Sodium Hexafluorosilicate
[CASRN 16893-85-9]

and

Fluorosilicic Acid
[CASRN 16961-83-4]

Review of Toxicological Literature

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Executive Summary

Nomination

Sodium hexafluorosilicate and fluorosilicic acid were nominated for toxicological testing based on their widespread use in water fluoridation and concerns that if they are not completely dissociated to silica and fluoride in water that persons drinking fluoridated water may be exposed to compounds that have not been thoroughly tested for toxicity.

Nontoxicological Data

Analysis and Physical-Chemical Properties

Analytical methods for sodium hexafluorosilicate include the lead chlorofluoride method (for total fluorine) and an ion-specific electrode procedure. The percentage of fluorosilicic acid content for water supply service application can be determined by the specific-gravity method and the hydrogen titration method. The American Water Works Association (AWWA) has specified that fluorosilicic acid contain 20 to 30% active ingredient, a maximum of 1% hydrofluoric acid, a maximum of 200 mg/kg heavy metals (as lead), and no amounts of soluble mineral or organic substance capable of causing health effects. Recently, single-column ion chromatography with conductometric detection and sodium hydroxide-methanol-water eluent was used for the simultaneous determination of fluorosilicic acid, Ca^{2+}, Mg^{2+}, Al^{3+}, Cl^-, and NO_3^- and successfully applied to the analysis of mineral water and composite tablets.

When heated to decomposition, sodium hexafluorosilicate releases toxic fumes of hydrogen fluoride and sodium oxide, while contact with metals releases hydrogen gas. In water, the compound readily dissociates to sodium ions and hexafluorosilicate ions and then to hydrogen gas, fluoride ions, and hydrated silica. At the pH of drinking water (6.5-8.5) and at the concentration usually used for fluoridation (1 mg fluoride/L), the degree of hydrolysis is essentially 100%. Fluorosilicic acid is a moderately strong acid that can corrode glass and stoneware. Like its salt, its degree of hydrolysis is essentially 100% in drinking water, and when reacted with steam or water or when heated to decomposition or highly acidified, toxic and corrosive fumes of fluorides (e.g., hydrogen fluoride and silicon tetrafluoride) are released. It also reacts with metals, producing hydrogen gas.

Commercial Availability, Production, and Uses

Sodium hexafluorosilicate is usually commercially available in technical and C.P. grades; it was formally available in insecticides of up to ~98% purity such as granular baits. A typical product contains 59.34% fluorine and a maximum of 0.50% each of water moisture, water-insoluble matter, and heavy metals (as lead). Fluorosilicic acid is commercially available as aqueous solutions (up to 70%) in technical and C.P. grades. A typical product contains a maximum of 23% of the acid, a minimum of 18.22% fluorine, a maximum of 0.02% heavy metals (as lead), and <1.00% hydrofluoric acid. Many U.S. producers and suppliers are available for both compounds (over 20 for each). Bulk producers/suppliers include Lucier Chemical Industries and Creanova Inc.

Sodium hexafluorosilicate is produced by treating fluorosilicic acid with sodium hydroxide, sodium carbonate, or sodium chloride; alkalinity is adjusted to avoid the release of the fluoride. Fluorosilicic acid is mainly produced as a byproduct of the manufacture of phosphate fertilizers

where phosphate rock is treated with sulfuric acid. It can also be made by the reaction of sulfuric acid on barium hexafluorosilicate, apatite, or fluorite (fluorspar).

The latest available figure for U.S. production of sodium hexafluorosilicate is 19,600 metric tons (43.2 million pounds) in 1984. In that same year, 3000 metric tons (6.61 million pounds) was imported. In 1995, ten phosphate rock processing plants produced 55,900 metric tons (123 million pounds) of fluorosilicic acid as a byproduct. In 1999, ten plants again reported on the production of fluorosilicic acid as a byproduct from phosphate rock processing; 69,200 metric tons (153 million pounds) was produced. This was an almost 3% increase in output from the previous year.

The major use of sodium hexafluorosilicate and fluorosilicic acid is as fluoridation agents for drinking water. Sodium hexafluorosilicate has also been used for caries control as part of a silicophosphate cement, an acidic gel in combination with monocalcium phosphate monohydrate, and a two-solution fluoride mouth rinse. Both chemicals are also used as a chemical intermediate (raw material) for aluminum trifluoride, cryolite (Na_3AlF_6), silicon tetrafluoride, and other fluorosilicates and have found applications in commercial laundry.

Other applications for sodium hexafluorosilicate include its use in enamels/enamel frits for china and porcelain, in opalescent glass, metallurgy (aluminum and beryllium), glue, ore flotation, leather and wood preservatives, and in insecticides and rodenticides. It has been used in the manufacture of pure silicon, as a gelling agent in the production of molded latex foam, and as a fluorinating agent in organic synthesis to convert organodichlorophosphorus compounds to the corresponding organodifluorophosphorus compound. In veterinary practice, external application of sodium hexafluorosilicate combats lice and mosquitoes on cattle, sheep, swine, and poultry, and oral administration combats roundworms and possibly whipworms in swine and prevents dental caries in rats. Apparently, all pesticidal products had their registrations cancelled or they were discontinued by the early 1990s.

Fluorosilicic acid is used in the tanning of animal hides and skins, in ceramics and glass, in technical paints, in oil well acidizing, in the manufacture of hydrogen fluoride, for the sterilization of equipment (e.g., in brewing and bottling establishments and for copper and brass vehicles), and in electroplating. It is also employed as an impregnating ingredient to preserve wood and harden masonry and for the removal of mold as well as rust and stain in textiles.

Environmental Occurrence and Persistence

Fluorosilicic acid (30-35%) can readily be recovered in the hydrogen fluoride process from the silicon tetrafluoride-containing plant vent gases, as well as from wet-process phosphoric acid plants. In the manufacture of phosphate fertilizer in Central Florida, fluorides and radionuclides (radium and uranium) are released as toxic pollutants. During the acidulation process, radon gas can be released and carried into the fluorosilicic acid, while polonium can be captured during the scrubbing process and combined with fluoride.

For drinking water fluoridation, the maximum use level (MUL) for sodium hexafluorosilicate is 2 mg/L; for fluorosilicic acid, the level is 6 mg/L of a 25% fluorosilicic acid solution. Both values correspond to a fluoride concentration of 1.2 mg/L, which is below the U.S.

Environmental Protection Agency's (EPA's) Maximum Contaminant Level (MCL) of 4.0 mg/L and the Secondary Maximum Contaminant Level (SMCL) of 2.0 mg/L. The National Sanitation Foundation (NSF) has established a Maximum Drinking Water Level of 16 mg/L for silicates and a Maximum Allowable Level (MAL) of 1.2 mg fluoride/L for its certified products used in drinking water.

Human Exposure

Potential exposure to sodium hexafluorosilicate and fluorosilicic acid is via inhalation and eye and skin contact. Another route for the former compound is ingestion. Although current data indicate that silicofluorides are used in over 9200 U.S. water treatment systems, serving over 120 million individuals, exposure via drinking water is expected to be minimal since both compounds hydrolyze almost completely under these conditions.

In the workplace, exposure to both chemicals is possible during their manufacture, transportation, or use in water treatment. In the National Institute for Occupational Safety and Health (NIOSH) 1983 National Occupation Exposure Survey (NOES), 79,556 employees were potentially exposed to sodium hexafluorosilicate, while 10,867 were potentially exposed to fluorosilicic acid.

Regulations

Workers treating agricultural products with insecticides such as weevil baits and persons using roach baits and other insecticidal products containing sodium hexafluorosilicate in the home may have been exposed by inhalation or the skin, and by hand-to-mouth contact. In the United States, all pesticide uses of sodium hexafluorosilicate have been cancelled. (It is noted that its use as an insecticide is currently listed in the *2001 Farm Chemicals Handbook*, which does not note discontinuation of the product Safsan.) Both sodium hexafluorosilicate and fluorosilicic acid are listed in Section 8(b) of the Toxic Substances Control Act (TSCA; chemical inventory section). Both are also exempt from reporting under the Inventory Update Rule (i.e., Partial Updating of the TSCA Inventory Data Base Production and Site Reports [40CFR, Section 710(b)]). The Occupational Safety and Health Administration (OSHA) and American Conference of Governmental Industrial Hygienists (ACGIH) have established an eight-hour time-weighted average (TWA) of 2.5 mg/m^3 fluorides, as fluorine, for work place exposure. NIOSH has also recommended an air exposure level to inorganic fluorides of 2.5 mg F/m^3 but as a ten-hour TWA.

Toxicological Data

Human Data

Chronic exposure to sodium hexafluorosilicate dust at levels above the eight-hour TWA can result in severe calcification of the ribs, pelvis, and spinal column ligaments; effects on the enzyme system; pulmonary fibrosis; stiffness; irritation of the eyes, skin, and mucous membranes; weight loss; anorexia; anemia; cachexia; wasting; and dental effects. Long-term or repeated exposure to the skin can result in skin rash. A probable oral lethal dose of 50-500 mg/kg, classified as very toxic, has been reported for a 150-pound (70-kg) person receiving between 1 teaspoon and 1 ounce of sodium hexafluorosilicate. Cases of sodium hexafluorosilicate ingestion reported symptoms such as acute respiratory failure, ventricular

tachycardia and fibrillation, hypocalcemia, facial numbness, diarrhea, tachycardia, enlarged liver, and cramps of the palms, feet, and legs.

The symptoms of inhalation of fluorosilicic acid include burning of the eyes and numbness around the lips. Symptoms do not necessarily occur immediately; they can appear 24 hours after exposure. A spill incident of the chemical on an interstate in Florida, covering an area 600 feet long and 60 feet wide, resulted in the visit of more than 50 people to hospitals. Individuals complained of skin and respiratory irritation, including burning in the throat, and headaches. A man riding in a truck with his arm out the window experienced burning on his forearm. The effects of long-term exposure to fluorosilicic acid are changes in bone, corrosivity of the mucous membranes (e.g., ulceration of the nose, throat, and bronchial tubes), coughing, shock, pulmonary edema, fluorosis, coma, and even death. In workers engaged for approximately 30 years in the production of phosphate fertilizers, nine out of the 50 observed workers had increased bone densities. When swallowed, severe irritation of the lungs, nose, and throat can occur, as well as severe damage to the throat and stomach. A probable oral lethal dose of 50-5000 mg/kg, classified as very toxic, has been reported for doses between 1 teaspoon and 1 ounce for a 150-pound (70-kg) person; a probable oral lethal dose of 5-50 mg/kg, classified as extremely toxic, has been reported for doses between 7 drops and 1 teaspoon for the same individual.

Chemical Disposition, Metabolism, and Toxicokinetics

In a female chemical plant worker who ingested sodium hexafluorosilicate in a suicide attempt, fluoride levels in serum and fresh urine were 5.130 and 235.60 mg/dm^3, respectively, on day 2 of hospitalization; treatment with calcium compounds (calcium carbonate and calcium lactogluconate) immediately returned levels to normal. In 50 workers engaged for approximately 30 years in the production of phosphate fertilizers and exposed to gaseous fluoride (hydrogen fluoride, silicon tetrafluoride, and fluorosilicic acid), urine fluoride excretion ranged from 1.0 to 9.6 mg F^-/L (controls: 0.3 to 1.2).

In rats fed a diet containing 0.16% sodium hexafluorosilicate supplemented in a corn-soybean oilmeal-casein ration *ad libitum* for 22-23 days, the average amounts of fluorine were 94.4 mg in feces and 91.9 mg in urine. The mean amount of fluorine absorbed was 65.1% and that retained was 31.0%.

Fluorine concentrations in stomach/rumen contents, urine, and blood serum have been determined in domestic animals experiencing sodium hexafluorosilicate poisoning. Significantly elevated levels were initially found, which decreased with time.

Acute Toxicity

In mice, an oral LD_{50} of 70 mg/kg (0.37 mmol/kg) for sodium hexafluorosilicate was reported. In rats, oral LD_{50} values of 125 and 430 mg/kg (0.665 and 2.29 mmol/kg, respectively) were calculated, while a TD_{Lo} of 248 mg/kg (1.32 mmol/kg) was calculated. A subcutaneous LD_{Lo} of 70 mg/kg (0.37 mmol/kg) was also reported in the animals. In rabbits, the oral LD_{50} value was 125 mg/kg (0.665 mmol/kg). In guinea pigs, an LC_{Lo} value of 33 mg/kg (0.18 mmol/kg) for sodium hexafluorosilicate was observed; additionally, an oral LD_{50} of 200 mg/kg (1.39 mmol/kg) was reported for fluorosilicic acid.

Sodium Hexafluorosilicate: Mice orally given sodium hexafluorosilicate (70 mg/kg; 0.37 mmol/kg) exhibited toxic effects in the peripheral nerves, sensation, and in behavior. In rats, an oral dose (248 mg/kg; 1.32 mmol/kg) administered intermittently for one month produced toxic effects in the kidney, ureter, and/or bladder, as well as musculoskeletal and biochemical effects. Using guinea pigs, inhalation experiments (13-55 mg/m^3 [1.7-7.2 ppm] sodium hexafluorosilicate in air for ≥6 hours) resulted in pulmonary irritation; the lowest concentration that caused death was 33 mg/m^3 (4.3 ppm).

When sodium hexafluorosilicate (500 mg; 2.66 mmol) was applied to the skin of adult rabbits, mild irritation occurred. When applied to the eyes (100 mg; 0.532 mmol), severe irritation was observed; following a four-second rinse, the effect was still severe.

Sodium hexafluorosilicate poisoning has been reported in domestic animals (cattle, sheep, a horse, and a pigeon). Animals exhibited drowsiness, constipation, loss of appetite, paresis of the rumen, severe abdominal pain, and diarrhea. Sheep also exhibited grinding of the teeth (an indication of pain) and frothing at the mouth in most cases of lethal poisoning, while the horse also had bradycardia. In a study in which sheep were orally administered technical sodium hexafluorosilicate (25, 50, 200, 1500, and 2000 mg/kg; 0.13, 0.27, 1.06, 7.976, and 10.63 mmol/kg) via stomach tube, the animals exhibited similar symptoms. Animals died 6 days after administration of 200 mg/kg and 2.5 hours after administration of 2000 mg/kg. When a dairy herd of 600 animals was acutely poisoned from railcar contamination of feed, 95% of the animals had decreased neuromuscular transmission. The poisoning resembled calcium depletion.

Fluorosilicic Acid: In rats orally given fluorosilicic acid (430 mg/kg; 2.98 mmol/kg), somnolence and/or general depressed activity was observed. Other rat studies with fluorosilicic acid (single oral doses of 215, 464, 1000, and 2100 mg/kg [1.49, 3.22, 6.939, and 14.57 mmol/kg]) led to its classification as "moderately toxic." Percutaneous administration of the compound (amounts not provided) in rats, guinea pigs, and pigs resulted in continuously spreading necrosis in the deeper regions of injured skin. Hypocellular necrosis, consisting of sharp leukocyte demarcations, and edema up to the subcutis were also observed. In rabbits, it was corrosive to the skin (0.5 mL [4 mol] for 1, 24, or 72 hours) and eyes (0.1 mL [0.8 mol] instilled into left eye).

Synergistic/Antagonistic Effects

Fluoride, administered in the form of sodium hexafluorosilicate, had a strong affinity for calcium and magnesium. When orally given to sheep via a stomach tube at doses of 25, 50, 200, 1500, and 2000 mg/kg, increased changes in serum calcium and magnesium levels were observed at the two highest doses within 30 minutes after dose administration. At 200 mg/kg, recovery of both levels occurred after five days. With the 1500 mg/kg dose group, changes in phosphorus and sugar levels in whole blood were also significantly increased.

Genotoxicity

Sodium hexafluorosilicate was negative in the Salmonella/microsome test (concentrations up to 3600 g/plate, –S9), the micronucleus test on mouse bone marrow (37.2 mg/kg; 0.198 mmol/kg), and in the *Bacillus subtilis* rec-assay system (0.001-10 M; 188 g/mL-1.9 g/mL).

The compound (0.25 mM; 47 g/mL) did not induce sex-linked recessive lethal mutations in *Drosophila*.

Other Data

Within one week after beginning work in a foam rubber plant, a 23-year-old man exhibited skin lesions consisting of "diffuse, poorly delineated, erythematous plaques with lichenoid papules and large pustules" on his arms, wrists, thighs, and trunk. Although scratch and patch tests with sodium hexafluorosilicate (2% aqueous) were negative, tests in rabbits (topical application of a 1, 5, 10, and 25% solution) showed the compound to be a pustulogen.

No short-term or subchronic exposure, chronic exposure, cytotoxicity, reproductive toxicity, teratology, carcinogenicity, or initiation/promotion studies were available.

Structure-Activity Relationships

For the same fluorine content, sodium fluoride, sodium hexafluorosilicate, cryolite (Na_3AlF_6), and barium sulfate were observed to have the same extent of chronic fluorine intoxication in rats. Ammonium fluoride, potassium fluoride, barium fluorosilicate, potassium fluorosilicate, and sodium fluorosilicate exhibited the same acute toxicity as sodium fluoride in the animals.

In a comparative study of absorption and excretion of fluorine in rats fed sodium fluoride, calcium fluoride, and sodium hexafluorosilicate, the percent fluorine retained was the same for the two sodium compounds. Several experiments on growing rats orally given 5, 10, 15, 25, and 50 ppm fluorine as sodium fluoride or sodium hexafluorosilicate for 90-100 days found no differences in the quantity of fluorine deposited and the contents of ash, calcium, and phosphorus in the incisor teeth, molar teeth, mandibles, and femurs. Furthermore, there were no differences in the percent of ingested fluorine retained in the body, and a combination of sodium silicate (15 ppm silicon) with sodium fluoride (25 ppm fluorine) did not affect the amount of fluorine deposited. The growth rate was normal in all rats. A separate study using litters of female weanling Osborne-Mendel rats that were given 50 ppm fluorine as sodium fluoride or ammonium fluorosilicate in drinking water for 99 days observed similar results.

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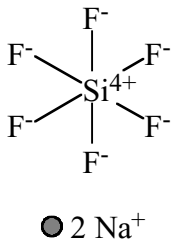
1.0 Basis for Nomination

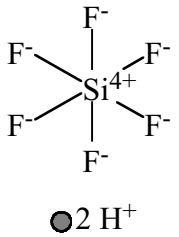
Sodium hexafluorosilicate and fluorosilicic acid were nominated for toxicological testing based on their widespread use in water fluoridation and concerns that if they are not completely dissociated to silica and fluoride in water that persons drinking fluoridated water may be exposed to compounds that have not been thoroughly tested for toxicity.

2.0 Introduction

Sodium Hexafluorosilicate
[16893-85-9]



Fluorosilicic Acid
[16961-83-4]



2.1 Chemical Identification and Analysis

2.1.1 Sodium Hexafluorosilicate

Sodium hexafluorosilicate ([Na_2SiF_6]; mol. wt. = 188.06) is also called:

Destruxol applex
Disodium hexafluorosilicate[a,b,d]
Disodium silicofluoride
Ens-zem weevil bait
ENT 1,501
Fluorosilicate de sodium
Fluosilicate de sodium
Ortho earwig bait
Ortho weevil bait
Prodan
Prodan (pesticide)
PSC Co-Op weevil bait
Safsan

Salufer
Silicate (2^-), hexafluoro-, disodium (8CI, 9CI)
Silicon sodium fluoride[a,b,c]
Sodium fluoride silicate
Sodium fluorosilicate[a,b]
Sodium fluosilicate[a,b,e]
Sodium hexafluosilicate
Sodium silicofluoride[a,b]
Sodium silicon fluoride[a,b]
Super prodan
UN2674 (DOT)

May be written as the following: [a]without any appended formula; [b]with Na_2SiF_6 appended in parentheses, [c]with $SiNa_2F_6$ appended in parentheses, [d]with (2^-) appended in parentheses, or [e]with ACN (accepted common name) appended in parentheses.

Sources: HSDB (2000b); Registry (2000); RTECS (2000); SANSS (2000)

Other CAS Registry Numbers (CASRNs) that have been used for the compound are 1310-02-7, 1344-04-3, 12656-12-1, 39413-34-8, 221174-64-7 (Registry, 2000). CASRNs for the hydrates are 10213-79-3 (pentahydrate), 15630-83-8 (hexahydrate), 27121-04-6 (octahydrate), and 13517-24-3 (nonahydrate). AOAC (Association of Official Analytical Chemists) Method 945.05 has been used to detect fluorine as sodium hexafluorosilicate in pesticide formulations (HSDB, 2000b). The chemical composition of sodium hexafluorosilicate used in water supply service applications can be determined by test procedures specified in AWWA (American Water Works Association) B702-99 (AWWA, 1999).

2.1.2 Fluorosilicic Acid

Fluorosilicic acid[e] ([H_2SiF_6]; mol. wt. = 144.11) is also called:

Dihydrogen hexafluorosilicate[a,c]
FKS
Fluosilicic acid[a,d] (6CI)
Hexafluorosilicic acid
Hexafluorosilicate (2^-), dihydrogen
Hexafluosilicic acid
Hydrofluorosilicic acid[a,e]
Hydrofluosilicic acid[a,d]
Hydrogen hexafluorosilicate[a,b]
Hydrogen hexafluorosilicic
Hydrosilicofluoric acid[a,e]
Sand acid[a,e]
Silicate (2^-), hexafluoro-, dihydrogen (8CI, 9CI)
Silicic acid (H_2SiF_6)
Silicofluoric acid[a,e]
Silicofluoride
Silicon hexafluoride dihydride
UN1778 (DOT)

May be written as the following: [a]without any appended formula; [b]with H_2SiF_6 appended in parentheses, [c]with (2^-) appended in parentheses, [d]with ACN (accepted common name) appended in parentheses, or [e]with DOT (Department of Transportation) appended in parentheses.

Sources: HSDB (2000a); Registry (2000); RTECS (2000); SANSS (2000)

Other CASRNs that have been used for the compound are 1309-45-1 and 12672-67-2 (Registry, 2000). Total fluorine in fluorosilicates can be detected by the lead chlorofluoride method. In air, an ion-specific electrode procedure with a range of 0.05 to 475 mg fluoride/m^3 has been used (HSDB, 2000a). The percentage of fluorosilicic acid content for water supply service application can be determined by the specific-gravity method and the hydrogen titration method (specified in AWWA B703-94); the latter is the preferred method, since the former procedure provides a "very rough estimation." AWWA has specified that fluorosilicic acid must contain 20 to 30% active ingredient, a maximum of 1% hydrofluoric acid, a maximum of 200 mg/kg heavy metals (as lead), and no amounts of soluble mineral or organic substance that can cause health effects (AWWA, 2000; HSDB, 2000a). Analyses of tap water treated with silicofluorides (e.g., samples from Seattle, WA, San Francisco, CA, and Ft. Collins, CO) have revealed insignificant lead and arsenic levels (CSDS, 2001). Recently, single-column ion chromatography with conductometric detection and sodium hydroxide-methanol-water eluent was used for the simultaneous determination of fluorosilicic acid, Ca^{2+}, Mg^{2+}, Al^{3+}, Cl^-, and NO_3^-; the detection limit for the anion of the acid was 1.25 x 10^6 M. It was successfully applied to the analysis of mineral water and composite tablets (Xu et al., 2001).

2.2 Physical-Chemical Properties

Property	Information	Reference(s)
Sodium hexafluorosilicate		
Physical State	white, granular, crystalline, or free-flowing powder; white hexagonal crystals	HSDB (2000b)
Odor	odorless	
Boiling Point (^oC)	decomposes at 500	LCI, Ltd. (2000b)
Melting Point (^oC)	melts at red heat with decomposition	HSDB (2000b)
Specific Gravity (g/cm^3)	2.7	
pH Value	neutral (solution in cold water)	
	3.0-4.5 (1% solution)	LCI, Ltd. (2000b)
Water Solubility	soluble in cold water (150 parts) and boiling water (40 parts)	HSDB (2000b)
mg/L or g/m^3 at 17.5 ¡C	6,500	Worthing (1987; cited by Shiu et al., 1990)
mg/L or g/m^3 at 20 ¡C	72,000	Dean (1985; cited by Shiu et al., 1990)
Insoluble in	alcohol (e.g., ethanol)	HSDB (2000b)
Fluorosilicic acid		
Physical State	colorless liquid; white crystals	HSDB (2000a)
Odor	sour, pungent	
Density @ 25 ¡C	1.4634 (60.97% solution)	
Boiling Point (^oC)	decomposes (60.97% solution)	
	105 (25% solution)	LCI, Ltd. (2000a)
Freezing Point (^oC)	-15.5 (25% solution)	
Specific Gravity (g/cm^3)	1.234 (25% solution) @ 16 ¡C	LCI, Ltd. (2000a)
pH Value	1.2 (1% solution)	LCI, Ltd. (undated-a)
Soluble in	alkali; cold and hot water	HSDB (2000a)

In alkaline medium, fluorosilicate solutions are readily hydrolyzed; in acidic conditions, silicon tetrafluoride and hydrogen fluoride are released. Thermal decomposition of fluorosilicates releases gaseous silicon tetrafluoride and forms solid fluoride. When heated to decomposition,

sodium hexafluorosilicate releases toxic fumes of hydrogen fluoride and sodium oxide; contact with metals can release hydrogen gas (HSDB, 2000b; NICNAS, 2001).

Fluorosilicic acid is a moderately strong acid that can corrode glass and stoneware. At about 19 ˚C, a 60-70% solution solidifies, forming crystalline dihydrate. A 13.3% solution may be distilled without decomposition. Fluorosilicic acid is deliquescent that is, it absorbs moisture from the air and becomes liquid (HSDB, 2000a). It produces toxic and corrosive fumes of fluorides (e.g., hydrogen fluoride and silicon tetrafluoride) when reacted with water or steam or when the compound is heated to decomposition or highly acidified with sulfuric acid (HSDB, 2000a; NICNAS, 2001). It also reacts with many metals, producing hydrogen gas (HSDB, 2000a; LCI, Ltd., undated-a).

Aqueous Chemistry

In water, the compound readily dissociates to sodium ions and hexafluorosilicate ions. At the pH of drinking water (6.5-8.5) and at the concentration usually used for fluoridation (1 mg fluoride/L), essentially 100% of sodium hexafluorosilicate dissociates to fluoride ions and hydrated silica (Crosby, 1969; Urbansky and Schock, 2000). In a quasi-constant composition titration study using high concentrations of hydrogen ion (H^+) and calcium ion (Ca^{2+}), the promoting effect of Ca^{2+} on the hydrolysis of sodium hexafluorosilicate was observed to be stronger than the inhibiting effect of H^+, thereby causing faster hydrolysis at low pH (Eidelman and Chow, 1991).

$$Na_2SiF_6(aq) + 4\ H_2O \quad 4\ HF(aq) + 2\ NaF(aq) + Si(OH)_4(aq)$$

In water, fluorosilicic acid readily hydrolyzes to hydrofluoric acid and various forms of amorphous and hydrated silica. At the concentration usually used for water fluoridation, 99% hydrolysis occurs and the pH drops to 4.2. As pH increases, hydrolysis increases. At the pH of drinking water, the degree of hydrolysis is "essentially 100%" (Crosby, 1969; Urbansky and Schock, 2000).

$$H_2SiF_6(aq) + 4\ H_2O \quad 6\ HF(aq) + Si(OH)_4(aq)$$

2.3 Commercial Availability

Sodium hexafluorosilicate is available as granular bait and in technical and C.P. grades. It is usually commercially available as ~98% pure (HSDB, 2000b). A typical product contains 59.34% fluorine and a maximum of 0.50% each of moisture as water, water-insoluble matter, and heavy metals (as lead) (LCI, Ltd., 2000b). Chemical producers include Chemtech Products Inc. (Alorton, IL), IMC-Agrico Company (Faustina, LA), and Kaiser Aluminum and Chemical Corporation (Mulberry, FL) (SRI Int., 2000). Lucier Chemical Industries produces and ships sodium hexafluorosilicate in 25-kg bags and 50-pound bags (LCI, Ltd., 2000b). It is supplied by GFS Chemicals Inc. (Powell, OH) and Spectrum Chemical Manufacturing Corporation (Gardena, CA) (Chemcyclopedia Online, 2001). Chem Sources (2001) has identified 24 suppliers of the compound; bulk suppliers include Creanova Inc. (Somerset, NJ) and Seal Chemical Industries (Newport Beach, CA). RIMI Chemicals Company Ltd. formulates the chemical as the product Safsan (Farm Chem. Handbook, 2001).

Fluorosilicic acid is commercially available as aqueous solutions of 5, 10, 15, 20, 25, 30, 34, and 60-70% in technical and C.P. grades (HSDB, 2000a). A typical product contains a minimum of 23% of the acid, a minimum of 18.22% fluorine, a maximum of 0.02% heavy metals (as lead), and <1.00% hydrofluoric acid (LCI, Ltd., 2000a). It is produced by Cargill Fertilizer, Inc. (Riverview, FL), Chemtech Products Inc. (Alorton, IL), Farmland Hydro, L.P. (Bartow, FL), IMC-Agrico Company (Faustina, LA; Nichols, FL; South Pierce, FL; Uncle Sam, LA), PCS Phosphate Company, Inc. (Aurora, NC), Royster-Clark Inc. (Americus, GA; Florence, AL; Hartsville, SC), and U.S. Agri-Chemicals Corporation (Fort Meade, FL) (SRI Int., 2000). Cargill Fertilizer, Inc. produces fluorosilicic acid as a primary nutrient (Farm Chem. Handbook, 2001). Another producer, Lucier Chemical Industries (Jacksonville Beach, FL) ships its product in tank cars, tank trucks, and drums (LCI, Ltd., 2000a). Chem Sources (2001) has identified 16 suppliers of fluorosilicic acid; bulk suppliers include Creanova Inc. (Somerset, NJ), Fluka (Milwaukee, WI), and Spectrum Laboratory Products, Inc. (Gardena, CA). Under the name hydrofluorosilicic acid [56977-47-0], it is supplied by Alfa Aesar/Johnson Matthey (Ward Hill, MA) and Solvay Fluorides Inc. (St. Louis, MO) (Chemcyclopedia Online, 2001).

3.0 Production Processes

Sodium hexafluorosilicate is produced by the neutralization of fluorosilicic acid with sodium hydroxide, sodium carbonate, or sodium chloride under vigorous agitation. The amount of the alkali is controlled so as not to result in the fluoride (HSDB, 2000b).

Fluorosilicic acid is mainly produced as a byproduct of the manufacture of phosphate fertilizers where phosphate rock, containing fluorides and silica or silicates, is treated with sulfuric acid. The gases released, hydrogen fluoride and silicon tetrafluoride, are sprayed with water in condensing towers or drawn into a series of scrubbers and dissolved in water, forming an aqueous solution of fluorosilicic acid (CSDS, 2001; Farm Chem. Handbook, 2001; NICNAS, 2001). This is the crude form of fluorosilicic acid; the purified form is obtained by distillation of the crude acid or by reacting pure silica with hydrofluoric acid. The compound can also be made by the reaction of sulfuric acid on barium hexafluorosilicate (HSDB, 2000a). Furthermore, fluorosilicic acid is manufactured by the reaction of apatite and/or fluorite (fluorspar) with sulfuric acid (LCI, Ltd., 2000a). Its production from phosphoric acid producers supplements fluorspar as a domestic source of fluorine (Miller, 1995, 1999).

4.0 Production and Import Volumes

The latest available figure for U.S. production of sodium hexafluorosilicate is 19,600 metric tons (43.2 million pounds) in 1984. In that same year, 3000 metric tons (6.61 million pounds) was imported (HSDB, 2000b).

In 1995, ten phosphate rock processing plants produced 55,900 metric tons (123 million pounds) of fluorosilicic acid as a byproduct. Of this amount, 45% was used in water fluoridation, directly or as the sodium salt, while 34% went toward the production of aluminum trifluoride and 20% went toward other uses (Miller, 1995). In 1999, ten plants again reported on the production of fluorosilicic acid as a byproduct from phosphate rock processing; 69,200 metric tons (153 million pounds) was produced, and 69,100 metric tons (152 million pounds) was sold or used. This was an almost 3% increase in output from the previous year. The amount used for water fluoridation was 34, 900 metric tons (51%), while 19,000 metric tons (27%) was used for aluminum trifluoride production, and 15,300 metric tons (22%) was used for other uses such as

sodium hexafluorosilicate production (Miller, 1999). The latest figures are definitely an increase compared to the 1975 and 1976 U.S. production of the acid at 30,000 metric tons (66 million pounds) from phosphoric acid manufacturing. No import data were found (HSDB, 2000a).

5.0 Uses

The major use of sodium hexafluorosilicate and fluorosilicic acid is as fluoridation agents for drinking water (HSDB, 2000a,b; Urbansky and Schock, 2000). They have been added to water since the mid-1940s to prevent tooth decay (Chem. Mark. Rep., 2000). Sodium hexafluorosilicate has also been used for caries control as part of a silicophosphate cement and as an acidic gel in combination with monocalcium phosphate monohydrate (Jinks et al., 1982 abstr.; Takagi et al., 1992). As part of a two-solution fluoride mouth rinse, it resulted in enhanced remineralization of human enamel lesions and root lesions (Takagi et al., 1997; Chow et al., 2000).

Both chemicals are also used as a chemical intermediate (raw material) for aluminum trifluoride, cryolite (Na_3AlF_6), silicon tetrafluoride, and other fluorosilicates (HSDB, 2000a,b). In addition, they have found applications in commercial laundry; sodium hexafluorosilicate acts as a laundry souring agent and the acid acts as a neutralizer for alkalis (LCI, Ltd., 2000a,b).

Other applications for sodium hexafluorosilicate include its use in enamels/enamel frits for china and porcelain, in opalescent glass, metallurgy (aluminum and beryllium), glue, ore flotation, leather and wood preservatives, and in insecticides and rodenticides (e.g., moth repellent and for the control of Noctuid larvae [i.e., cotton leafworms, mole crickets, grasshoppers, locusts, crane flies, earwigs, and sowbugs]) (HSDB, 2000b; LCI, Ltd. 2000b; Farm Chem. Handbook, 2001). It has been used in the manufacture of pure silicon and as a gelling agent in the Dunlop process (production of molded latex foam) (HSDB, 2000b). Recently, it has been used in organic synthesis as a fluorinating agent to convert organodichlorophosphorus compounds to the corresponding organodifluorophosphorus compound in low to moderate yields (up to 75%) (Farooq, 1998). In veterinary practice, externally applied sodium hexafluorosilicate has been used to combat lice and mosquitoes on cattle, sheep, swine, and poultry. It has been given orally to combat roundworms and possibly whipworms in swine and added to feed (50 ppm) to prevent dental caries in rats (HSDB, 2000b). Sodium hexafluorosilicate is listed as an oral care agent on the International Nomenclature of Cosmetic Ingredients inventory established under a European Commission Directive (96/335/EC) (INCI, 1998).

Fluorosilicic acid is used in the tanning of animal hides and skins, in ceramics and glass (glass etching), in technical paints, in oil well acidizing, and in the manufacture of hydrogen fluoride. It is also employed as an impregnating ingredient to preserve wood and harden masonry and for the removal of mold as well as rust and stain in textiles. It has been used for the sterilization of equipment (e.g., in brewing and bottling establishments and for copper and brass vehicles) as well as in electroplating (HSDB, 2000a; LCI, Ltd., 2000a). A typical electrolyte contains 95 g/L free fluorosilicic acid (King and Ramachandran, 1995). In the electrolytic refining of lead, the electrolyte contains 33% of the acid (Howe, 1981).

6.0 Environmental Occurrence and Persistence

In the hydrogen fluoride process, fluorosilicic acid (30-35%) can readily be recovered from the silicon tetrafluoride-containing plant vent gases, which are absorbed in water. It can also be

recovered from wet-process phosphoric acid plants and then processed to form hydrogen fluoride (Smith, 1994; Woytek, 1980). In this process, 45-60% gaseous fluorine compounds are recoverable. The fluorosilicic acid is usually disposed of by converting it into inert and harmless waste products; usually, neutralization with limestone or milk of lime is done to precipitate the acid as a mixture of calcium fluoride and silica. However, small amounts of poisonous fluorine compounds remain in the effluent (Denzinger et al., 1979).

The manufacture of phosphate fertilizer in Central Florida releases not only fluorides as a toxic pollutant but also radionuclides. Radium wastes come from the filtration systems. Uranium and its decay-rate products are found in the phosphate rock and fertilizer as well as the byproduct fluorosilicic acid. During the wet-process procedure, trace amounts of both radium and uranium are captured in the scrubbers and therefore are in the fluorosilicic acid. During the acidulation process yielding phosphoric acid, radon gas in the phosphate pebbles can be released and carried into the fluorosilicic acid, while polonium can be captured during the scrubbing process and then can combine with fluoride (Glasser, undated).

The Centers for Disease Control (CDC) and EPA recommended levels for fluoride in drinking water ranges from 0.6-1.2 ppm (CSDS, 2001). For drinking water fluoridation, the maximum use level (MUL) for sodium hexafluorosilicate is 2 mg/L; for fluorosilicic acid, the level is 6 mg/L of a 25% fluorosilicic acid solution. Both values correspond to a fluoride concentration of 1.2 mg/L, which is below the U.S. Environmental Protection Agency's (EPA's) Maximum Contaminant Level (MCL) of 4.0 mg/L and the Secondary Maximum Contaminant Level (SMCL) of 2.0 mg/L. Although EPA has no MCL for silicate in drinking water, the National Sanitation Foundation (NSF) has established a Maximum Drinking Water Level of 16 mg/L for silicates. For NSF Certified Products used in drinking water, the Maximum Allowable Level (MAL) for fluoride is 1.2 mg/L; the MUL of the products ranges from 4 to 6.6 mg/L (NSF Int., 2000a). At its plant in Riverview, FL, Cargill Fertilizer, Inc. had an MUL of 8 mg/L sodium hexafluorosilicate (equivalent to 1.2 mg/L fluoride) for fluoridation (NSF Int., 2001). While the majority of 29 manufacturers of fluorosilicic acid had an MUL of 6 mg/L, a level of 6.6 mg/L was measured at the IMC-Agrico Company plant at Uncle Sam, LA. [The Hydrite Chemical Company's MUL was 1.7 mg/L at three plants, while the American Development Corporation had an MUL of 4 mg/L at two plants] (NSF Int., 2000b).

7.0 Human Exposure

Potential exposure to sodium hexafluorosilicate is via inhalation of dusts, ingestion, and eye and skin contact (HSDB, 2000b). The main routes of entry of fluorosilicic acid are inhalation and eye and skin contact (HSDB, 2000a; LCI, Ltd., undated-a).

Exposure to sodium hexafluorosilicate is possible from its use to control crawling insects in homes and work buildings. The chemical has "high inherent toxicity," and children may ingest the material from crawling on the floors of treated houses (U.S. EPA, 1999).

In 1992, 5876 U.S. public water suppliers were using fluorosilicic acid and 1635 utilities were using its sodium salt for water fluoridation, serving greater than 80 and 36 million persons, respectively (Urbansky and Schock, 2000). Currently, silicofluorides are used in over 9200 U.S. water treatment systems, serving over 120 million individuals (CSDS, 2001). Exposure via drinking water is, however, expected to be minimal, since at concentrations used in water

fluoridation and at the normal pH of drinking water, both compounds hydrolyze almost completely (see Section 2.2) (Urbansky and Schock, 2000). At equilibrium, the hexafluorosilicate remaining in drinking water is estimated to be <<1 parts per trillion (Urbansky and Schock, 2000). In addition, exposure to impurities in the fluoridating agent is judged to be of low health risk when properly treated water is ingested. For example, in fluorosilicic acid, iron and iodine are usually below the levels considered useful as a dietary supplement; the phosphorus level is reported to be insignificant; and silver is usually <4 parts per septillion in the fluoridated water (CSDS, 2001).

In the workplace, exposure to both chemicals is possible during their manufacture, transportation, or use in water treatment (HSDB, 2000a,b). In the NIOSH 1983 National Occupational Exposure Survey (NOES) of 8057 facilities, 74 industries, and 60 occupations, 79,556 employees were potentially exposed to sodium hexafluorosilicate; the total number of female employees potentially exposed was 22,185. In the 1983 NOES of 1758 facilities, 19 industries, and 15 occupations, 10,867 employees were potentially exposed to fluorosilicic acid; the total number of females potentially exposed was 2068 (RTECS, 2000).

8.0 Regulatory Status

Under EPA's Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), sodium hexafluorosilicate as a pesticide was subject to registration or re-registration in 1988 (RTECS, 2000). In August 1995, the act was amended, eliminating fluorosilicate compounds from the registration list and their sale for pesticide use (40CFR153, Subpart H) (U.S. EPA, 1995). In the United States, all pesticide uses have been cancelled (U.S. EPA, 1999). The registrations of insecticide formulations containing 0.18% to 98.5% sodium hexafluorosilicate, some on the market since the late 1940s, were cancelled in the late 1980s and early 1990s. Target organisms included roaches, moths, and weevils. Other cancelled fluorosilicate products were formulated with sodium aluminum fluorosilicate or aluminum fluorosilicate (NPIRS[¤], 2001). [It is noted that the use of sodium hexafluorosilicate as an insecticide is currently listed in the *2001 Farm Chemicals Handbook* (see Section 5.0).] Both sodium hexafluorosilicate and fluorosilicic acid are listed in Section 8(b) of the Toxic Substances Control Act (TSCA; chemical inventory section). Both are also exempt from reporting under the Inventory Update Rule (i.e., Partial Updating of the TSCA Inventory Data Base Production and Site Reports [40CFR, Section 710(b)]) (TSCAINV, 2000). The Occupational Safety and Health Administration (OSHA) and American Conference of Governmental Industrial Hygienists (ACGIH) have established an eight-hour time-weighted average (TWA) of 2.5 mg/m^3 fluorides, as fluorine. OSHA has established this Permissible Exposure Limit (PEL) for the general industry (29CFR1910.1000), construction (29CFR1915.1000), shipyard (29CFR1926.55), and federal contracts (41CFR50-204.50). The ACGIH short-term excursion limit (STEL) recommendation is that excursions in worker exposure levels may exceed three times the threshold limit value (TLV)-TWA for no more than 30 minutes during a work day and not exceed five times the TLV-TWA, provided that the TLV-TWA is not exceeded. ACGIH has listed fluorides, as fluorine, as "A4 not classifiable as a human carcinogen" (HSDB, 2000b; RTECS, 2000). NIOSH has also recommended an air exposure level to inorganic fluorides of 2.5 mg F/m^3 but as a ten-hour TWA (RTECS, 2000).

9.0 Toxicological Data

9.1 General Toxicology

Chronic ingestion of excessive amounts of fluoride produces osteosclerosis and mottled tooth enamel. Chronic exposure increases osteoblastic activity as well as the density and calcification of bone (Gilman et al., 1980; cited by HSDB, 2000a).

9.1.1 Human Data

Sodium Hexafluorosilicate

Chronic exposure to dust at levels above the PEL or TLV can result in severe calcification of the rib, pelvis, and spinal column ligaments; effects on the enzyme system; pulmonary fibrosis; stiffness; irritation of the eyes, skin, and mucous membranes; weight loss; anorexia; anemia; cachexia; wasting; and dental effects. Long-term or repeated exposure to the skin can result in skin rash (LCI, Ltd., undated-b). Contact with the molten forms of the chemical may cause severe burns to the skin and eyes (HSDB, 2000b).

The clinical signs and symptoms after ingestion of soluble fluoride salts occur in the following five stages: (I) salty or soapy taste, salivation, nausea, abdominal pain, vomiting, (bloody) diarrhea, dehydration, and thirst; (II) muscle weakness, tremors, and in rare instances transient epileptiform convulsions, which may lead to central nervous depression; (III) shock characterized by pallor, weak and thready pulse, shortness of breath, weak heart sounds, wet and cold skin, cyanosis, dilated pupils, followed by death in two to four hours; (IV) when death has not occurred, paralysis of muscle deglutition, carpopedal spasm, and spasm of extremities; and (V) occasionally localized or generalized urticaria. A probable oral lethal dose of 50-500 mg/kg, classified as very toxic, has been reported for a 150-pound (70-kg) person receiving between 1 teaspoon and 1 ounce of the chemical (Gosselin et al., 1976; cited by HSDB, 2000b).

A girl (2.5 years old) who ingested sodium hexafluorosilicate "developed acute respiratory failure, a prolonged AT interval, ventricular tachycardia and fibrillation, hypokalemia, hypocalcemia (3 to 4 mg/100 mL), and aspiration pneumonia" (Ellenhorn et al., 1997; cited by HSDB, 2000b). In a suicide attempt, a female chemical plant worker (32 years old) who ingested three teaspoons of sodium hexafluorosilicate immediately began vomiting, and then experienced facial numbness, diarrhea, diaphoresis, muscle spasms, weakness, abdominal pain, dyspnea, shallow breathing, and cramps of the palms, feet, and legs. Tachycardia and tachypnea were observed. After 12 hours, generalized weakness and enlargement of the liver continued. Treatment with calcium compounds (calcium carbonate initially; calcium lactogluconate for ten days after life-threatening symptoms had diminished) resulted in recovery within 21 days (Dadej et al., 1987).

Fluorosilicic Acid

Contact with the molten forms of fluorosilicic acid may cause severe burns to the skin and eyes. It is also extremely corrosive to the respiratory tract (Hawley, 1981; cited by HSDB, 2000a). The symptoms of inhalation include burning of the eyes and numbness around the lips. Symptoms do not necessarily occur immediately; they can appear 24 hours after exposure.

On the morning of September 6, 1994, a tanker truck spilling 4500 gallons of fluorosilicic acid on Interstate 4 near Deltona, Florida, covering an area 600 feet long and 60 feet wide, resulted in the evacuation of approximately 2300 people from their homes into shelters. Later in the day, fumes were detected in the Deltona Woods neighborhood; because the acid could be carried by the wind, everyone within a mile radius was evacuated, which included 1,750 people in Orange County and 500 people in Deltona. More than 50 people went to hospitals, complaining of skin and respiratory irritation, including burning in the throat, and headaches. An individual riding in a truck with his arm out the window experienced burning on his forearm (Lancaster, 1994).

The effects of long-term exposure to fluorosilicic acid are changes in bone, corrosivity of the mucous membranes (e.g., ulceration of the nose, throat, and bronchial tubes), coughing, shock, pulmonary edema, fluorosis, coma, and even death (LCI, Ltd., undated-a). In a study of 50 workers engaged for approximately 30 years in the production of phosphate fertilizers, the concentration of gaseous fluoride (hydrogen fluoride, silicon tetrafluoride, and fluorosilicic acid) ranged from 0.04 to 0.17 mg/m^3. Nine workers had increased bone densities (Fabbri et al., 1978; cited by HSDB, 2000a).

When swallowed, severe irritation of the lungs, nose, and throat can occur, as well as severe damage to the throat and stomach (LCI, Ltd., undated-a). A probable oral lethal dose of 50-5000 mg/kg, classified as very toxic, has been reported for doses between 1 teaspoon and 1 ounce for a 150-pound (70-kg) person; a probable oral lethal dose of 5-50 mg/kg, classified as extremely toxic, has been reported for doses between 7 drops and 1 teaspoon for the same individual (Gosselin et al., 1984; cited by HSDB, 2000a).

9.1.2 Chemical Disposition, Metabolism, and Toxicokinetics

In a female chemical plant worker who ingested sodium hexafluorosilicate (see Section 9.1.1), fluoride levels in serum and urine (fresh) were 5.130 and 235.60 mg/dm^3, respectively, on day 2 of hospitalization. Treatment with calcium compounds (calcium carbonate and calcium lactogluconate) immediately returned levels to normal. The following day, the levels dropped to 0.399 and 15.39 mg/dm^3, respectively; by day 20, the levels were 0.067 and 0.87 mg/dm^3, respectively (Dadej et al., 1987).

In 50 workers engaged for approximately 30 years in the production of phosphate fertilizers and exposed to gaseous fluoride (hydrogen fluoride, silicon tetrafluoride, and fluorosilicic acid), urine fluoride excretion ranged from 1.0 to 9.6 mg F^-/L (controls: 0.3 to 1.2) (Fabbri et al., 1978; cited by HSDB, 2000a).

In rats fed a diet containing 0.16% sodium hexafluorosilicate supplemented in a corn-soybean oilmeal-casein ration *ad libitum* for 22-23 days, the average amounts of fluorine were 94.4 mg in feces and 91.9 mg in urine. The mean amount of fluorine absorbed was 65.1% and that retained was 31.0% (Kick et al., 1935).

From 1965 to 1974, 170 cases of suspected fluorosilicate poisoning were reported in domestic animals. For positive cases, the animals were poisoned from ingestion of bait, which had not been disposed of after use. Of these, 27 cases were used in the chemical diagnosis of sodium hexafluorosilicate poisoning (13 for cattle, 11 for sheep, and 1 each for horse, pigeon, and concentrate for sheep) (see also Section 9.1.3). In cattle and sheep, measured fluorine

concentrations ranged from 120 to 2900 ppm (wet weight) in stomach/rumen contents and up to 75 ppm in urine. In blood serum, 8 and 3 ppm fluorine were determined in one animal from the groups of poisoned cattle and sheep, respectively (Egyed and Shlosberg, 1975).

When sheep were given sodium hexafluorosilicate via stomach tube (25, 50, 200, 1500, and 2000 mg/kg; 0.13, 0.27, 1.06, 7.976, and 10.63 mmol/kg), blood serum concentrations and urine levels of fluoride initially significantly increased and then decreased with time. For example, the low-dose group had blood serum concentrations ranging from 0.1-0.165 ppm fluoride prior to treatment and 4.2 ppm fluoride six hours after dose administration. By day 4, levels dropped to 0.38 ppm fluoride. Corresponding urine levels of fluoride were 1.35-6.75, 175, and 25 ppm, respectively (Egyed and Shlosberg, 1975).

9.1.3 Acute Exposure

Acute toxicity values for sodium hexafluorosilicate and fluorosilicic acid are presented in **Table 1**. The details of selected studies discussed in this section are presented in **Table 2**.

Table 1. Acute Toxicity Values for Sodium Hexafluorosilicate and Fluorosilicic Acid

Route	Species (sex and strain)	$LC_{Lo}/LD_{50}/LD_{Lo}/TD_{Lo}$	Reference(s)
Sodium hexafluorosilicate			
oral	mouse (sex and strain n.p.)	LD_{50} = 70 mg/kg; 0.37 mmol/kg	RTECS (1997)
	rat (sex and strain n.p.)	LD_{50} = 125 mg/kg; 0.665 mmol/kg	HSDB (2000b)
	rat (F, Sprague-Dawley albino white)	LD_{50} = 430 mg/kg; 2.29 mmol/kg	Rhone-Poulenc Inc. (1971)
	rat (sex and strain n.p.)	TD_{Lo} = 248 mg/kg; 1.32 mmol/kg	RTECS (1997)
	rabbit (sex and strain n.p.)	LD_{50} = 125 mg/kg; 0.665 mmol/kg	
s.c.	rat (sex and strain n.p.)	LD_{Lo} = 70 mg/kg; 0.37 mmol/kg	
inh	guinea pig (sex and strain n.p.)	LC_{Lo} = 33 mg/kg; 0.18 mmol/kg	Patty (1963; cited by HSDB, 2000b)
Fluorosilicic acid			
oral	guinea pig (sex and strain n.p.)	LD_{50} = 200 mg/kg; 1.39 mmol/kg	LCI, Ltd. (undated-a)

Abbreviations: F = female(s); inh = inhalation; LC_{Lo} = lethal concentration low; LD_{50} = lethal dose for 50% of test animals; LD_{Lo} = lethal dose low; n.p. = not provided; s.c. = subcutaneous(ly); TD_{Lo} = toxic dose low

Sodium Hexafluorosilicate

Mice orally given sodium hexafluorosilicate (70 mg/kg; 0.37 mmol/kg) exhibited toxic effects in the peripheral nerves, sensation, and in behavior. In rats, an oral dose (248 mg/kg; 1.32 mmol/kg) administered intermittently for one month produced toxic effects in the kidney, ureter, and/or bladder, as well as musculoskeletal and biochemical effects (RTECS, 1997). Using guinea pigs, inhalation experiments (13-55 mg/m^3 [1.7-7.2 ppm] sodium hexafluorosilicate in air for ≥6 hours) resulted in pulmonary irritation; the lowest concentration that caused death was 33 mg/m^3 (4.3 ppm) (Patty, 1963; cited by HSDB, 2000b).

Table 2. Acute Exposure to Sodium Hexafluorosilicate and Fluorosilicic Acid

Species, Strain, and Age, Number, and Sex of Animals	Chemical Form and Purity	Route, Dose, Duration, and Observation Period	Results/Comments	Reference
Sodium hexafluorosilicate				
Mouse strain, age, number, and sex n.p.	sodium hexafluoro-silicate, purity n.p.	oral; 70 mg/kg (LD_{50}; 0.37 mmol/kg); duration and observation period n.p.	Toxic effects were observed in the peripheral nerves and sensation (flaccid paralysis without anesthesia, generally neuromuscular blockage) and in behavior (ataxia and muscle contraction or spasticity).	RTECS* (1997)
Rats, strain, age, number, and sex n.p.	sodium hexafluoro-silicate, purity n.p.	oral; 248 mg/kg (1.32 mmol/kg) for 30 days intermittent; observation period n.p.	Toxic effects in the kidney, ureter, and/or bladder (other changes in urine composition) were observed. Musculoskeletal (other changes) and biochemical (enzyme inhibition, induction, or changes in blood or tissue [phosphatases] levels) effects were seen.	RTECS* (1997)
Rats, strain, age, number, and sex n.p.	sodium hexafluoro-silicate, purity n.p.	s.c.; 70 mg/kg (LD_{Lo}; 0.37 mmol/kg); duration and observation period n.p.	Fatty liver degeneration and other changes in the liver and toxic effects in the kidney, ureter, and bladder primarily changes in glomeruli were observed.	RTECS* (1997)
Guinea pigs, strain, age, number, and sex n.p.	sodium silicofluoride as dust, purity n.p.	inhalation; 13-55 mg/m^3 (1.2-7.2 ppm) in air for ≥6 h; observation period n.p.	Pulmonary irritation was observed. The lowest concentration that caused death when inhaled for 6 h was 33 mg/m^3.	Patty (1963; cited by HSDB, 2000b)
Sheep, Awassi breed, 1- to 3-yr-old, 5F	technical sodium hexafluorosilicate, purity n.p.	oral (via stomach tube); 25, 50, 200, 1500, and 2000 mg/kg (0.13, 0.27, 1.06, 7.976, and 10.63 mmol/kg) suspended in water; duration and observation period n.p.	With the 25- and 50-mg/kg doses, animals exhibited grinding of teeth (an indication of pain), dullness, and mild diarrhea. At 200 mg/kg, additional symptoms were experienced and included staggering and severe diarrhea. Animals died on day 6. With the two higher doses, licking of the lips, kicking of the belly, grinding of the teeth, falling down (after 1.5 h), frothing at the mouth, congested conjunctiva, protrudation of the tongue, forced and labored breathing, fever, and increased respiration and heart rates were observed. Animals died 3 h after administration of 1500 mg/kg and 2.5 h after administration of 2000 mg/kg. Post-mortem examination showed serous pericardial fluid (few milliliters), a slightly friable liver, mild edema in the lungs, and froth in the trachea. Hemorrhages occurred on the spleen and mucosal folds of the abomasum, and a gelatinous fluid was present in the colon. For the 1500 mg/kg-dose group, the change in GOT went from 132% (of pretreatment activity) at 1.5 hours to 230% at 2.5 hours. For LDH, the change was 158% at death. The serum ICDH change increased from 168% after one hour to 984% at death.	Egyed and Shlosberg (1975)

Table 2. Acute Exposure to Sodium Hexafluorosilicate and Fluorosilicic Acid (Continued)

Species, Strain, and Age, Number, and Sex of Animals	Chemical Form and Purity	Route, Dose, Duration, and Observation Period	Results/Comments	Reference
Fluorosilicic acid				
Rats, strain, age, number, and sex n.p.	fluorosilicic acid, purity n.p.	oral; 430 mg/kg (LD_{50}; 2.98 mmol/kg); duration and observation period n.p.	Somnolence and/or general depressed activity was observed.	RTECS* (2000)
Rats, Sprague-Dawley albino, age n.p., 5F per dose level	fluorosilicic acid (~23%, neat), purity n.p.	oral (via stomach tube); single doses of 215, 464, 1000, and 2100 mg/kg (1.49, 3.22, 6.939, and 14.57 mmol/kg) dissolved in water. Animals were observed for 14 days and then necropsied.	With 464 mg/kg, 3 out of 5 rats died; at ≥1000 mg/kg, 100% mortality was observed. At ≥464 mg/kg, acute depression was observed. Necropsy showed that animals in the low-dose group were "grossly normal" and that dead rats had massive hemorrhages in the entire gastrointestinal tract.	Rhone-Poulenc Inc. (1971)
Rats, guinea pigs, and swine tested as a group; no other data were provided	fluorosilicic acid, purity n.p.	percutaneous; amounts, duration, and observation period n.p.	The intact skin was not affected. When areas were injured before application of the acid, necrosis, continuously spreading, occurred in the deeper regions. Hypocellular necrosis, consisting of sharp leukocyte demarcations, and edema up to the subcutis were observed.	Alhassan and Zink (1982; cited by HSDB, 2000a)
Rabbits, New Zealand, age n.p., 6, sex n.p.	fluorosilicic acid (~23%, neat), purity n.p.	dermal; 0.5 mL (4 mol) to the intact and abraded skin for 1, 24, or 72 h	Severe erythema and edema were observed, indicating the material to be a primary irritant.	Rhone-Poulenc Inc. (1971)
Rabbits, New Zealand, age n.p., 6, sex n.p.	fluorosilicic acid (~23%, neat), purity n.p.	instillation; 0.1 mL (0.8 mol) into the left eye. Eyes were observed at 24, 48, and 72 h following treatment.	Severe and permanent corneal opacity with scar tissue occurred.	Rhone-Poulenc Inc. (1971)

Abbreviations: GOT = glutamate oxaloacetate transaminase; h = hour(s); ICDH = isocitric dehydrogenase; LDH = lactate dehydrogenase; n.p. = not provided

*RTECS uses codes for Toxic Effects. For some codes, it is unclear whether the effects occur in all organs (e.g., M02 — KIDNEY, URETER, BLADDER [Changes primarily in glomeruli]). In these instances, "and/or" has been used.

When sodium hexafluorosilicate (500 mg; 2.66 mmol) was applied to the skin of adult rabbits, mild irritation occurred. When applied to the eyes (100 mg; 0.532 mmol), severe irritation was observed; following a four-second rinse, the effect was still severe (RTECS, 1997).

Sodium hexafluorosilicate poisoning in domestic animals from the ingestion of bait which had not been disposed of after use (13 cases for cattle, 11 for sheep, and 1 each for horse, pigeon, and concentrate for sheep) resulted in drowsiness, constipation, loss of appetite, paresis of the rumen, severe abdominal pain, and diarrhea. Sheep also exhibited grinding of the teeth (an indication of pain) and frothing at the mouth in most cases of lethal poisoning, while the horse also had bradycardia. In an acute study in which sheep were orally administered technical sodium hexafluorosilicate (25, 50, 200, 1500, and 2000 mg/kg; 0.13, 0.27, 1.06, 7.976, and 10.63 mmol/kg) via stomach tube, the animals exhibited similar symptoms. In addition, with the two highest doses, falling down (after 1.5 hours), congested conjunctiva, forced and labored breathing, fever, and increased respiration and heart rates were observed. Animals died 6 days after administration of 200 mg/kg and 2.5 hours after administration of 2000 mg/kg (Egyed and Shlosberg, 1975). When a dairy herd of 600 animals was acutely poisoned from railcar contamination of feed, 95% of the animals had decreased neuromuscular transmission. The poisoning, which resembled calcium depletion, was effectively treated with calcium gluconate intravenously (HSDB, 2000b [original source was not cited]).

Fluorosilicic Acid

In rats orally given fluorosilicic acid (430 mg/kg; 2.98 mmol/kg), somnolence and/or general depressed activity was observed (RTECS, 2000). Other rat studies with fluorosilicic acid (single oral doses of 215, 464, 1000, and 2100 mg/kg [1.49, 3.22, 6.939, and 14.57 mmol/kg]) led to its classification as "moderately toxic" (Rhone-Poulenc, Inc., 1971). Percutaneous administration of the compound (amounts not provided) in rats, guinea pigs, and pigs resulted in continuously spreading necrosis in the deeper regions of injured skin. Hypocellular necrosis, consisting of sharp leukocyte demarcations, and edema up to the subcutis were also observed (Alhassan and Zink, 1982; cited by HSDB, 2000a). In rabbits, it was corrosive to the skin (0.5 mL [4 mol] for 1, 24, or 72 hours) and eyes (0.1 mL [0.8 mol] instilled into left eye) (Rhone-Poulenc Inc., 1971).

9.1.4 Short-term and Subchronic Exposure

No data were available.

9.1.5 Chronic Exposure

No data were available.

9.1.6 Synergistic/Antagonistic Effects

Fluoride, administered in the form of sodium hexafluorosilicate, had a strong affinity for calcium and magnesium. When orally given to sheep via a stomach tube at doses of 25, 50, 200, 1500, and 2000 mg/kg, increased changes in serum calcium and magnesium levels were observed at the two highest doses within 30 minutes after dose administration. At 200 mg/kg, recovery of both levels occurred after five days. With the 1500 mg/kg dose group, changes in phosphorus and sugar levels in whole blood were also significantly increased (16% [of pretreatment levels] at 1.5 hours to 146% at 2.5 hours for phosphorus; 300% to 374%, respectively, for sugar levels) (Egyed and Shlosberg, 1975).

9.1.7 Cytotoxicity
No data were available.

9.2 Reproductive and Teratological Effects
No data were available.

9.3 Carcinogenicity
No studies with sodium hexafluorosilicate or fluorosilicic acid were available. IARC (1987) concluded that there was inadequate evidence for carcinogenicity to humans and to animals for inorganic fluorides used in drinking water.

9.4 Initiation/Promotion Studies
No data were available.

9.5 Anticarcinogenicity
No data were available.

9.6 Genotoxicity
Sodium hexafluorosilicate was negative in the Salmonella/microsome test (concentrations up to 3600 g/plate, –S9) and the micronucleus test on mouse bone marrow (37.2 mg/kg; 0.198 mmol/kg) (Gocke et al., 1981). The compound (0.25 mM; 47 g/mL) did not induce sex-linked recessive lethal mutations in *Drosophila* (Gocke et al., 1981; IARC, 1987). In the *Bacillus subtilis* rec-assay system, sodium hexafluorosilicate (0.001-10 M; 188 g/mL-1.9 g/mL) also gave negative results (Kada et al., 1980; Kanematsu et al., 1980).

9.7 Cogenotoxicity
No data were available.

9.8 Antigenotoxicity
No data were available.

9.9 Other Data
Within one week after beginning work in a foam rubber plant, a 23-year-old man exhibited skin lesions consisting of "diffuse, poorly delineated, erythematous plaques with lichenoid papules and large pustules" on his arms, wrists, thighs, and trunk. Although scratch and patch tests with sodium hexafluorosilicate (2% aqueous) were negative, animal testing showed the compound to be a pustulogen. When rabbits received topical application of a 1, 5, 10, and 25% solution of sodium hexafluorosilicate in petroleum, pustules occurred on normal skin only with the high concentration, while all concentrations produced pustules on stabbed skin (Dooms-Goossens et al., 1985).

10.0 Structure-Activity Relationships
At levels of 14-16 ppm fluorine, sodium fluoride, sodium hexafluorosilicate, and cryolite (Na_3AlF_6) had the same extent of chronic fluorine intoxication in rats (De Eds and Thomas, 1933-1934; cited by McClure, 1950). At 40 and 80 ppm, the chronic toxicity (observations on growth rate, fecundity, mortality, tooth development, pathology, and disease) of barium fluorosilicate and cryolite in rats was "substantially the same as that of sodium fluoride for the same fluorine content" (Smyth and Smyth, 1932; cited by McClure, 1950). At 14 ppm fluorine,

ammonium fluoride, potassium fluoride, barium fluorosilicate, potassium fluorosilicate, and sodium fluorosilicate exhibited the same acute toxicity as sodium fluoride in the animals (Smith and Leverton, 1934; cited by McClure, 1950).

In a comparative study of absorption and excretion of fluorine in rats fed sodium fluoride, calcium fluoride, and sodium hexafluorosilicate, the percent fluorine retained was the same for the two sodium compounds (Kick et al., 1935 [see Section 9.1.2 for details regarding sodium hexafluorosilicate]). Several experiments on growing rats orally given 5, 10, 15, 25, and 50 ppm fluorine as sodium fluoride or sodium hexafluorosilicate for 90-100 days found no differences in the quantity of fluorine deposited and the contents of ash, calcium, and phosphorus in the incisor teeth, molar teeth, mandibles, and femurs. Furthermore, there were no differences in the percent of ingested fluorine retained in the body, and a combination of sodium silicate (15 ppm silicon) with sodium fluoride (25 ppm fluorine) did not affect the amount of fluorine deposited. The growth rate was normal in all rats (McClure, 1950).

In a separate study, litters of female weanling Osborne-Mendel rats were given 50 ppm fluorine as sodium fluoride or ammonium fluorosilicate in drinking water for 99 days. The cariostatic effect was similar for the two compounds i.e., both inhibited caries to the same extent. There were no differences in the amounts of fluorine and ash deposited in the molars, incisors, mandibles, and femurs. There were no differences in growth rate and in the production of incisor striations (Zipkin and McClure, 1954).

11.0 Online Databases and Secondary References

11.1 Online Databases

Chemical Information System Files
SANSS (Structure and Nomenclature Search System)
TSCAINV (Toxic Substances Control Act Inventory)
TSCATS (Toxic Substances Control Act Test Submissions)

National Library of Medicine Databases
EMIC and EMICBACK (Environmental Mutagen Information Center)

STN International Files

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

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

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Appendix: Units and Abbreviations

°C = degrees Celsius

µg/L = microgram(s) per liter

µg/m^3 = microgram(s) per cubic meter

µg/mL = microgram(s) per milliliter

µM = micromolar

ACGIH = American Conference of Governmental Industrial Hygienists

AOAC = Association of Official Analytical Chemists

AWWA = American Water Works Association

bw = body weight

C.P. = Commercially Pure

CSDS = Colorado Springs Dental Society

EPA = Environmental Protection Agency

F = female(s)

FIFRA = Federal Insecticide, Fungicide, and Rodenticide Act

g = gram(s)

g/mL = gram(s) per milliliter

h = hour(s)

HSDB = Hazardous Substances Data Bank

IARC = International Agency for Research on Cancer

i.p. = intraperitoneal(ly)

kg = kilogram(s)

L = liter(s)

LC_{50} = lethal concentration for 50% of test animals

LC_{Lo} = lethal concentration low

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

LD_{Lo} = lethal dose low

M = male(s)

MAL = Maximum Allowable Level

MCL = Maximum Contaminant Level

MUL = maximum use level

mg/kg = milligram(s) per kilogram

mg/m^3 = milligram(s) per cubic meter

mg/mL = milligram(s) per milliliter

min = minute(s)

mL/kg = milliliter(s) per kilogram

mm = millimeter(s)

mM = millimolar

mmol = millimole(s)

mmol/kg = millimoles per kilogram

mo = month(s)

mol = mole(s)

mol. wt. = molecular weight

NICNAS = National Industrial Chemicals Notification and Assessment Scheme

NIOSH = National Institute for Occupational Safety and Health

NSF = National Sanitation Foundation

NOES = National Occupational Exposure Survey

NOHS = National Occupational Hazard Survey

n.p. = not provided

OSHA = Occupational Safety and Health Administration

PEL = permissible exposure limit

ppb = parts per billion

ppm = parts per million

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

REL = relative exposure limit

RTECS = Registry of Toxic Effects of Chemical Substances

s.c. = subcutaneous(ly)

SMCL = Secondary Maximum Contaminant Level

STEL = short-term exposure limit

TD_{Lo} = toxic dose low

TLV = threshold limit value

TSCA = Toxic Substances Control Act

TWA = time-weighted average

wk = week(s)

yr = year(s)