight for the first six weeks, 0.2 mg/g body weight for the next six weeks, and 0.4 mg/g body weight for the last six weeks), serum and tissue (liver, kidney, lung, and aorta) silicon levels were significantly increased compared to those of controls (Najda et al., 1992, 1993a). When rats were dosed with sodium silicate [6834-92-0] (40, 200, or 1000 mg/kg body weight), urinary silicon excretion increased rapidly, and within 24 hours, the peak excretion rate occurred. The half-life was 24 hours. For the first 24-hour collection period at the low dose and for the next two 24-hour collection periods (i.e., 24-48 hours and 48-72 hours) at the high dose, sodium silicate produced greater urinary silicon concentrations than sodium aluminosilicate, magnesium trisilicate, and zeolite NaA. Although urinary silicon excretion correlated with dose level for all four compounds, the percentage of silicon excreted decreased as dose increased, which was suggested to be caused by the saturation of some process in the absorption or excretion of silicon (Benke and Osborn, 1979). In another rat study, 3% of an oral dose of sodium metasilicate (100 mg) was excreted in urine within 72 hours (Keeler and Lovelace, 1959; cited by FASEB, 1981). When young rats (and young adult Beagle dogs) were given sodium metasilicate (2.4 g/kg/day) in a semisynthetic (and highly palatable) diet, urine and blood measurements were within normal limits [study details are provided in Section 9.1.4 and Table 5] (Newberne and Wilson, 1970).

When guinea pigs were orally administered radiolabeled sodium [^{31}Si]metasilicate, the majority of silica was quickly absorbed and excreted in urine but a significant amount remained in the tissues, emphasizing the important role of silicon as a trace element for bone formation (Clayton and Clayton, 1981-1982; cited by HSDB, 2000). Single oral doses of sodium metasilicate in solution (80 mg as SiO_2 [about 160 mg/kg]) resulted in maximum urinary excretion after 48 hours; levels returned to baseline value after eight days. Four doses administered at 48-hour intervals to the guinea pigs resulted in 96% silica excretion in the urine and feces (~18% of this value was total urinary excretion) as urinary levels returned to baseline level (Sauer et al., 1959a; cited by FASEB, 1981). A solution of sodium metasilicate pentahydrate (15-mL dose containing 20 mg SiO_2/mL) administered intraperitoneally produced siliceous deposits in kidney tubules of the animals (Settle and Sauer, 1960).

Table 2. Chemical Disposition, Metabolism, and Toxicokinetic Studies with Sodium Metasilicate

Species, Strain, and Age, Number, and Sex of Animals	Chemical Form and Purity	Route, Dose, Duration, and Observation Period	Results/Comments	Reference
Rats, Wistar, 2-mo-old, 100M (40 were controls)	sodium metasilicate nonahydrate ($Na_2SiO_3 \cdot 9H_2O$) (containing 10.11% Si), reagent grade	p.o.; average daily dose of Si of 0.1 mg/g bw (0.05% Si soln.) for the first 6 wk, 0.2 mg/g bw (0.1% soln.) for the next 6 wk, and 0.4 mg/g bw (0.2% soln.) for the last 6 wk. One-third of animals from each group was killed after 6, 12, and 18 wk.	Serum and tissue (liver, kidneys, lungs, and aorta) Si levels were significantly increased in the test rats compared to those in controls. (Noted: The low dose produced no increase in tissues after 6 wk.) The difference in all parameters between the two groups increased with time and dose. Only data for 18 wk are given here (test animals vs. controls). Serum (µmol/L): 39 vs. 36 Tissues (µmol/g wet weight): liver: 0.51 vs. 0.35 lungs: 0.95 vs. 0.82 kidneys: 1.1 vs. 0.91 aorta: 1.7 vs. 1.4	Najda et al. (1992)
Rats, Wistar, 2-mo-old, 100M (40 were controls)	$Na_2SiO_3 \cdot 9H_2O$ (containing 10.11% Si), reagent grade	p.o.; average daily dose of Si of 0.1 mg/g bw (0.05% Si soln.) for the first 6 wk, 0.2 mg/g bw (0.1% soln.) for the next 6 wk, and 0.4 mg/g bw (0.2% soln.) for the last 6 wk. One-third of animals from each group was killed after 6, 12, and 18 wk.	Serum Si levels were significantly increased in test rats compared to those of controls after 12 and 18 wk. Tissue Si concentrations (liver, kidneys, lungs, and aorta) were also higher in the test rats after both weeks (but no statistical significance was found for aortas after 12 wk). These differences increased with time and dose. Only data for 18 wk are given here (test animals vs. controls). Serum (µmol/L): 39 vs. 36 Tissues (µmol/g wet weight): liver: 0.51 vs. 0.35 lungs: 0.99 vs. 0.81 kidneys: 1.1 vs. 0.91 aorta: 1.75 vs. 1.38	Najda et al. (1993a)
Rats, Sprague-Dawley Cox, 4M	sodium silicate [6834-92-0] (manufactured under the tradename Britesil® C24, containing 25.9% Si) purity n.p.	oral (via a feeding tube); 40, 200, or 1000 mg/kg bw. Animals were sacrificed after the 8-h collection period of urine.	After dosing, urinary silicon (Si) excretion increased rapidly, and within 24 h, the peak excretion rate was found. Sodium silicate (SS) had a half-life of 24 h. For the first 24-h collection period at 40 mg/kg, SS had the greatest Si excretion, followed by magnesium trisilicate (MgTS), zeolite NaA (ZA), and then sodium aluminosilicate (SAS), while at 1000 mg/kg, the order was ZA>SS>MgTS>SAS. For the 24- to 48-h and 48- to 72-h collection periods, at 40 mg/kg, the order of Si excretion was MgTS>SS>SAS=ZA, and at 1000 mg/kg, it was SS>SAS>MgTS>ZA. Urinary Si excretion correlated with dose level for all compounds. The magnitude of the increased (two- to eightfold), however, was not as great as the increase in the amount dosed (25-fold), and therefore the percentage of silicon excreted was decreased as dose was increased.	Benke and Osborn (1979)

Table 2. Chemical Disposition, Metabolism, and Toxicokinetic Studies with Sodium Metasilicate (Continued)

Species, Strain, and Age, Number, and Sex of Animals	Chemical Form and Purity	Route, Dose, Duration, and Observation Period	Results/Comments	Reference
Rats, strain, age, number, and sex n.p.	sodium metasilicate, purity n.p.	oral (via stomach tube); 100 mg; duration and observation period n.p.	Within 72 h, 3% of the oral dose was excreted in urine.	Keeler and Lovelace (1959; cited by FASEB, 1981)
Guinea pigs, strain, age, and number n.p., M	sodium [^{31}Si]metasilicate (partially neutralized), purity n.p.	oral; dose, duration, and observation period n.p.	The majority of silica was quickly absorbed and excreted in the urine but a significant amount was retained in the tissues.	Clayton and Clayton (1981-1982; cited by HSDB, 2000)
Guinea pigs, strain, age, number, and sex n.p.	sodium metasilicate soln. (80 mg as SiO_2), purity n.p.	oral; single doses; observed for ≥8 days	Maximum urinary excretion occurred after 48 h. Levels returned to baseline values after 8 days.	Sauer et al. (1959a; cited by FASEB, 1981)
Guinea pigs, strain, age, number, and sex n.p.	sodium metasilicate soln. (80 mg as SiO_2), purity n.p.	oral; four doses at 48-h intervals	Silica urinary and fecal excretion reached 96% as urinary levels returned to baseline values. Total urinary excretion was ~18% of the amount given.	Sauer et al. (1959a; cited by FASEB, 1981)
Guinea pigs, strain n.p., "adult", number and sex n.p.	sodium metasilicate pentahydrate ($Na_2SiO_3 \cdot 5H_2O$), purity n.p.	i.p. injection; 15-mL dose containing 20 mg SiO_2/mL). Animals were killed 24 h after administration of silica.	Siliceous deposits were found in the renal tubules.	Settle and Sauer (1960)
Rabbits, strain, age, number, and sex n.p.	1% neutralized sodium metasilicate soln., purity n.p.	i.v.; dose, duration, and observation period n.p.	Within 48 h, 20 to 56% of doses was excreted in the urine.	Gajatto (1944; cited by FASEB, 1981)
Ducklings, Pekin, 50-days-old, 500 (100/group), sex n.p.	sodium silicate [6834-92-0], purity n.p.	oral; 1, 1.5, 2, or 2.5 g per 100 g feed in a mixed meal for 56 days	Increased Si levels were found in feathers.	Kiriliv et al. (1989b)
Lambs, strain, age, and number n.p., M	1.0% sodium metasilicate, purity n.p.	oral; dietary supplements of the compound; duration and observation period n.p.	Although Si excretion in the urinary tract can result in siliceous stones, no increased rate of stone formation was observed.	Emerick et al. (1959; cited by FASEB, 1981)
Cows, strain, age, number, and sex n.p.	sodium metasilicate, purity n.p.	oral; supplement of 1.0 g of compound daily for 2 mo	There were no significant changes in Si concentration of milk.	Archibald and Fenner (1957; cited by FASEB, 1981)

Abbreviations: bw = body weight; h = hour(s); i.p. = intraperitoneal(ly); i.v. = intravenous(ly); M = male(s); mo = month(s); n.p. = not provided; p.o. = *per os*, peroral(ly); Si = silicon; soln. = solution

When rabbits were injected intravenously with 1% neutralized sodium metasilicate solution, 20 to 56% of the dose was excreted in urine within 48 hours (Gajatto, 1944; cited by FASEB, 1981). In ducks given sodium silicate [6834-92-0] (1, 1.5, 2, or 2.5 g per 100 g feed) in a mixed meal, increased silicon levels were found in the feathers (Kiriliv et al., 1989b). When male lambs were fed dietary supplements of 1.0% sodium metasilicate, there was no increased rate of formation of siliceous stones (Emerick et al., 1959; cited by FASEB, 1981). Cows fed a daily supplement of 1.0 g sodium metasilicate for two months showed no significant changes in silicon concentration of milk (Archibald and Fenner, 1957; cited by FASEB, 1981).

9.1.3 Acute Exposure

Acute toxicity values for sodium metasilicate are presented in **Table 3**. The details of studies discussed in this section, except where noted, are presented in **Table 4**.

Table 3. Acute Toxicity Values for Sodium Metasilicate and Its Pentahydrate

Route	Species (sex and strain)	LD_{50} (range)/LD_{Lo}	Reference
Sodium Metasilicate			
n.p.	Mouse (M, strain n.p.)	LD_{50} = 820 (66.7-1087.6) mg/kg; 6.72 (0.546-8.9096) mmol/kg	Ito et al. (1986 abstr.) *RTECS (2000c) reported these values with the oral route.
	Mouse (F, strain n.p.)	LD_{50}* = 770 mg/kg; 6.31 mmol/kg	
	Rat (M, strain n.p.)	LD_{50}* = 1152.8 (9947-13,359) mg/kg; 9.4438 (81.49-109.44) mmol/kg	
	Rat (F, strain n.p.)	LD_{50} = 1349.3 (1189.6-1530.4) mg/kg; 11.053 (9.7452-12.537) mmol/kg	
oral	Mouse (sex and strain n.p.)	LD_{50} = 2400 mg/kg; 19.66 mmol/kg	Clayton and Clayton (1981-1982; cited by HSDB, 2000)
	Rat (sex and strain n.p.)	LD_{50} = 1280 mg/kg; 10.49 mmol/kg	
	Dog (sex and strain n.p.)	LD_{Lo} = 250 mg/kg; 2.05 mmol/kg	RTECS (2000c)
	Pig (sex and strain n.p.)	LD_{Lo} = 250 mg/kg; 2.05 mmol/kg	
i.p.	Guinea pig (sex and strain n.p.)	LD_{Lo} = 200 mg/kg; 1.64 mmol/kg	
dermal	Rabbit (M and F, New Zealand white)	LD_{50} > 200 mg/kg; 1.64 mmol/kg	Rhone-Poulenc, Inc. (1976; cited by CIR, 2001)
Sodium Metasilicate Pentahydrate			
oral	Rat (sex and strain n.p.)	LD_{50} = 847 mg/kg; 6.94 mmol/kg	RTECS (2000c)

Abbreviations: F = female(s); i.p. = intraperitoneal(ly); LD_{50} = lethal dose for 50% of test animals; LD_{Lo} = lethal dose low; M = male(s); n.p. = not provided

Table 4. Acute Exposure to Sodium Metasilicate

Species, Strain, and Age, Number, and Sex of Animals	Chemical Form and Purity	Route, Dose, Duration, and Observation Period	Results/Comments	Reference
Rats, Wistar, age, number, and sex n.p.	sodium metasilicate, purity n.p.	peroral; "high doses" (n.p.), "acute" (duration and observation n.p.)	Bleeding in the stomach and duodenum and erosion down to the middle of the small intestine were observed.	Ito et al. (1986 abstr.)
Rats, Sprague-Dawley, age n.p., 5 M/dose	20% sodium metasilicate soln., purity n.p.	oral (via gastric intubation); 464, 1000, 2150, and 4640 mg/kg; animals were observed for 14 days	At the lowest dose, no signs of toxicity were produced. At 1000 and 2150 mg/kg, rats experienced gasping, dyspnea, and acute depression. At the highest dose, rats had the same symptoms and nasal discharge. Additionally, all rats given 4640 mg/kg died; gross gastrointestinal hemorrhages with congestion of the kidneys, adrenal glands, liver, lungs, and heart were observed.	Rhone-Poulenc, Inc. (1971b; cited by CIR, 2001)
Rats, species, age, number, and sex n.p.	sodium metasilicate nonahydrate ($Na_2SiO_3 \cdot 9H_2O$), purity n.p.	i.p. injection; 300 mg on day 1 and 200 mg on days 2 and 3 (neutral soln.)	Lesions in the spleen and lymph nodes and mitotic changes in the nuclei of cells similar to those produced by ionizing radiation or hypoxia were observed.	Clayton and Clayton (1981-1982; cited by HSDB, 2000)
White rats, strain, age, number, and sex n.p.	neutralized 2.0% sodium metasilicate soln., purity n.p.	i.p. injection; ~1200 mg/kg on day 1 and 800 mg/kg on days 2 and 3	Spleen weight was decreased by 60%, while the relative weight of kidneys was increased. Microscopic lesions of the lymphatic tissues and cellular damage in the intestinal mucosa were observed.	Nanetti (1973; cited by FASEB, 1981)
Guinea pigs, strain n.p., "adult", number and sex n.p.	sodium metasilicate pentahydrate ($Na_2SiO_3 \cdot 5H_2O$), purity n.p.	i.p. injection; 15-mL dose containing 20 mg SiO_2/mL). Animals were killed 24 h after administration of silica.	Preliminary tests: Many animals did not survive longer than 48 h. At necropsy, kidneys were pale and enlarged and had rough surfaces. Siliceous deposits were found in the renal tubules.	Settle and Sauer (1960)
Guinea pigs, strain, age, number, and sex n.p.	sodium metasilicate, purity n.p.	dermal; 250 mg applied to the skin for 24 h	Moderate irritation of the skin was observed.	RTECS (2000c)
Rabbits, strain n.p., age n.p., 10, sex n.p.	detergent containing sodium metasilicate (37%) and sodium carbonate, purity n.p.	dermal; 50% w/v aqueous applied to intact and abraded skin for 4 h; responses graded at 4, 24, and 48 h after patch applications	Tissue destruction was observed in the intact and abraded skin of all animals. The compound was classified as corrosive.	Nixon et al. (1975; cited by CIR, 2001)
Rabbits, strain, age, number, and sex n.p.	sodium metasilicate, purity n.p.	dermal; 250 mg applied to the skin for 24 h	Severe irritation of the skin was observed.	RTECS (2000c)
Rabbits, New Zealand, age n.p., 6, sex n.p.	sodium metasilicate (42.4% water), purity n.p.	eye exposure (instillation?); 0.1 mL in one eye; duration and observation period n.p.	Test sample was corrosive to the eye; all animals had total destruction of the eye.	Rhone-Poulenc, Inc. (1971b; cited by CIR, 2001)

Table 4. Acute Exposure to Sodium Metasilicate (Continued)

Species, Strain, and Age, Number, and Sex of Animals	Chemical Form and Purity	Route, Dose, Duration, and Observation Period	Results/Comments	Reference
Dogs, strain, age, number, and sex n.p.	sodium metasilicate, purity n.p.	oral; 200 mg/kg; duration and observation period n.p.	Damage (unspecified) to the kidneys, ureters, bladder, gastrointestinal tract, and the lungs, thorax, or respiration were observed.	RTECS (2000c)
Dogs, Beagle, age n.p., 3/dose group, sex n.p.	commercially available detergent containing sodium metasilicate (percentage n.p.)	oral; single doses of 100, 250, 500, 1000, and 2500 mg/kg; observed for >54 h	Doses of ≥250 mg/kg produced gross lesions in the oral cavity, pharynx, esophagus, stomach, larynx, lungs, and kidneys. Microscopic lesions included acute necrosis of the epithelial lining of the digestive tract; necrosis, ulceration, and edema of the larynx; edematous lungs; and necrosis of the proximal renal tubules. At the highest dose, all dogs died within 54 h.	Muggenberg et al. (1974; cited by CIR, 2001)
Pigs, strain, age, number, and sex n.p.	commercially available detergent containing sodium metasilicate (percentage n.p.)	oral; single dose of 250; observed for >95 h	Lesions were similar to those found in dogs (see above entry). One animal died 95 h after dose administration.	Muggenberg et al. (1974; cited by CIR, 2001)
Ducklings, Pekin, 50-days-old, number and sex n.p.	sodium silicate [6834-92-0], purity n.p.	oral; single dose of 40 or 50 g (animal weight n.p.)	Illness and/or death occurred in some animals.	Kiriliv et al. (1989b)

Abbreviations: h = hour(s); i.p. = intraperitoneal; min. = minute(s); n.p. = not provided; soln. = solution

Administration of the oral LD_{50} doses of sodium metasilicate in rats and mice (1153 and 770 mg/kg, respectively) produced ulceration or bleeding in the stomach, duodenum, and small intestine (Ito et al., 1986 abstr.; RTECS, 2000c). In rats, oral doses of a 20% solution (464, 1000, 2150, and 4640 mg/kg) produced gasping, dyspnea, acute depression, and/or nasal discharge at ≥1000 mg/kg. All rats receiving the highest dose died; gross intestinal hemorrhages with congestion of the kidneys, adrenal glands, liver, lungs, and heart were observed (Rhone-Poulenc, Inc., 1971b; cited by CIR, 2001). Intraperitoneal (i.p.) injection of the nonahydrate form (300 mg on day 1 and 200 mg on days 2 and 3) to rats resulted in lesions in the spleen and lymph nodes and mitotic changes in nuclei of cells (Clayton and Clayton, 1981-1982; cited by HSDB, 2000). In another study, i.p. injection of a neutralized 2.0% sodium metasilicate solution (~1200 mg/kg on day 1 and 800 mg/kg on days 2 and 3) decreased rat spleen weight by 60% and increased kidney weight. Microscopic lesions of the lymphatic tissues and cellular damage in the intestinal mucosa were also observed (Nanetti, 1973; cited by FASEB, 1981).

In adult guinea pigs, a solution of sodium metasilicate pentahydrate (15-mL dose containing 20 mg SiO_2/mL) administered intraperitoneally produced siliceous deposits in kidney tubules within 24 hours. Many animals did not survive longer than 48 hours. At necropsy, kidneys were pale and enlarged and had rough surfaces (Settle and Sauer, 1960). Sodium metasilicate (250 mg) applied to the skin for 24 hours of guinea pigs produced moderate irritation (RTECS, 2000c).

When a laundry detergent containing sodium metasilicate and sodium carbonate was applied to the eyes of rabbits, damage to the cornea, with opacification, occurred, which correlated with its alkalinity (study details not provided) (Grant, 1986; cited by HSDB, 2000). A detergent containing 37% sodium metasilicate, applied to the intact and abraded skin of rabbits for four hours, caused tissue destruction in all animals (Nixon et al., 1975; cited by CIR, 2001). Sodium metasilicate (250 mg) applied to the skin for 24 hours of the animals produced severe irritation (RTECS, 2000c). Other skin irritation studies (details not provided in table) with varying amounts of sodium metasilicate also classified the chemical as corrosive (Rhone-Poulenc, Inc., 1971b, 1976; cited by CIR, 2001). It was also corrosive to the eyes of rabbits (Rhone-Poulenc, Inc., 1971b; cited by CIR, 2001).

When dogs were orally given sodium metasilicate (LD_{Lo} = 200 mg/kg), unspecified damage to the kidneys, ureters, bladder, gastrointestinal tract, lungs, thorax, and/or respiration was observed (RTECS, 2000c). Single doses of a commercially available detergent containing sodium metasilicate (percentage not specified) caused gross lesions in the oral cavity, pharynx, esophagus, stomach, larynx, lungs, and kidneys with ≥250 mg/kg. When pigs were given a single oral dose of 250 mg/kg of the same detergent, one animal died 95 hours after ingestion; lesions were similar to those observed in the dogs (Muggenberg et al., 1974; cited by CIR, 2001).

A single oral dose of sodium silicate [6834-92-0] (40 or 50 g) caused illness and/or death in some ducklings (Kiriliv et al., 1989b).

9.1.4 Short-term and Subchronic Exposure

The details of the following studies are presented in **Table 5**.

Table 5. Short-term and Subchronic Exposure to Sodium Metasilicate

Species, Strain, and Age, Number, and Sex of Animals	Chemical Form and Purity	Route, Dose, Duration, and Observation Period	Results/Comments	Reference
Albino mice, strain and age n.p., 210, sex n.p.	sodium metasilicate, purity n.p.	route n.p.; "dosed daily" with 200-300 mg/kg for 1 mo	Cellular proliferation in internal organs was observed.	Shakhbazyan and Karapetyan (1963; cited by FASEB, 1981)
Rats, Wistar, age, number, and sex n.p.	sodium metasilicate, purity n.p.	peroral; "high doses" (n.p.); "subchronic" (duration and observation period n.p.)	Slight degenerative changes in the epithel of renal tubules were observed, which were sporadically scattered. The maximum safety concentration was therefore calculated to be 1500 ppm/L/day (792 mg/kg/day) and the concentration for practical use to be 5 ppm (safety index = 475).	Ito et al. (1986 abstr.)
Rats, Charles River Cesarean-Derived (CD), age n.p., 15M and 15F	sodium metasilicate, purity n.p.	oral; 2.4 g (0.020 mol)/kg/day in a semisynthetic diet for 4 wk. At the end of the exposure period, the animals were sacrificed.	Polydipsia, polyuria, and soft stools were observed in some animals.	Newberne and Wilson (1970)
Rats, Fisher 344, "weanling", number and sex n.p.	sodium metasilicate nonahydrate ($Na_2SiO_3 \cdot 9H_2O$), purity n.p.	oral; 100 mg Si/kg/day added to "Si-depleted, chemically defined diets;" duration and observation periods n.p.	Rats showed a 25-34% increase in growth rates compared with controls (Si-depleted diets).	Schwarz and Milne (1972; cited by FASEB, 1981)
Rabbits, strain and age n.p., 20, sex n.p.	sodium metasilicate, purity n.p.	route n.p.; "dosed daily" with 200-300 mg/kg for 1 mo	Cellular proliferation in internal organs was observed.	Shakhbazyan and Karapetyan (1963; cited by FASEB, 1981)
Dogs, purebred Beagle, 6-mo-old, 8M and 8F	sodium metasilicate, purity n.p.	oral; 2.4 g (0.020 mol)/kg/day in a highly palatable diet for 4 wk. At the end of the exposure period, the animals were sacrificed.	Polydipsia, polyuria, and soft stools were observed in some animals. Gross cortical lesions of the kidney, which resembled focal, subcapsular hemorrhages and cortical infarcts, occurred in all males and in all but one female. Affected tubules were in juxtaposition to normal ones. Within localized areas of the kidney, hypertrophy of tubular epithelium (with or without degenerative changes), inflammatory cell infiltration into the interstitium, and dilatation or collapse of other tubules occurred to varying degrees. Renal function, however, was not affected.	Newberne and Wilson (1970)

Abbreviations: F = female(s); M = male(s); n.p. = not provided; wk = week(s)

Albino mice and rabbits dosed daily with sodium metasilicate (200-300 mg/kg) for one month exhibited cellular proliferation in internal organs (Shakhbazyan and Karapetyan, 1963; cited by FASEB, 1981).

When rats were orally given sodium metasilicate (100 mg Si/kg/day to 2.4 g/kg/day), increased body weights in males and decreased body weights in females, slight degenerative changes in the epithelia of renal tubules, polydipsia, polyuria, soft stools, and an increase in growth rates were observed (Ito et al., 1986 abstr.; Newberne and Wilson, 1970; Schwarz and Milne, 1972; cited by FASEB, 1981).

Some dogs given sodium metasilicate (2.4 g/kg/day) in a highly palatable diet for one month had polydipsia, polyuria, and soft stools. The incidence of renal lesions was 100% for males and 87.5% for females; renal function, however, was not affected as detected by clinical tests of serum and urine (Newberne and Wilson, 1970).

9.1.5 Chronic Exposure

No data were available. Nutritional requirements of silicon using sodium metasilicate have been studied in several livestock species. See Section 9.10.1.

9.1.6 Synergistic/Antagonistic Effects

Using solutions of sodium metasilicate nonahydrate (average daily dose of silicon: 0.1 mg/g body weight with a 0.05% solution for the first six weeks, 0.2 mg/g body weight with a 0.1% solution for the next six weeks, and 0.4 mg/g body weight with a 0.2% solution for the last six weeks), the effects of silicon on the mineral metabolism, lipid levels, and enzyme activities of rats have been studied by Najda and co-workers. A synergistic effect between silicon and copper was observed, while an antagonistic relationship was seen between silicon and zinc. [Noted: Compared to sodium metasilicate, the silicates of calcium, magnesium, and zinc are insoluble in water (Budavari, 1996).] For the effects on lipid levels and enzyme activities, see Section 9.10.2.

Serum and tissue (liver, kidney, lung, and aorta) copper levels were significantly higher in the test animals compared to those in controls, while serum and tissue zinc levels were lower in the former group compared to those of the latter group (Najda et al., 1992). In another study, under the same conditions, serum calcium levels were increased in test rats versus in controls, while serum magnesium levels were decreased. In contrast, calcium levels were lower and magnesium levels were higher in the liver, kidneys, and lungs of test animals versus those of controls (Najda et al., 1993b).

In an *in vitro* study evaluating the effect of sodium metasilicate on liposomes, 8-hydroxyquinoline-5-sulfonic acid was toxic when added with the silicate (i.e., it increased the silicate's destabilizing effect) (Erdogdu and Hasirci, 1983). See also Section 9.10.3.

9.2 Reproductive and Teratological Effects

No data were available. [Note: RTECS (2000c) listed two reproductive studies for the CASRN 6834-92-0; however, the original papers used "sodium silicate." (See Section 10.1.)]

9.3 Carcinogenicity
No data were available.

9.4 Initiation/Promotion Studies
No data were available.

9.5 Anticarcinogenicity
No data were available.

9.6 Genotoxicity
In assays using *Bacillus subtilis* strains without metabolic activation, sodium metasilicate (0.005-0.5 M) was not genotoxic (Kada et al., 1960; cited by CIR, 2001).

9.7 Cogenotoxicity
No data were available.

9.8 Antigenotoxicity
No data were available.

9.9 Immunotoxicity
A delayed-type hypersensitivity response was observed in the mouse ear swelling test (female BALB/c mice were sensitized on the back with 4% sodium metasilicate and then challenged on the ear with 6% sodium metasilicate). Negative results occurred in the murine local lymph node assay (NTP, 2000; cited by CIR, 2001).

9.10 Other Data

9.10.1 Nutritional Requirements for Silicon
Silicon has been found to be essential to the growth and skeletal development of rats and chicks (Underwood, 1977; cited by Ure and Berrow, 1982; Carlisle, 1974; cited by National Research Council, 2001). When added to purified or chemically defined diets, a concentration of 250 mg/kg silicon has been set as a guideline (National Research Council, 1984).

Several studies in livestock (broilers, pigs, and lambs) have investigated nutritional requirements for silicon using sodium metasilicate. When chicks were fed a low-silicon diet, growth retardation and a disturbance in bone formation occurred. However, when the diet was supplemented with sodium metasilicate nonahydrate, the chicks exhibited normal growth and development (Carlisle, 1972, 1974, 1980; all cited by FASEB, 1981). When broiler chickens and ducks were fed sodium metasilicate (0.5-2.5%) in feed mixtures up to 60-days-old, no adverse effects occurred. Carcass yield, feed utilization efficiency, percentage survival, and activity of digestive enzymes were greater compared to controls (diets without silicate). A level of 2 g per 100 g feed was safe to use as a growth promoter (Kiriliv et al., 1989a; b; 1991). In a similar study, chickens had increased vitamin B_{12} and niacin in the muscles and gizzard (Lagodyuk et al., 1990). When sodium metasilicate (providing 120 ppm sodium and 74 ppm silicon) was supplemented to the drinking water, no effects on growth rate, feed conversion, mortality, or litter conditions were observed. Loss of humeri strength in wings was not

significant (versus broilers given sodium fluoride). Sodium metasilicate had intermediate results on the breaking strength and ash content of humeri and tibiae (Merkley and Miller, 1983).

When lambs were given sodium silicate [6834-92-0] in water (solution equivalent to 800 mg SiO_2/L) for a period of 75 days, a significant interaction between silica and sex was observed. The weight gain of males was increased while that of females was slightly reduced. The effect was generally greater in diets without urea (Smith et al., 1972).

Growing pigs fed a basal diet supplemented with sodium metasilicate (amount not provided) gained 5.06 kg more in body weight and consumed 0.36 feed units less to gain 1 kg compared to controls (fed diet alone) (Kokorev et al., 1994). The average daily silicon requirements for young pigs were reported to be 39.8 and 161.3 mg/kg body weight at the beginning and end of the experiment (slaughtered when 3 or 7.5 months old), respectively (Kokorev et al., 1993).

9.10.2 Other Beneficial Effects in Domestic Animals

Studies in poultry found that sodium metasilicate, as the anhydrous form or nonahydrate (up to 2.5% feed mixture or diets supplemented with 300 mg/kg), had a positive effect on bone mineralization (i.e., increased alkaline phosphatase levels) and on metabolism (e.g., increased amino nitrogen and total phosphorus in plasma, increased glycogen in liver) (Kiriliv et al., 1989a, 1991; Lagodyuk et al., 1989; Tekeli and Zohouri, 1998).

In a balance trial with steers, sodium metasilicate (solubilized in drinking water at 800 ppm as SiO_2) as a high-energy (HE) density diet produced the following digestibilities for plain and silicated treatments: 75.5% versus 69.2% for nitrogen, 80.0% versus 77.0% for dry matter, and 71.0% versus 65.0% for cellulose. For the low-energy (LE) density diet, digestibilities were 54.0% versus 59.0%, respectively, for nitrogen. A digestion trial, designed to compare heifers and bulls, showed that when fed the HE diet, heifers had reduced digestion coefficients for nitrogen, dry matter, and cellulose, while these were all increased in bulls. For the LE diet, heifers showed increases in digestibility of all compounds, while bulls only showed an increase in cellulose digestibility (Hall and Anthony, 1979 abstr.).

Hens given sodium metasilicate nonahydrate (0.5, 1.0, or 1.5 g per 100 g) in a standard mixed feed from 150- to 330-days-old had increased numbers and weights of eggs and increased egg shell quality; best results were obtained with the mid dose (Lagodyuk et al., 1989). In another study, laying hens were given sodium metasilicate (0.5 or 1%) in diets containing (a) 3.4% calcium and 0.34% phosphorus or (b) 2.7% calcium and 0.27% phosphorus for 15 weeks. At 32 weeks of age, egg production was increased and the lower dose decreased egg specific gravity more than the higher dose with diet A. At 52 weeks of age, increased egg production and feed efficiency were observed with both diets. Additionally, diet B with 1% sodium metasilicate significantly reduced egg specific gravity (Mir Abdalbaghy and Nik-Khah, 1997).

9.10.3 Effects of Silicon on Lipid Levels and Enzyme Activities

Rats perorally given solutions of solutions of sodium metasilicate nonahydrate (average daily dose of silicon: 0.1 mg/g body weight using a 0.05% solution for the first six weeks, 0.2 mg/g body weight using a 0.1% solution for the next six weeks, and 0.4 mg/g body weight using a 0.2% solution for the last six weeks) exhibited increases in serum HDL-cholesterol and HDL-

phospholipid concentrations, as well as significant increases in serum thyrotropin levels, suggesting a role for sodium silicate in functions of the pituitary gland (Najda et al., 1991, 1993c). In the liver and kidney, the activities of superoxide dismutase, catalase, and glutathione peroxidate were decreased in test animals (Najda et al., 1994). In another study (details not provided), the activities of alanine and aspartate aminotransferases, alkaline phosphatase, and γ-glutamyl transpeptidase in serum were not changed, further emphasizing the lack of sodium metasilicate's toxicity on the animals (Najda et al., 1993; cited by HSDB, 2000). Lastly, there were no statistically significant differences in hydroxyproline and hydroxylysine blood serum concentrations and elastin levels in aortic walls between both groups (Najda et al., 1993a). The difference in all parameters between the test and control groups increased with time of experiment and dose of solution. No compound-related toxic effects or behavioral changes in the animals were observed. The results seemed to indicate that several mechanisms of silicon antiatheromatous actions are present. It was concluded that "the arterial wall is probably not the only site of silicon action. … There could also exist an alternative mechanism of silicon action *in vivo*, combined with a modification of enzymatic system activity, responsible for the metabolism of lipids" (Najda et al., 1991).

9.10.4 Miscellaneous Studies

Sodium metasilicate destabilized liposomes with cholesterol (i.e., increased their permeability) *in vitro*. The effect, caused by the dissolution of monosilicic acid from silicate, decreased as concentration increased (Erdogdu and Hasirci, 1983). Neutralized sodium metasilicate at concentrations up to 0.025 M inhibited urease and invertase *in vitro* but did not significantly affect other enzymes (e.g., pepsin, trypsin, lipase, catalase, and cholinesterase) (Kind et al., 1954; Alexander, 1968; both cited by FASEB, 1981). In Skin^2 ZK 1350 cultures, sodium metasilicate was corrosive; the mean cell viability was 66% (Liebsch et al., 1995; cited by CIR, 2001). In an *in vitro* system using pig platelets, sodium metasilicate nonahydrate was found to be a strong inducer of histamine release (Ainsworth et al., 1979; cited by FASEB, 1981).

10.0 Structure-Activity Relationships

In this section, toxicity data for sodium silicate, amorphous nonfibrous silica, simple three-element silicates (metal, silicon, and oxygen) and their hydrates, sodium carbonate, and sodium hydroxide are presented. For amorphous silica and the simple three-element silicates, focus was placed on *inhalation studies* in both humans and animals. Numerous studies in which animals (e.g., rabbits and mice) were treated intratracheally were available. For example, such experiments were conducted with aluminum silicate. Observation included the development of alveolar macrophagic responses and the induction of IgE antibody production (Marinescu et al., 1981; Fujimaki et al., 1986).

10.1 Sodium Silicate

In several reviews, studies with sodium silicate have been presented with those conducted with sodium metasilicate (e.g., FASEB [1981] and CIR [2001]).

Human Data: A 57-year-old man who had come in contact with sodium silicate in a dyeing process experienced recurrent ulcerative lesions on his left hand for two years, as well as contact urticaria. Positive patch tests and a scratch test pointed to sodium silicate as the culprit (Tanaka et al., 1982). In another case report, a man who had drunk 200 mL of a neutralized sodium

silicate solution (waterglass; ~100 g sodium silicate) experienced vomiting, diarrhea, and gastrointestinal bleeding and had albumin, casts, acetone, sugar, and blood in the urine; he recovered (Eichhorst, 1920; cited by FASEB, 1981).

ADME: In experimental animals, enteral administration of silicates was observed to result in increased urinary silicate excretion but no significant effect on blood levels (Joint FAO/WHO Expert Committee on Food Additives, 1974; King et al., 1933; Sauer et al., 1959a,b; all cited by FASEB, 1981). When guinea pigs were orally given 10 mL of a 0.6% sodium silicate solution with labeled ^{31}Si, initial urinary absorption and excretion were rapid, and after four hours the former process decreased. Increasing the pH from 10.6 to 11.4 increased the amount of labeled silica in tissues and in urine by threefold at four hours after administration (Sauer et al., 1959b; cited by FASEB, 1981).

Chronic Toxicity: When three-week-old Sprague-Dawley rats were orally given sodium silicate (600 and 1200 ppm silica/L [120 and 240 mg/kg bw at the start of the experiment and 72 and 144 mg/kg bw at the end]) in drinking water for 180 days, male rats were 6.0% heavier, while female rats were 5.0% lighter than controls at the low dose. At 1200 ppm, no changes in body weights were observed. Furthermore, it appeared that nitrogen and phosphorus retentions were increased (Smith et al., 1973; cited by FASEB, 1981).

Reproductive Toxicity: When three-week-old Sprague-Dawley rats were orally given sodium silicate (600 and 1200 ppm silica/L [120 and 240 mg/kg bw at the start of the experiment and 72 and 144 mg/kg bw at the end]) in drinking water for 180 days, the numbers of offspring and survival rates were decreased (Smith et al., 1973; cited by FASEB, 1981 and RTECS, 2000c).

Adult albino rats were given sodium silicate (TD_{Lo}=9766 µg/kg [80.00 µmol/kg] for one day) via intratesticular injection into the left testis (right one served as control) had an increased mean testis weight compared to controls at two days but a decreased weight at seven days. No morphological or histological changes and no effect on the residual spermatozoa in the ductus deferens were seen. Additionally, s.c. injection of the same dose into the animals did not affect morphology, histology, or spermatozoa (Kamboj and Kar, 1964; RTECS, 2000c).

Genotoxicity: Sodium silicate (concentrations of 0.025-0.300% for 3 hours) did not induce back-mutations in Sd-4 (streptomycin-dependent) *Escherichia coli* treated cells. The percent survival ranged from 66% (at the lowest dose) to 0.11% (at the highest dose), and the mutants per 10^8 bacteria ranged from 0.0 (at the highest dose) to 11.4 (at a concentration of 0.100%) (Demerec et al., 1951).

Immunotoxicity: In women with silicone breast implants, preincubation of sera with sodium silicate inhibited more than 90% of the binding of immunoglobulin G (IgG) and IgM antibodies with silicate. Silicon dioxide, on the other hand, failed to inhibit the activity (Shen et al., 1996).

10.2 Amorphous Silica

Amorphous silicas, which are naturally occurring and synthetic, include diatomaceous earth, precipitated silica, silica gel, fumed silica, and silica fume (thermally generated). Fumed silica [7631-86-9] is synthetically produced by vapor phase hydrolysis, whereas silica fume is the

byproduct of the reaction of coke and silica sand in an electric arc furnace (NOHSC, undated-a). OSHA has set a PEL of 6 mg/m^3 for amorphous silica and classifies it as a nuisance dust (OSHA, 1989; Waddell and Evans, 1997). The Exposure Standards Expert Working Group recommended a TWA of 2 mg/m^3 (respirable dust) for silica, amorphous fume (thermally generated) containing <1% quartz and that no STEL be set (NOHSC-undated b).

The limited data on the effects of inhaled amorphous silica on the respiratory tract suggest that effects following exposure may be reversible upon termination of the exposure (U.S. EPA, 2001a). A review of the toxicity of amorphous silica observed that some tissue reaction occurred but no collagen formation (Jahr, 1981; cited by NOHSC, undated-a).

Human Data: The health effects of amorphous silicas in humans are unclear. In general, limited studies indicated minimal effects, including a negative carcinogenic effect (McLaughlin et al., 1997; Table 1 of the paper summarizes epidemiological studies.) The Working Group concluded that there was inadequate evidence in humans for the carcinogenicity of amorphous silica; the evaluation was abased ion inhalation exposures in the workplace (IARC, 1997).

Airflow limitation in workers from exposure to amorphous silica (potato workers and grape workers) has been suggested, but the studies failed to find pneumoconiotic effects (Jorna et al., 1994; Gamsky et al., 1992; both cited by IARC, 1997). Pulmonary fibrosis was a common result from prolonged occupational exposure to the dust (e.g., in workers at a metallurgical company) (Vitums et al., 1977). Silicosis has not been observed in individuals exposed to amorphous silica, including those experiencing chronic exposure to the product (Wilson, 1981; cited by Waddell and Evans, 1997). However, several cases of pneumoconiosis or silicosis among those exposed to diatomaceous earth have been reported (McLaughlin et al., 2000). In a study of 165 workers exposed to precipitated silica for an average of 8.6 years, no ill effects were reported (OSHA, 1989). Studies of 353 workers exposed to fumed silica (1.6-53 mg/m^3) for up to 32 years found pulmonary dysfunction only in smokers (ASTM, 1987; cited by NOHSC, undated-a). In comparison to fumed silica, silica fume has been observed to have a "more significant pneumoconiotic effect" (ACGIH, 1986; cited by NOHSC, undated-a). An association between silica fume and the development of silicosis in exposed individuals working in silicon smelters was suggested (van Niekerk et al., 2000). Its toxicity is currently under review by the Exposure standards Working Group (NOHSC, undated-a).

Animal Studies: Animals studies have indicated limited and mostly reversible cytotoxic and possibly fibrogenic effects with some forms, and the few carcinogenicity studies available do not suggest that amorphous silica is carcinogenic (McLaughlin et al., 1997). The Working Group concluded that there was inadequate evidence in experimental animals for the carcinogenicity of synthetic amorphous silica and uncalcined diatomaceous earth (IARC, 1997).

When rats were exposed to fumed silica (50 mg/m^3) (exposure time not provided), the majority died from pulmonary obstruction and emphysema after three to five months. Upon termination of exposure, surviving rats immediately recovered (Schepers et al., 1957; cited by NOHSC, undated-a). When rats, guinea pigs, and monkeys were exposed to fumed silica, silica gel, or precipitated silica (15 mg/m^3 total dust; 6.9-9.9 mg/m^3 respirable dust) for 5.5 to 6 hours/day, 5 days/week for up to 18 months, few or no silicon-containing macrophages were found in the

lungs of the rats and guinea pigs, but early nodular fibrosis induced by fumed silica was found in the lungs of the monkeys (Groth et al., 1981; cited by NOHSC, undated-a). Upon termination of exposure to the dust, cell aggregate lesions in the lungs regressed (Schepers et al., 1957; cited by Waddell and Evans, 1997). Fumed silica was therefore more toxic than precipitated silica and silica gel. It was noted that full toxic potential of fumed silica might not have been observed, since the exposure period of 18 months might be short for the monkeys (NOHSC, undated-a).

When male and female rats were exposed by inhalation to three types of amorphous silica (Aerosil 200, Aerosil R 974, and Sipernat 22S) for six hours/day, five days/week for 13 weeks, non-neoplastic pulmonary changes, consisting of slight to severe accumulation of alveolar macrophages, intra-alveolar granular material, cellular debris and polymorphonuclear leukocytes in the alveolar spaces, and increased septal cellularity, were seen at the end of the exposure period. In addition, focal interstitial fibrosis was found in all animals. During the post-exposure period, the changes disappeared partly or completely (Reuzel et al., 1991; cited by IARC, 1997). Exposure to 10.91 mg/m^3 quartz glass (amorphous glass dust VP 203-006) for seven hours/day, five days/week for a year resulted in a non-neoplastic pulmonary change consisting of slight, focal cellular reaction with minimal fibrosis; mediastinal lymph nodes were enlarged and exhibited severe fibrosis with bundles of hyalinized collagen fibers (Rosenbruch et al., 1990; cited by IARC, 1997).

A more recent rat study of subchronic inhalation of amorphous silica (precipitated silica; Aerosil 200 Degussa) (50 mg/m^3 for 6 hours/day, five days/week for up to 13 weeks) found a high degree of pulmonary inflammation and cytotoxicity (e.g., an increased lung burden and increased numbers of neutrophils and macrophages immediately after exposure) but no genotoxic effects in alveolar epithelial cells (Johnston et al., 2000).

When mice were exposed by inhalation in a chamber with a capacity of 600 L to about 0.5 g per day precipitated silica for one year, pulmonary tumors (adenomas and adenocarcinomas) and nodular fibrotic overgrowth or hyperplasia of the tracheobronchial lymph nodes were observed (Campbell, 1940; cited by IARC, 1997).

A study using natural amorphous silicas (including diatomaceous earth) found that total silica content per lung increased linearly in guinea pigs exposed by inhalation to atmospheric suspensions of the silica; furthermore, total ash weight increased more quickly than the accumulation of dust (Pratt, 1983).

10.3 Metal Silicates (Calcium, Aluminum, and Magnesium [Talc])

Calcium silicate [10101-39-0], potassium silicate [1312-76-1], and sodium silicate [1344-09-8] are not U.S. EPA registered pesticides (Orme and Kegley, 2000a, b, e). However, all are listed as "inert" ingredients in pesticide products registered by the agency (U.S. EPA, 2001b; see document for specific categories and additional listing of silicate compounds). The reregistration of calcium silicate (List D, Case No. 4081) was cancelled in September 1991 (U.S. EPA, 1998). [The registration status for the product Silikil S, which contained 55% calcium silicate and 37% diatomaceous earth, was cancelled on October 10, 1989 (Orme and Kegley, 2000c).]

Inhalation of silicates causes fibrogenesis in the lungs but to a lesser extent than silica. Heavy prolonged exposure to silicates, however, produces characteristic lesions. The gross and microscopic features of silicosis and silicate diseases have been reviewed by the Silicosis and Silicate Disease Committee (1988).

Calcium Silicate

Animal Studies: When 192 outbred white male Wistar SPF rats of the AF/HAN strain were exposed to the dust of three commercially produced calcium silicate insulation materials (10 mg/m^3 respirable dust) for seven hours/days, five days/week for a total of 224 over one year, no major pulmonary damage was observed; only small amounts of dust were recovered from the lungs. Calcium silicates had no effect on the survival or health of the animals. [A single i.p. injection of 25 mg of the dust preparations from the calcium silicate composites produced no mesotheliomas. Autopsy showed little dust or dust-related fibrosis in the peritoneal cavity of the animals] (Bolton et al., 1986). In guinea pigs, inhalation of dust particles of calcium silicate (dose and exposure period not provided) induced "excised lungs respiratory ampliation to constrict down to a state of severe hypoventilation" (Dautrebande et al., 1958).

Aluminum Silicate

Long-term retention of inhaled fused aluminosilicate particles (FAP) has been studied in several animal species and in humans.

Human Data: In seven volunteers who inhaled monodisperse FAP (diameters of 1.2 and 3.9 μm labeled with ^{85}Sr and ^{88}Y, respectively), approximately 8% of the smaller particles and 40% of the larger particles were cleared within six days. The fractions were calculated to be deposited within the conducting airways, therefore causing no immediate alveolar clearance. Approximately 4% of the smaller particles and 11% of the larger particles retained at six days were cleared with a half-time of about 20 days; the rest was cleared with half-times of 330 and 420 days, respectively. For both, mechanical clearance was slow with a half-time of about 600 days (Bailey et al., 1982). Close pathogenic relationships between pulmonary fibrosis and inhalation exposure to pesticides, including kaolin powder (with aluminum silicate) and talcum or soapstone powder (with magnesium and aluminum silicate) have been suggested (Barthel, 1974).

Animal Studies: Fischer 344 male rats were exposed nose-only for 45 minutes to an aerosol of ^{57}Co-labeled FAP with 3.95 μm activity median aerodynamic diameter (AMAD). Clearance of FAP from the alveolar compartment of the lung (measured as thoracic retention of ^{57}Co) was 60% at 112 days after inhalation; the rate of clearance was indicated by the half-time of 85 days in the thorax counts. The total amounts of ^{57}Co recovered in the washings and in the tissues of the trachea and bifurcation one day after inhalation were 98 and 87%, respectively, and decreased with time but never fell below 30% during the study period. There were no significant amounts of ^{57}Co in the gastrointestinal tract, liver, spleen, kidneys, or the remainder of the carcass. Less than 1% was distributed in the thoracic lymph nodes during the study period and 100 times less was in the cervical lymph nodes. Most of the small quantities dissolving from the FAP remaining in the lung were excreted in urine and feces (Patrick et al., 1996).

In another study, rats, mice, and dogs were "briefly exposed" to ^{134}Cs-labeled FAP (monodisperse particles of 0.7-, 1.5-, or 2.8-µm AMAD or polydisperse particles with 1.5- to 2.0-µm AMAD). In dogs, the dominant factor in long-term (i.e., up to 850 days after exposure) lung clearance for particles was solubilization; most of the deposited particles went to lung-associated lymph nodes. In rats and mice, the dominant factor was mechanical clearance; rapid clearance occurred from the pulmonary region. In all animals, a small portion of the initial deposit was found in the upper respiratory tract (Snipes et al., 1983).

In Syrian hamsters exposed to aerosols of ^{137}Cs-labeled FAP (a monodisperse aerosol with AMAD of 1.53 µm and a polydisperse aerosol with AMAD of 1.87 µm), an estimated relative lung deposition of 9.5% of inhaled aerosols was observed. The right apical lobe contained more activity on a per gram lung weight basis than the total lung, while the right cardiac and right diaphragmatic lobe had less activity [exposure period not provided in abstract] (Thomas and Raabe, 1978).

Using a model with a two-lung compartment for lung retention (half-life of 10,000 days in one, and a half-life of 50, 200, and 400 days for mice, rats, and dogs, respectively, in the other), the predicted different retention patterns for the animals at the same concentration of aerosol of FAP were attributed to interspecies differences in the anatomy of the lung (Thomas, 1971).

Magnesium Silicate (Talc)

The resulting lung injury from the inhalation of talc is partly caused by its contaminants, asbestos and crystalline silica. The irritation induced can lead to inflammation at the deposition site in the lung tissue and then attraction and activation of neutrophils, which may increase the lung injury. Talc was also toxic to the lung via intravenous injection but not via oral ingestion (Kehrer, 1990).

Human Data: Of five reported cases of accidental inhalation of talcum powder (consisting of 90% anhydrous magnesium silicate) in children (one to two years old), three died within one to 20 hours. Their symptoms included respiratory distress, choking, tachycardia, cyanosis, intercostal retraction, and bronchitis. Inflammatory exudate was found in the larynx, trachea, bronchi, and bronchioles, with gross obstruction of the lower air passages, and atelectasis and compensatory emphysema were seen in the lungs. Microscopic examination revealed cellular desquamation and leucocytic infiltration (Anonymous, 1969).

Animal Studies: The National Toxicology Program (NTP) performed toxicology and carcinogenicity studies of non-asbestiform talc (CASRN 14807-96-6; also called non-fibrous talc) in F344/N rats and $B6C3F_1$ mice. The animals were exposed to aerosols containing 0, 6, or 18 mg/m^3 talc for 6 hours/day, 5 days/week for up to 113 weeks for male rats, 122 weeks for female rats, and 104 weeks for all mice. There was some evidence of carcinogenicity of talc in male rats (increased incidence of benign or malignant pheochromocytomas of the adrenal gland), clear evidence in female rats (increased incidences of alveolar/bronchiolar adenomas and carcinomas of the lung and benign or malignant pheochromocytomas of the adrenal gland), and no evidence in male or female mice (NTP, 1993).

10.4 Sodium Carbonate

Human Data: The effects of overexposure to dusts or vapors of sodium carbonate can range from irritation of the mucous membranes, which leads to coughing and shortness of breath, to damage of the nasal septum. Sodium carbonate is non-irritating to intact skin. However, on abraded skin, symptoms of dermal contact can range from minor irritation and redness (erythema with concentrated solutions) to sensitization, dermatitis, and vesicular skin reactions (particularly with high concentrations). Severe irritation may also occur in the eyes; sodium carbonate can be corrosive and cause conjunctival edema and corneal destruction. Other symptoms can also appear from its absorption into the bloodstream via the eyes (Budavari, 1996; FMC Wyoming Corp., 2001; Mallinckrodt Baker, Inc., 1998).

Oral administration of sodium carbonate (LD_{Lo} = 714 mg/kg) was a general anesthetic in man. It produced ulceration or bleeding from the small intestine as well as other unspecified gastrointestinal changes (RTECS, 2000a). The symptoms occurring from corrosion of the gastrointestinal tract include severe abdominal pain, vomiting, diarrhea, collapse, and death (Mallinckrodt Baker, Inc., 1998).

Acute Toxicity: In mice, the following LD_{50} values were reported: 6600 mg/kg (oral), 117 mg/kg (i.p.), and 2210 mg/kg (s.c.). In the rat, the oral LD_{50} was calculated as 4090 mg/kg (RTECS, 2000a).

In mice, rats, and guinea pigs, inhalation studies were conducted using LC_{50} values for each species (1200, 2300, and 800 mg/m^3, respectively, for two hours). All animals had dyspnea and other gastrointestinal changes (RTECS, 2000a).

In rabbits, dermal exposure to sodium carbonate (500 mg) for 24 hours produced mild irritation. A lower dose (100 mg) applied to the eyes for 24 hours caused moderate irritation. The dose, followed by a 30-second rinse, reduced the effect to mild irritation. At an even lower dose (50 mg), severe irritation was observed (duration was not provided) (RTECS, 2000a).

Short-Term and Subchronic Toxicity: When mammals (species not specified) inhaled sodium carbonate (TC_{Lo} = 16.2 mg/m^3) intermittently for 17 weeks, changes in the sensation of smell, lowering of blood pressure (other than as an effect on the autonomic nervous system), and respiratory depression were observed (RTECS, 2000a).

Reproductive Toxicity: In mice, sodium carbonate (TD_{Lo} = 8.48 µg/kg) injected into the uterus for four days of pregnancy resulted in pre-implantation mortality (e.g., reduction in the number of implants per female and the total number of implants per corpora lutea) (RTECS, 2000a).

10.5 Sodium Hydroxide

Human Data: Sodium hydroxide is corrosive to all body tissues regardless of the route of exposure. Dermal exposure to sodium hydroxide can cause nasal irritation, pneumonitis, temporary loss of hair, intercellular edema, erythema, keratin material decomposition, and burns. Contact with the eyes can result in ulceration, perforation, opacification, and blindness (Budavari, 1996; OEHHA, 1999). Besides burns, oral ingestion of sodium hydroxide has been indirectly "implicated in the production of esophageal cancer" (i.e., the result of scar formation

and tissue destruction). Persons exposed to sodium hydroxide in the workplace have described nose and throat irritation, respiratory irritation, chest pains, and shortness of breath. Cases of irreversible obstructive lung disease have also been reported (OEHHA, 1999).

Acute Toxicity: An i.p. LD_{50} of 40 mg/kg was reported in mice. In rabbits, the dermal LD_{50} was calculated as 1350 mg/kg and the oral LD_{Lo} as 500 mg/kg (OxyChem, 1998; RTECS, 2000b). In mice and rats, dermal application of sodium hydroxide (dose not provided) caused severe irritation, leading to necrosis and death (OEHHA, 1999). When applied to the skin of rabbits for 24 hours, sodium hydroxide (500 mg) produced severe irritation. When administered to the eyes (0.050-1 mg and 1 mg followed with a 30-second rinse) for 24 hours, severe irritation was observed (RTECS, 2000b). Other observed effects have included ulceration, perforation, corneal necrosis and opacification, vascularization, and increased intraocular pressure (OEHHA, 1999).

Short-Term and Subchronic Toxicity: Inhalation studies in rats with sodium hydroxide from an aerosolized 40% solution (dose not provided) for one-half hour two times daily for 2.5 months produced alveolar wall thickening, accompanied with cell proliferation and congestion, ulceration and flattening of the bronchial epithelium, and proliferation of lymphadenoid tissue (OEHHA, 1999). In another study where exposure was two times weekly for one month, all rats died; the major cause was bronchopneumonia. Exposure to aerosol produced from lower concentrations caused dilatation and damage to the alveolar septae (20% solution) and bronchial dilatation and mucous membrane degeneration (5% solution) (OEHHA, 1999).
Carcinogenicity: An inhalation study with sodium hydroxide from an aerosolized 40% solution (dose not provided) for one-half hour two times daily for 2.5 months produced "undescribed, isolated tumors" in three of ten rats (OEHHA, 1999). No long-term studies with appropriate numbers of rodents were identified.

Genotoxicity: In Chinese hamster V79 lung and ovary cells, sodium hydroxide (10 and 16 mmol/L, respectively) presumably induced cytogenic effects (RTECS, 2000b).

11.0 Online Databases and Secondary References

11.1 Online Databases

Chemical Information System Files
TSCATS (Toxic Substances Control Act Test Submissions)

DIALOG Files
DIOGENES (Chemical Economics Handbook)

STN International Files

AGRICOLA	CAPLUS	NIOSHTIC	TOXLINE
BIOSIS	EMBASE	NTIS	
CA	HSDB	PROMT	
CABA	LIFESCI	Registry	
CANCERLIT	MEDLINE	RTECS	

TOXLINE includes the following subfiles:

Toxicity Bibliography	TOXBIB
International Labor Office	CIS
Hazardous Materials Technical Center	HMTC
Environmental Mutagen Information Center File	EMIC
Environmental Teratology Information Center File (continued after 1989 by DART)	ETIC
Toxicology Document and Data Depository	NTIS
Toxicological Research Projects	CRISP
NIOSHTIC®	NIOSH
Pesticides Abstracts	PESTAB
Poisonous Plants Bibliography	PPBIB
Aneuploidy	ANEUPL
Epidemiology Information System	EPIDEM
Toxic Substances Control Act Test Submissions	TSCATS
Toxicological Aspects of Environmental Health	BIOSIS
International Pharmaceutical Abstracts	IPA
Federal Research in Progress	FEDRIP
Developmental and Reproductive Toxicology	DART

In-House Databases
CPI Electronic Publishing Federal Databases on CD
Current Contents on Diskette®
The Merck Index, 1996, on CD-ROM

11.2 Secondary References [Data Compilations and Reviews]

ACGIH (American Conference of Governmental Industrial Hygienists). 1986. Documentation of the Threshold Limit Values and Biological Exposure Indices,5th ed. Cincinnati, OH. Cited by NOHSC (undated-a).

ASTM (American Society for Testing and Materials). 1987. Health Requirements for Occupational Exposure to Synthetic Amorphous Silica. ASTM Standard E1156-87, Philadelphia, PA. Cited by NOHSC (undated-a).

Budavari, S., Ed. 1996. The Merck Index, 12th ed. Merck & Co., Inc., Whitehouse Station, NJ.

CIR (Cosmetic Ingredient Review). 2001. Tentative report: Safety assessment of potassium silicate, sodium metasilicate, and sodium silicate (January 29, 2001). CIR, Washington, DC, 30 pp.

Clayton, G.D., and F.E. Clayton, Eds. 1981-1982. Patty's Industrial Hygiene and Toxicology, 3rd ed. Vol. 2A, 2B, and 2C: Toxicology. John Wiley and Sons, New York, NY, pp. 3066-3067. Cited by HSDB (2000).

Falcone, J.S., Jr. 1985. Silicon compounds. In: Grayson, M, and D. Eckroth, Eds. Kirk-Othmer Concise Encyclopedia of Chemical Technology. John Wiley and Sons, New York, NY, pp. 1058-1060.

Falcone, J.S., Jr. 1997. Silicon compounds. In: Kroschwitz, J., and M. Howe-Grant, Eds. Kirk-Othmer Encyclopedia of Chemical Technology, 4th ed. Vol. 22. John Wiley and Sons, New York, NY, pp. 1-30.

FASEB (Federation of American Societies for Experimental Biology). 1981. Evaluation of the health aspects of sodium metasilicate and sodium zinc metasilicate as food ingredients. (Final report). 26 pp.

Grant, W.M. 1986. Toxicology of the Eye, 3rd ed. Charles C. Thomas Publisher, Springfield, IL, pp. 841 ff. Cited by HSDB (2000).

IARC (International Agency for Research on Cancer). 1997. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Silica, some silicates, coal dust and *para*-aramid fibrils, Vol. 68., WHO, Lyon, France, 506 pp.

Joint FAO/WHO Expert committee on Food Additives. 1974. Toxicological evaluation of some food additives including anticaking agents, antimicrobials, antioxidants, emulsifiers and thickening agents. WHO Food Addit. Ser. (No. 5):21-30. Cited by FASEB (1981).

Lowenheim, F.A., and M.K. Moran. 1975. Faith, Keyes, and Clark's Industrial Chemicals, 4th ed. John Wiley and Sons, Inc., New York, NY, pp. 755-761. Cited by FASEB (1981).

Mark, H.F., J.J. McKetta, Jr., and D.F. Othmer, Eds. 1969. Kirk-Othmer Encyclopedia of Chemical Technology, 2nd ed. Vol. 18. John Wiley and Sons, Inc., New York, NY, pp. 134-165. Cited by FASEB (1981).

Stokinger, H.E. 1981. The halogens and the nonmetals boron and silicon. In: Clayton, G.D., and F.E. Clayton, Eds. Patty's Industrial Hygiene and Toxicology, 3rd revised ed. John Wiley and Sons, Inc., New York, NY, pp. 2937-3043.

Underwood, E.J. 1977. Trace Elements in Human and Animal Nutrition, 4th ed. Academic Press, London, 545 pp. Cited by Ure and Berrow (1982).

Ure, A.M., and M.L. Berrow. 1982. The elemental constituents of soil. In: Environmental Chemistry (Specialist Periodical Report), Vol. 2. The Royal Society of Chemistry, Burlington House, London, pp. 94-204.

Waddell, W.H., and L.R. Evans. 1997. Amorphous silica. In: Kroschwitz, J.I., and M. Howe-Grant, Eds. Kirk-Othmer Encyclopedia of Chemical Technology, 4th ed. Vol. 21. John Wiley and Sons, New York, NY, pp. 1005-1032.

Weissler, A. 1978. Monograph on sodium metasilicate. Report No. FDA/BF-79/11. NTIS, Springfield, VA, 27 pp.

12.0 References Cited

Abe, K., S. Tanimori, N. Tobari, and Y. Yonejima. 1966. Analysis of compounds in detergents. VII. Analysis of inorganic compounds in household detergents. Kogyo Kagaku Zasshi 69(10):1908-1912. Abstract from CAPLUS 1967:77263.

Abe, M., T. Yamaguchi, M. Nakamae, K. Watanabe, and K. Ogino. 1988. Simultaneous determination of anionic surfactants and inorganic electrolytes by an isotachophoretic method. Yukagaku 37(11):1000-1005. Abstract from CAPLUS 1989:195178.

Ainsworth, S.K., R.E. Neuman, and R.A. Harley. 1979. Histamine release from platelets for assay of byssinogenic substances in cotton mill dust and related materials. Br. J. Ind. Med. 36:35-42. Cited by FASEB (1981).

Aldrich. 1998-1999. Sodium metasilicate. Inorganics and Organometallics from Aldrich. Milwaukee, WI, p. 410.

Alexander, A.G. 1968. *In vitro* effects of silicon on the action patterns of sugarcane acid invertase. J. Agric. Univ. Puerto Rico 52:311-322. Cited by FASEB (1981).

Anonymous. 1969. Accidental inhalation of talcum powder. Br. Med. J. 4:5-6. Abstract from NIOSHTIC 1997:95669.

Archibald, J.G., and H. Fenner. 1957. Silicon in cow's milk. J. Dairy Sci. 40:703-706. Cited by FASEB (1981).

Bailey, M.R., F.A. Fry, and A.C. James. 1982. The long-term clearance kinetics of insoluble particles from the human lung. Ann. Occup. Hyg. 26(1-4):273-290. Abstract from EMBASE 83006085.

Barthel, E. 1974. Pulmonary fibrosis in persons occupationally exposed to pesticides (Ger.). Z. Erkr. Atmungsorgane 141(1):7-17. Abstract from EMBASE 75141881.

Baumann, H. 1960. *Verhalten der Kieselsäure in menschlichen Blut und Harn.* [Silica concentration in human blood and urine.] Hoppe-Seyler's Z. Physiol. Chem. 320:11-20. Cited by FASEB (1981).

Benke, G.M., and T.W. Osborn. 1979. Urinary silicon excretion by rats following oral administration of silicon compounds. Food Cosmet. Toxicol. 17(2):123-128.

Bolton, R.E., J. Addison, J.M.G. Davis, K. Donaldson, A.D. Jones, B.G. Miller, and A. Wright. 1986. Effects of the inhalation of dusts from calcium silicate insulation materials in laboratory rats. Environ. Res. 39(1):26-43.

Buckley, L.E. 1968. Letter, dated July 29, responding to an inquiry about the use of sodium metasilicate pentahydrate as a component of a fruit and vegetable washing mixture. Food and Drug Administration, Washington, DC. Cited by FASEB (1981).

Campbell, J.A. 1940. Effects of precipitated silica and of iron oxide on the incidence of primary lung tumours in mice. Br. Med. J. ii:275-280. Cited by IARC (1997).

Carlisle, E.M. 1972. Silicon: An essential element for the chick. Science 178:619-621. Cited by FASEB (1981).

Carlisle, E.M. 1974. Silicon as an essential element. Fed. Proc. Am. Soc. Exp. Biol. 33:1758-1766. Cited by FASEB (1981) and National Research Council (2001).

Carlisle, E.M. 1980. A silicon requirement for normal skull formation in chicks. J. Nutr. 110:352-359. Cited by FASEB (1981).

Cassidy, F.A. 1962. Letter, dated October 2, responding to an inquiry about the status of sodium metasilicate pentahydrate as a component of a fruit and vegetable washing mixture. Food and Drug Administration, Washington, DC. Cited by FASEB (1981).

Chemcyclopedia Online. 2001. Sodium metasilicate and sodium metasilicate pentahydrate. American Chemical Society, Washington, DC. Internet address: http://chemcyclopedia.ims.ca/ Last accessed on June 1, 2001.

Clairol. 2000. Sodium metasilicate modified soap chamber test (00041). Unpublished data submitted by CTFA (Cosmetic, Toiletry, and Fragrance Association), 207 pp. Cited by CIR (2001).

Clairol. 2000b. Sodium metasilicate modified soap chamber test (97057). Unpublished data submitted by CTFA (Cosmetic, Toiletry, and Fragrance Association), 52 pp. Cited by CIR (2001).

Coppock, R.W., M.S. Mostrom, and L.E. Lillie. 1988. The toxicology of detergents, bleaches, antiseptics, and disinfectants in small animals. Vet. Hum. Toxicol. 30(5):463-473.

Dautrebande, L., A.L. Delaunois, and C. Heymans. 1958. New studies on aerosols. IV. Effect of fine dust particles on excised guinea pig's lung before and after sympathomimetic aerosols. Arch. Int. Pharmacodyn. Ther. CXVI(1-2):187-208. Abstract from NIOSHTIC 1997:19474.

Demerec, M., G. Bertani, and J. Flint. 1951. A survey of chemicals for mutagenic action on *E. coli*. Am. Nat. 85:119-136.

Eichhorst, H. 1920. Water-glass poisoning. Schweiz. Med. Wochenschr. 50:1081. (J. Am. Med. Assoc. 76:275-276 [1921].) Cited by FASEB (1981).

Emerick, R.J., L.B. Embry, and O.E. Olson. 1959. Effect of sodium silicate on the development of urinary calculi and the excretion of various urinary constituents in sheep. J. Anim. Sci. 18:1025-1030. Cited by FASEB (1981).

Erdogdu, G., and V.N. Hasirci. 1983. Liposomes in silicosis investigations. Environ. Health Perspect. 51:325-329.

FMC Wyoming Corp. 2001. Material safety data sheet: Sodium carbonate, anhydrous. MSDS Ref. No. 497-19-8. FMC Wyoming Corporation, Philadelphia, PA. Internet address: http://www.fmc.com/msds/70729xup.htm. Last updated on April 13, 2001. Last accessed on May 30, 2001.

Fujimaki, H., M. Ozawa, T. Ashikawa, K. Kubota, and N. Watanabe. 1986. Induction of IgE antibody production to aerosolized ovalbumin in mice treated intratracheally with aluminum silicate. Int. Arch. Allergy Appl. Immunol. 79(2):206-210.

Gajatto, S. 1944. *Studi sulla farmacologia del silicio. II. Tossicità del silicato di sodio. Modalità della sua eliminazione urinaria.* [Pharmacology studies on silicon. II. Sodium silicate toxicity, modality of its urinary excretion.] Studi Sessaresi 22:279-287. Cited by FASEB (1981).

Gamsky, T.E., S.A. McCurdy, S.J. Samuels, and M.B. Schenker. 1992. Reduced FVC among California grape workers. Am. Rev. Resp. Dis. 145:257-262. Cited by IARC (1997).

Grosvenor, V.L. 1982. Aqueous potentiometric titration of silicate and hydroxide in alkali silicate solutions. Anal. Chem. 54(4):837-838. Abstract from CAPLUS 1982:115093.

Groth, D.H. [et al.] 1981. Chronic effects of inhaled amorphous silicas in animals. In: Dunnom, D.D., Ed. Health Effects of Synthetic Silica Particulates, ASTM STP 732, American Society for Testing and Materials, pp. 118-143. Cited by NOHSC (undated-a).

Hall, P.A., and W.B. Anthony. 1979 abstr. The response of female, male and castrate male cattle to diets containing solubilized sodium silicate. J. Anim. Sci. 49(1):372. Abstract #567.

HSDB (Hazardous Substances Data Bank). 2000. Sodium metasilicate. HSDB No. 753. Last updated on June 12, 2000. National Library of Medicine (NLM), Bethesda, MD.

Huang, L., C. Le, B. Dai, and X. Yang. 1990. Volumetric analysis of sodium silicate. Huaxue Shijie 31(8):358-360. Abstract from CAPLUS 1991:94264.

Ito, R., S. Saito, S. Nakai, Y. Tokunaga, T. Kubo, K. Hiraga, S. Iwahara, and K. Yuki. 1986 abstr. Safety of anticorrosives in building water-pipe metal inhibitors sodium polyphosphate and sodium meta-silicate. Fourth International Congress of Toxicology, Tokyo, Japan, July 21-25, 1986. Toxicol. Lett. (AMST) 31(Suppl.):44. Abstract.

Jahr, J. 1981. Possible health hazards from different types of amorphous silicas. In: Dunnom, D.D., Ed. Health Effects of Synthetic Silica Particulates, ASTM STP 732, American Society for Testing and Materials, pp. 118-143. Cited by NOHSC (undated-a).

Johnston, C.J., K.E. Driscoll, J.N. Finkelstein, R. Baggs, M.A. O'Reilly, J. Carter, R. Gelein, and G. Oberdörster. 2000. Pulmonary chemokine and mutagenic responses in rats after subchronic inhalation of amorphous and crystalline silica. Toxicol. Sci. 56(2):405-413.

Jorna, T.H.J.M., P.J.A. Borm, K.D. Koiter, J.J.M. Slangen, P.T. Henderson, and E.F.M. Wouters. 1994. Respiratory effects and serum type III procollagen in potato sorters exposed to diatomaceous earth. Int. Arch. Occup. Environ. Health 66:217-222. Cited by IARC (1997).

Kada, T., E. Brun, and H. Marcovich. 1960. *Comparison de l'induction de mutants prototrophs par les rayons X et UV chez Escherichia coli B/r try*$^-$ [Fr.]. Ann. Inst. Pasteur 99:547-566. Cited by CIR (2001).

Kamboj, V.P., and A.B. Kar. 1964. Antitesticular effect of metallic and rare earth salts. J. Reprod. Fertil. 7:21-28.

Kawauchi, A. 1999. Nonsolvent quantitation of anionic surfactants and other inorganic ingredients in laundry detergent products by X-ray fluorescence spectrometry. J. Surfactants Deterg. 2(1):79-83. Abstract from CAPLUS 1999:108220.

Keeler, R.F., and S.A. Lovelace. 1959. The metabolism of silicon in the rat and its relation to the formation of artificial siliceous calculi. J. Exp. Med. 109:601-614. Cited by FASEB (1981).

Kehrer, J.P. 1990. "Pulmonary toxicity of inhaled and intravenous talc" by M.A. Hollinger. (Commentary.) Toxicol. Lett. 52(2):117-119.

Kind, P.R.N., E.J. King, V. Pash, W. Roman, and E. Schmidt. 1954. Inhibition of enzymes by silicic acid. Biochem. J. 56:xlv. Cited by FASEB (1981).

King, E.J., H. Stantial, and M. Dolan. 1933. The biochemistry of silicic acid. III. The excretion of administered silica. Biochem. J. 27:1007-1014. Cited by FASEB (1981).

Kiriliv, Y.I., I.B. Ratych, and P.Z. Lagodyuk. 1989a. Changes in carbohydrate metabolism in relation to productivity and meat quality of broiler chickens given hydrated sodium silicate. Vestn. Skh. Nauki (Moskva) (No.6):163-164. Abstract from CABA 90:46309.

Kiriliv, Y.I., I.B. Ratych, and P.Z. Lagodyuk. 1989b. Toxicity of sodium silicate fed to broiler ducks. Veterinariya, Moscow (No. 7):62-63. Abstract from CABA 89:110577.

Kiriliv, Y.I. I.B. Ratych, and P.Z. Lagodyuk. 1991. Effect of silicon on metabolism and productivity in broiler ducks. Skh. Biol. (No. 4):50-52. Abstract from CABA 93:54253.

Kokorev, V.A., A.S. Fedin, and V.G. Matyushkin. 1993. Biological bases for silicon requirements of young pigs. Skh. Biol. (No. 6):84-88. Abstract from CABA 94:102078.

Kokorev, V.A., A.S. Fedin, and N.F. Buyankin. 1994. Silicon-containing supplements in diets for pigs. Zootekhniya (No. 10):19-21. Abstract from CABA 96:35726.

Kupferman, E. 1998. Postharvest applied chemicals to pears: A survey of pear packers in Washington, Oregon, and California. Tree Fruit Postharvest J. 9(1):3-24. Abstract from CABA 1998:177052.

Lagodyuk, P.Z., I.B. Ratych, and Y.I. Kiriliv. 1989. Metabolism and productivity of laying hens given diets with silicon supplements. Skh. Biol. (No. 6):22-24. Abstract from CABA 91:106117.

Lagodyuk, P.Z., I.A. Kukovskaya, I.A. Patych, and Y.I. Kiriliv. 1990. Content of group B vitamins in the tissues and performance of broiler chickens given feed mixture supplemented with sodium sulphate and metasilicate. Dokl. Akad. Skh. Nauk im. V.I. Lenina (No. 2):42-44. Abstract from CABA 91:80098.

Liao, J. 1986. Rapid determination of sodium silicate in degreasing solution. Diandu Yu Huanbao 6(5):31 ff. Abstract from CAPLUS 1986:637600.

Liebsch, M., B. Doring, T.A. Donelly, P. Logemann, L.A. Rheins, and H. Spielmann. 1995. Application of the human dermal model Skin^2 ZK 1350 to phototoxicity and skin corrosivity testing. Toxic *in Vitro* 9:557-562. Cited by CIR (2001).

L'Oreal. 2000. Elbow crease test with sodium metasilicate. Unpublished data submitted by CTFA (Cosmetic, Toiletry, and Fragrance Association), 6 pp. Cited by CIR (2001).

L'Oreal. 2000b. Semi-occluded patch test with sodium metasilicate. Unpublished data submitted by CTFA (Cosmetic, Toiletry, and Fragrance Association), 6 pp. Cited by CIR (2001).

Mallinckrodt Baker, Inc. 1998. Material safety data sheet: Sodium carbonate anhydrous. MSDS No. S3242. Mallinckrodt Baker, Inc., Phillipsburg, NJ. Internet address: http://www.meto.umd.edu/~russ/MSDS/sodium_carbonate_anhydrous.htm. Last updated June 30, 1998. Last accessed on May 30, 2001.

Marinescu, D., V. Tapu., A. Serbescu, and A. Eskenasy. 1981. Alveolar macrophage reactions. III. Stereotyped development of alveolar responses to intratracheally administered agents. Morphol. Embryol. 27(2):155-166.

McLaughlin, J.K., W.-H. Chow, and L.S. Levy. 1997. Amorphous silica: A review of health effects from inhalation exposure with particular reference to cancer. J. Toxicol. Environ. Health 50(6):553-566.

Medvedev, V., V. Medvedev, and P. Szarvas. 1970. Combined method for the investigation of the components of detergents. Kolor. Ert. 12(3-4):76-85. Abstract from CAPLUS 1970:467892.

Merkley, J.W., and E.R. Miller. 1983. The effect of sodium fluoride and sodium silicate on growth and bone strength of broilers. Poult. Sci. 62(5):798-804. Abstract from MEDLINE 83273248.

Mir-Abdalbaghy, J., and Z. Nik-Khah. 1997. The use of zeolite and sodium metasilicate in laying hens. Iran. J. Agric. Sci. 28(4):1-10. Abstract from CABA 1998:169905.

Muggenburg, B.A., J.L. Mauderly, F.F. Hahn [et al.] 1974. Effects of the ingestion of various commercial detergent products on beagle dogs and pigs. Toxicol. Appl. Pharmacol. 30:134 ff. Cited by CIR (2001).

Najda, J., J. Gminski, M. Drózdz, and A. Flak. 1991. The effect of silicon (Si) on lipid parameters in blood serum and arterial wall. Biol. Trace Elem. Res. 31(3):235-247.

Najda, J., J. Gminski, M. Drózdz, and A. Danch. 1992. Silicon metabolism: The interrelations of inorganic silicon (Si) with systemic iron (Fe), zinc (Zn), and copper (Cu) pools in the rat. Biol. Trace Elem. Res. 34(2):185-195.

Najda, J. [et al.] 1993. [title not provided] Rev. Roum. Biochim. 30(1-2):35-42. Cited by HSDB (2000).

Najda, J., J. Gminski, and M. Drózdz. 1993a. Some aspects of connective tissue metabolism in the conditions of systemic hypersilicemia. Trace Elem. Med. 10(4):163-167.
Najda, J., J. Gminski, M. Drózdz, and A. Danch. 1993b. The action of excessive, inorganic silicon (Si) on the mineral metabolism of calcium (Ca) and magnesium (Mg). Biol. Trace Elem. Res. 37(2-3):107-114.

Najda, J., J. Gminski, M. Drózdz, and F. Zych. 1993c. The influence of inorganic silicon (Si) on pituitary-thyroid axis. Biol. Trace Elem. Res. 37(2-3):101-106.

Najda, J., M. Goss, J. Gminski, L. Wglarz, K. Siemianowicz, and A. Olszowy. 1994. The antioxidant enzymes activity in the conditions of systemic hypersilicemia. Biol. Trace Elem. Res. 42(1):63-70.

Nanetti, L. 1973. *Su taluni effetti lesivi del silicato di sodio*. [Injurious effects of sodium silicate.] Zacchia 9:96-128. Cited by FASEB (1981).

National Research Council. 1984. Nutrient Requirements of Poultry, 8th revised ed. National Academy Press, Washington, DC.

National Research Council. 2001. Nutrient Requirements of Dairy Cattle, 7th revised ed. National Academy Press, Washington, DC.

Newberne, P.M., and R.B. Wilson. 1970. Renal damage associated with silicon compounds in dogs. Proc. Natl. Acad. Sci. USA 65(4):872-875.

Nixon, G.A., C.A. Tyson, and W.C. Wertz. 1975. Interspecies comparisons of skin irritancy. Toxicol. Appl. Pharmacol. 31:481-490. Cited by CIR (2001).

NOHSC (National Occupational Health and Safety Commission). [undated-a] Exposure standards. Fumed silica. Commonwealth of Australia. Internet address: http://www.nohsc.gov.au/OHSInformation/Databases/ExposureStandards/az/Fumed_silica.htm. Last accessed on August 6, 2001.

NOHSC. [undated-b] Exposure standards. Silica, amorphous fume (thermally generated). Commonwealth of Australia. Internet address: http://www.nohsc.gov.au/OHSInformation/Databases/ExposureStandards/az/Silica_Amorphous_Fume_thermally_generated_.htm. Last accessed on August 7, 2001.

NTP (National Toxicology Program). 1993. Toxicology and carcinogenesis studies of talc (CAS No. 14807-96-6) (non-asbestiform) in F344/N rats and B6C3F$_1$ mice (inhalation studies). Technical Report No. 421. NTIS No. PB94-215985. Internet address: http://ntp-server.niehs.nih.gov/htdocs/LT-studies/tr421.html. (Abstract.) Last accessed on August 2, 2001.

NTP. 2000. Executive summary of local lymph node assay of sodium metasilicate. Unpublished data submitted by CTFA (Cosmetic, Toiletry, and Fragrance Association), 3 pp. Cited by CIR (2001).

OEHHA (Office of Environmental Health Hazard Assessment). 1999. Determination of acute reference exposure levels for airborne toxicants. Acute Toxicity Summary: Sodium hydroxide. Internet address: http://www.oehha.org/air/acute_refs/pdf/1310932A.pdf. Last updated in May 1999. Last accessed on June 7, 2001.

Office of the Federal Register, General Services Administration. 1980b. Code of Federal Regulations. Title 9 [USDA]: Animal and animal products, parts 200 to end rev. U.S. Government Printing Office, Washington, DC. Cited by FASEB (1981).

Orme, S., and S. Kegley. 2000a. Calcium silicate. PAN Pesticide Database, Pesticide Action Network, San Francisco, CA. Internet address: http://data.pesticideinfo.org/4DAction/GetChemRecord/PC35366. Last accessed on August 2, 2001.

Orme, S., and S. Kegley. 2000b. Potassium silicate. PAN Pesticide Database, Pesticide Action Network, San Francisco, CA. Internet address: http://data.pesticideinfo.org/4DAction/GetChemRecord/PC34243. Last accessed on August 2, 2001.

Orme, S., and S. Kegley. 2000c. Silikil S. PAN Pesticide Database, Pesticide Action Network, San Francisco, CA. Internet address:

http://data.pesticideinfo.org/4DAction/GetProdRecord/04198700009. Last accessed on August 22, 2001.

Orme, S., and S. Kegley. 2000d. Sodium metasilicate. PAN Pesticide Database, Pesticide Action Network, San Francisco, CA. Internet address: http://data.pesticideinfo.org/4DAction/GetChemRecord/PC34396. Last accessed on August 2, 2001.

Orme, S., and S. Kegley. 2000e. Sodium silicate. PAN Pesticide Database, Pesticide Action Network, San Francisco, CA. Internet address: http://data.pesticideinfo.org/4DAction/GetChemRecord/PC34427. Last accessed on August 2, 2001.

OSHA (Occupational Safety and Health Administration). 1989. Silica, amorphous, precipitated and gel. Toxicological Review of Selected Chemical. Internet address: http://www.cdc.gov/niosh/pel88/silicagl.html. Last accessed on August 6, 2001.

OxyChem. 1997. The OxyChem Sodium Silicates Handbook. Silicates Division, Specialty Business Group, Dallas, TX, 24 pp.

OxyChem. 1998. Material safety data sheet: Caustic soda anhydrous (all grades). MSDS No. M32413. Occidental Chemical Corporation, Dallas, TX, 17 pp.

Patrick, G., A.L. Batchelor, and C. Stirling. 1996. Long-term retention of inhaled fused aluminosilicate particles in the trachea and first bifurcation of the rat. J. Aerosol Sci. 27(1):161-172.

Pratt, P.C. 1983. Lung dust content and response in guinea pigs inhaling three forms of silica. Arch. Environ. Health 38(4):197-204. Abstract from MEDLINE 83307538.

Reuzel, P.G.J., J.P. Bruijntjes, V.J. Feron, and R.A. Woutersen. 1991. Subchronic inhalation toxicity of amorphous silicas and quartz dust in rats. Food Chem. Toxicol. 29:341-354. Cited by IARC (1997).

Rhone-Poulenc, Inc. 1971b. Initial submission: Comparative toxicology study of disilicates with cover letter dated 10/23/92. NTIS Report No. OTS0571941. Cited by CIR (2001).

Rhone-Poulenc, Inc. 1976. Initial submission: Toxicity lab report T-5362 with dry chlorecso with cover letter dated 10/16/92. NTIS Report No. OTS0571654. Cited by CIR (2001).

Rosenbruch, M., H. Idel, K.-H. Friedrichs, F.-J. Reiffer, and A. Brockhaus. 1990. Comparison of inhalatory effects of quartz-glass and quartz DQ-12 in rats [Ger.]. Zbl. Hyg. 189:419-440. Cited by IARC (1997).

RTECS (Registry of Toxic Effects of Chemical Substances). 2000a. Sodium carbonate. RTECS No. VZ4050000. Last updated in December 2000. National Institute for Occupational Safety and Health (NIOSH), Cincinnati, OH.

RTECS. 2000b. Sodium hydroxide. RTECS No. WB4900000. Last updated in December 2000. National Institute for Occupational Safety and Health (NIOSH), Cincinnati, OH.

RTECS. 2000c. Sodium metasilicate. RTECS No. VV9275000. Last updated in July 2000. National Institute for Occupational Safety and Health (NIOSH), Cincinnati, OH.

Sauer, F., D.H. Laughland, and W.M. Davidson. 1959a. Silica metabolism in guinea pigs. Can. J. Biochem. Physiol. 37:183-191. Cited by FASEB (1981).

Sauer, F., D.H. Laughland, and W.M. Davidson. 1959b. The silica content of guinea pig tissues as determined by chemical and isotopic techniques. Can. J. Biochem. Physiol. 37:1173-1181. Cited by FASEB (1981).

Schaefer, W.M. 1975. Memorandum, dated September 8, of telephone conversation with G. Alpert, Food additive consultant, Washington, DC. Food and Drug Administration, Washington, DC. Cited by FASEB (1981).

Schepers, G.W.H. [et al.] 1957. The biological action of Degussa Submicron amorphous silica dust (Down Corning Silica). Am. Med. Assoc. Arch. Ind. Health 16:125-146. Cited by NOHSC (undated-a) and Waddell and Evans (1997).

Schwarz, K., and D.B. Milne. 1972. Growth-promoting effects of silicon in rats. Nature (London) 239:333-334. Cited by FASEB (1981).

Settle, W.R., and F. Sauer. 1960. Demonstration of siliceous deposits in the kidney of the guinea pig. Am. J. Vet. Res. 21:709-711.

Shakhbazyan, F.A., and A.A. Karapetyan. 1963. A study of the toxic properties of sodium metasilicate (Russian). Zh. Eksp. Klin. Med. 3:85-87. Cited by FASEB (1981).

Shen, G.Q., E.A. Ojo-Amaize, M.S. Agopian, and J.B. Peter. 1996. Silicate antibodies in women with silicone breast implants: Development of an assay for detection of humoral immunity. Clin. Diagn. Lab. Immunol. 3(2):162-166. Abstract from MEDLINE 96265438.

Sigrist, T., and K. Flury. 1985. Death by peroral ingestion of soluble glass (sodium metasilicate). Z. Recht. Smed. 94:245-250. Cited by CIR (2001).

Silicosis and Silicate Disease Committee. 1988. Diseases associated with exposure to silica and nonfibrous silicate minerals. Arch. Pathol. Lab. Med. 112(7):673-720. Abstract from MEDLINE 88251251.

Smith, G.S., A.L. Neumann, A.B. Nelson, and E.E. Ray. 1972. Effects of "soluble silica" upon growth of lambs. J. Anim. Sci. 34(5):839-845. Abstract from CABA 73:74962.

Smith, G.S., A.L. Neumann, V.H. Gledhill, and C.A. Arzola. 1973. Effects of "soluble silica" on growth, nutrient balance and reproductive performance of albino rats. J. Anim. Sci. 36:271-278. Cited by FASEB (1981) and RTECS (2000c).

Snipes, M.B., B.B. Boecker, and R.O. McClellan. 1983. Retention of monodisperse or polydisperse aluminosilicate particles inhaled by dogs, rats, and mice. Toxicol. Appl. Pharmacol. 69(3):345-362. Abstract from MEDLINE 83276559.

SRI Int. 2000a. Supply and demand by region—United States—Sodium silicates—Salient statistics. Chemical Economics Handbook (CEH). Record No. 4976. CEH Accession No. 766.4001F. Issue date: March 1998, pp. 766.4001G-J. SRI International, Menlo Park, CA. Excerpt from DIALOG® File 359.

SRI Int. 2000b. 2000 Directory of Chemical Producers—United States. SRI International, Menlo Park, CA, pp. 887, 889, and 890.

Tanaka, T., Y. Miyachi, and T. Horio. 1982. Ulcerative contact dermatitis caused by sodium silicate. Coexistence of primary irritant contact dermatitis and contact urticaria. Arch. Dermatol. 118(7):518-520. Abstract from MEDLINE 82229977.

Tekeli, S.K., and A. Zohouri. 1998. *Broylerlerde silikonum metabolizma uzerindeki etkileri* (Turkish). [The effects on metabolism of silicon in broilers.] Turk Veterinerlik ve Hayvancilik Dergisi [Turk J. Vet. Anim. Sci.] 22(1):111-117. Abstract from CABA 1999:5763.

Thomas, R.G. 1971. Retention kinetics of inhaled fused aluminosilicate particles. In: Walton, W.H., Ed. Inhaled Particles III, Vol. 1, Unwin Brothers Limited, London, pp. 193-199. Abstract from NIOSHTIC 1997:74091.

Thomas, R.L., and O.G. Raabe. 1978. Regional deposition of inhaled ^{137}Cs-labeled monodisperse and polydisperse aluminosilicate aerosols in Syrian hamsters. Am. Ind. Hyg. Assoc. J. 39(12):1009-1018. Abstract from MEDLINE 79121707.

U.S. EPA (U.S. Environmental Protection Agency). 1998. Status of pesticides in registration, reregistration, and special review (Rainbow Report). Special Review and Reregistration Division, Office of Pesticide Programs, Washington, DC. Internet address: http://www.epa.gov/oppsrrd1/Rainbow/98rainbo.pdf. Last accessed on August 21, 2001.

U.S. EPA. 2001a. Toxicological studies of particulate matter, Chapter 11. [Internet address: http:/www.epa.gov/ncea/pdfs/partmatt/vol2/0671ch11.pdf.] Air Quality Criteria for Particulate Matter (Second External Review Draft). EPA 600/P-99/002aB, bB, March 2001. National Center for Environmental Assessment. Internet address: http://www.epa.gov.ncea/partmatt.htm. Last updated on May 21, 2001. Last accessed on August 1, 2001.

U.S. EPA. 2001b. Lists of other (inert) pesticide ingredients. Office of Pesticide Programs, Washington, DC. Internet address: http://www.epa.gov/opprd001/inerts/lists.html. Last updated on June 12, 2001. Last accessed on August 2, 2001.

van Niekerk, W.C.A., W.M. Coombs, S.F. Simpson, and W.L. Retief. 2000. Identification of health hazards to toxic substances in silicon smelters. The risk of occupational exposure. Safety In Mines Research Advisory Committee (SIMRAC) Project Health 709. Internet address: http://www.simrac.co.za/report/Reports/Health/health709/Health%20709%20project%20summary.pdf.

Vennekens, M.J.A., and C.R.I. Odding. 1988. The use of thermal analysis in water treatment related problems. Thermochim. Acta 143:445-450. Abstract from CAPLUS 1989:44382.

Vitmus, V.C., M.J. Edwards, N.R. Niles, J.O. Borman, and R.D. Lowry. 1977. Pulmonary fibrosis from amorphous silica dust, a product of silica vapor. Arch. Environ. Health 32(2):62-68. Abstract from NIOSHTIC 1997:50314.

Wilson, R.H. 1981. [Paper to D.H. Groth.] ASTM Spec. Tech. Publ. 732:143 ff. Cited by Waddel and Evans (1997).

13.0 References Considered but Not Cited

Feigin, D.S. 1989. Misconceptions regarding the pathogenicity of silicas and silicates. J. Thorac. Imaging 4(1):68-80.

Lagaly, G., D. Klose, W. Tufar, A. Minhan, and A. Lovell. 1993. Silicates. In: Elvers, B., S. Hawkins, W. Russey, and G. Schulz, Eds. Ullmann's Encyclopedia of Industrial Chemistry, 5th completely revised ed. Vol. A 23. VCH, New York, NY, pp. 661-719.

Mauderly, J.L. 1993. Differences in pulmonary responses of rats, other animals, and humans to chronic inhalation of silica and other particles. Technical Report. Symposium on silica, silicosis, and cancer sponsored by the Department of Energy, Washington, DC, held in San Francisco, CA, October 28-30, 1993, 19 pp.

Richards, R.J., T.D. Tetley, and J. Hunt. 1981. The biological reactivity of calcium silicate composites: *In vivo* studies. Environ. Res. 26(2):243-257.

Schulz, R.Z., and C.R. Williams. 1942. Commercial talc. J. Ind. Hyg. Toxicol. 24(4):75-79.

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Appendix: Units and Abbreviations

°C = degrees Celsius

ACGIH = American Conference of Governmental Industrial Hygienists

bw = body weight

CIR = Cosmetic Ingredient Review

EPA = Environmental Protection Agency

F = female(s)

FASEB = Federation of American Societies for Experimental Biology

FDA = Food and Drug Administration

g = gram(s)

g/cm^3 = gram(s) per cubic centimeter

h = hour(s)

HSDB = Hazardous Substances Data Bank

i.p. = intraperitoneal(ly)

i.v. = intravenous(ly)

kg = kilogram(s)

L = liter(s)

LD_{50} = lethal dose for 50% of test animals

LD_{Lo} = lethal dose low (lowest dose, other than LD_{50}, of a substance introduced by any route, other than inhalation, over any given period of time in one or more divided portions and reported to have caused death in humans or animals)

M = male(s)

mg/kg = milligram(s) per kilogram

mg/mL = milligram(s) per milliliter

min. = minute(s)

mL/kg = milliliter(s) per kilogram

mmol = millimole(s)

mmol/kg = millimoles per kilogram

mo = month(s)

mol = mole(s)

mol. wt. = molecular weight

NIOSH = National Institute of Occupational Safety and Health

n.p. = not provided

NTP = National Toxicology Program

OSHA = Occupational Safety and Health Administration

ppm = parts per million

p.o. = peroral(ly), *per os*

RTECS = Registry of Toxic Effects of Chemical Substances

Si = silicon

soln. = solution

TC_{Lo} = toxic concentration low (lowest concentration of a substance in air to which humans or animals have been exposed for any given period of time that has produced any toxic effect in humans or produced a carcinogenic, neoplastigenic, or teratogenic effect in animals or humans)

TD_{Lo} = toxic dose low (lowest dose of a substance introduced by any route, other than inhalation, over any given period of time and reported to produce any toxic effect in humans or to produce carcinogenic, neoplastigenic, or teratogenic effects in animals or humans)

wk = week(s)

yr = year(s)