SUMMARY OF DATA FOR CHEMICAL SELECTION

Nitrogen trifluoride

7783-54-2

BASIS OF NOMINATION TO THE CSWG

Nitrogen trifluoride is brought to the attention of the CSWG because of the rapidly increasing demand for this chemical in the semiconductor industry, projected to reach 3.2 million pounds worldwide in 2001. Given this increased demand, the lack of chronic toxicity and carcinogenicity information warrants consideration of nitrogen trifluoride for nomination to the National Toxicology Program (NTP).

As a strong oxidizer and a source of fluorine, nitrogen trifluoride is the preferred substitute for greenhouse gas-producing perfluoroethane and is used as a cleaning and etching agent in the semiconductor industry. Nitrogen trifluoride is also used in high-energy fuels, and in high-energy chemical lasers.

Although not found to be mutagenic or clastogenic, nitrogen trifluoride presents a potential carcinogenic risk due to its oxidizing properties. In view of its rapidly growing production levels, the apparent lack of data on carcinogenic potential of nitrogen trifluoride calls for investigation into chronic toxicity of this compound.

INPUT FROM GOVERNMENT AGENCIES/INDUSTRY

Dr. John Walker of the US Environmental Protection Agency (EPA) was consulted regarding production information on nitrogen trifluoride. Dr. Walker stated that the latest EPA annual production volume data available for inorganic compounds were collected in 1978 and are currently outdated. The EPA High Production Volume (HPV) chemical lists compiled in 1986, 1990, 1994, and 1998 contain information on select organic compounds only and do not include inorganic chemical production data.

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SELECTION STATUS

ACTION BY CSWG: 7/26/01

Studies requested:

- Short-term tests for genotoxicity
- Metabolism

Priority: High

Rationale/Remarks:

- Preferred substitute for perfluoroethane as a cleaning and etching agent in the semiconductor industry

- Rapid increase in production capacity to meet expanding demand

- As an inorganic chemical, not part of EPA's HPV Challenge Program

- Limited studies on toxicity show methemoglobin formation and changes in the liver and kidneys that could not be attributed to fluorosis caused by release of fluorine

- Concerns expressed by CSWG members that more information on exposure of workers is needed before chronic studies can be recommended

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CHEMICAL IDENTIFICATION

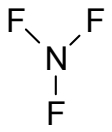
CAS Registry Number: 7783-54-2

CAS Name: Nitrogen fluoride (9CI)

Synonyms and Trade Names: Nitrogen trifluoride, trifluoramine, trifluoroamine, trifluoroammonia, perfluoroammonia

Structural Class: Inorganic fluoride (Praxair, 1999)

Structure, Molecular Formula, and Molecular Weight:



NF_3 Mol. wt.: 71.0

Chemical and Physical Properties:

Description: A colorless gas with a moldy odor (Merck, 2000).

Melting Point: -208.5°C (Merck, 2000)

Boiling Point: -129.0°C (Merck, 2000)

Density: 1.9 (liquid at bp) (Merck, 2000)

Specific gravity: 2.46 (air = 1) at 21.1°C and 1 atm (Praxair, 1999)

Vapor pressure: 1500 mm Hg at -119°C (Matheson Tri-Gas, 2000)

Solubility: Slightly soluble in water (Matheson Tri-Gas, 2000).

Reactivity: Stable at normal temperature and pressure, strong oxidizer, reacts explosively with reducing agents, decomposed by electric sparks (ACGIH, 1991; Matheson Tri-Gas, 2001; Merck, 2000).

Technical Products and Impurities: Nitrogen trifluoride is available at greater than 99% purity fromseveral US manufacturers (Chemcyclopedia Online, 2001; Matheson Tri-Gas, 2001; Praxair, 1999; Scott Specialty Gases, 2001). Common impurities include fluorides (e.g. difluorodiazine, N_2F_2; carbon tetrafluoride, CF_4; etc.), nitrogen and oxygen, carbon and nitrogen oxides, and water. Total fluorides can make up to 3900 ppm by volume in the commercial grade formulation (Henderson & Woytek, 1994; NLM, 2001a).

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Nitrogen trifluoride is shipped as a high pressure gas at 10 MPa (1450 psig) and is available in tube trailers and cylinders. The compound is available in three grades: commercial, used in chemical laser applications; VLSI (99.9% purity); and megaclass (99.996% purity), both used in the electronics industry. The commercial grade is sometimes divided further into electronic (99.7% purity) and CP (99.0% purity) grades (Air Products and Chemicals, 2001; Chemcyclopedia Online, 2001; Henderson & Woytek, 1994).

At temperatures above 200 – 300°C, nitrogen trifluoride is converted to tetrafluorohydrazine, which can slowly hydrolyze to highly toxic hydrogen fluoride and hydrazine, an animal carcinogen (Baxter, 1994; Henderson & Woytek, 1994).

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EXPOSURE INFORMATION

Production and Producers:

Manufacturing Process. Several methods for nitrogen trifluoride synthesis have been described in the literature. The compound can be prepared from ammonia using either cobalt trifluoride (Meshri, 1994) or a mixture of hydrogen fluoride and a metal fluoride (Tarancon, 2000).

Alternatively, nitrogen can be made to produce nitrogen trifluoride by radiochemistry, glow discharge, or plasma technology (Shia, 1994). The latter process involves: (1) passing gaseous nitrogen through a plasma arc at a temperature of at least 1000EC; (2) introducing gaseous elemental fluorine into the post arc region; and (3) rapid quenching of the exit gases to a temperature below 25EC. This method was developed as an alternative to the methods involving the reaction of ammonia and elemental fluorine or the electrolysis of molten fluorides, which yielded nitrogen trifluoride in admixture with many by-products (Fullam & Seklemian, 1967).

Large-scale production of nitrogen trifluoride currently involves one of two major methods. The first one constitutes direct fluorination of ammonia, whereby nitrogen trifluoride is synthesized by reacting ammonia and gaseous fluorine in the presence of molten ammonium acid fluoride. The second method involves electrolysis of molten ammonium acid fluoride, which results in production of nitrogen trifluoride at the anode and hydrogen gas at the cathode (Henderson & Woytek, 1994).

Development of electronic applications for nitrogen trifluoride resulted in the requirement for higher purity. Difluorodiazine is removed by pyrolysis over heated metal or metal fluoride. Other purification techniques are aimed at removal of moisture, nitrous oxide, carbon dioxide, and carbon tetrafluoride (Henderson *et al*., 1991; Henderson & Woytek, 1994; Hyakutake *et al*., 1990; Nagamura, 1998; Tarancon, 1997).

Production/Import Levels. Nitrogen trifluoride is listed in the EPA TSCA Inventory.

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According to Dr. John Walker of the EPA, who was consulted regarding nitrogen trifluoride production levels, production information on inorganic compounds is not included in the EPA HPV list. As a result, the latest EPA figures on inorganic compounds production date back to 1978 and are, therefore, outdated (STN, 2001; Walker, 2001).

Henderson and Woytek (1994) estimated annual US production of nitrogen trifluoride at less than 100 tons annually. However, the demand for the compound is expanding rapidly because of its use as a substitute for greenhouse gas-producing perfluoroethane to clean semiconductors and liquid crystal displays (Schumann, 2000). Indeed, Anderson Development Company, a subsidiary of Mitsui Chemicals, Inc., is reported to be in the process of doubling the capacity of its nitrogen trifluoride plant to approximately 55 tons a year (Anon., 1999), while Air Products and Chemicals, the major US manufacturer of nitrogen trifluoride with the current capacity of approximately 988 thousand lbs/yr, plans to expand production to about 2.8 million lbs/yr by mid-2002 (Schumann, 2000).

Producers and Importers: Nitrogen trifluoride is currently manufactured in the US by three companies: Air Products and Chemicals, Inc.; Anderson Development Co.; and Central Glass International, Inc. (Chemcyclopedia Online, 2001). Air Products and Chemicals is currently the largest producer of nitrogen trifluoride in the US, with a production capacity of 1.75 million lbs/year (Hunter, 2000a). Advanced Specialty Gases also manufactures nitrogen trifluoride. Its nitrogen trifluoride plant has been offline due to an explosion but is expected to resume production shortly (Schumann, 2000). Worldwide consumption is estimated to reach 3.2 million lbs in 2001 (Hunter, 2000a).

Other suppliers of nitrogen trifluoride include Advance Research Chemicals, Inc.; Airgas, Inc.; BOC Gases; East-West Global, Inc.; Especial Gas, Inc.; Matheson Tri-Gas, Inc.; Praxair Technology, Inc.; Scott Specialty Gases, Inc.; and Ozark Fluorine Specialties (BOC Gases, 2001; Chemcyclopedia Online, 2001; East-West Global, 2001; Especial Gas, 2001; Hunter, 2000b; Tilton, 2000; Matheson Tri-Gas, 2001; Scott Specialty Gases, 2001; Schumann, 2000).

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Use Pattern: The principal use of nitrogen trifluoride is as a fluorine source in the electronics industry. Nitrogen trifluoride offers significant advantages over traditional carbon-based etchants. These include high etch rates, high selectivities for nitride-over-oxide etching and single-crystal silicon over thermally grown oxide, and the production of only volatile reaction products resulting in an etch with no polymer or fluoride residues (Henderson & Woytek, 1994).

Nitrogen trifluoride is also used in *in situ* plasma or thermal cleaning of chemical vapor deposition (CVD) reactors. Nitrogen trifluoride plasma can remove these deposits as volatile fluorides in minutes. The cleaning is performed at the process temperature and eliminates the need to remove the internal CVD reactor components to be cleaned by acid tank immersion (Henderson & Woytek, 1994).

Another use of nitrogen trifluoride is as a fluorine source for hydrogen and deuterium fluoride (HF/DF) high-energy chemical lasers, where nitrogen trifluoride is preferred to fluorine because of its relative ease of storage and handling at ambient temperatures (Henderson & Woytek, 1994).

The use of nitrogen trifluoride as a cleaning and etching agent has been on the rise recently due to the drive in the semiconductor industry towards the reduction of perfluorocompound (PFC)-induced greenhouse gas emissions. Nitrogen trifluoride is itself a PFC and is classified as a greenhouse gas by the EPA. However, its unique structure reportedly allows more complete destruction and greater utilization, thus decreasing emissions by up to 90% as compared to other PFC gases. Nitrogen trifluoride cleaning processes are also 4 to 12 times faster than those involving carbon-fluorine compounds and are associated with lower abatement costs. Because of these advantages, CVD tool makers for the semiconductor industry have begun to standardize on nitrogen trifluoride clean processes for their equipment. The new uses drove demand to 1.5 million pounds in 2000 (EPA, 2001; Pruette *et al*., 1999; Schumann, 2000).

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Human Exposure: Inhalation constitutes the primary route of exposure to gaseous nitrogen trifluoride. The slight moldy odor of nitrogen trifluoride causes it to have poor warning properties (ACGIH, 1991). Five volunteers were exposed to 100 and 500 ppm of nitrogen trifluoride for 2 to 3 minutes. No odor was detected at 100 ppm, and one of the five volunteers was reported to have detected the odor at 500 ppm (Torkelson *et al*., 1962).

Occupational Exposure. The National Occupational Exposure Survey (NOES), conducted by the National Institute for Occupational Safety and Health (NIOSH) between 1981 and 1983, estimated that 1096 employees, including 140 female employees, were potentially exposed to nitrogen trifluoride in the workplace (STN, 2001). However, due to rapidly increasing demand for this compound in the semiconductor industry, these figures are likely to be out of date.

Consumer Exposure. No information on consumer exposure to nitrogen trifluoride was found in the available literature.

Environmental Occurrence: No information on the environmental occurrence of nitrogen trifluoride was found in the available literature.

Regulatory Status: The US Occupational Safety and Health Administration (OSHA) has set an 8-h time-weighted average (TWA) permissible exposure limit (PEL) of 10 ppm (29 mg/m^3) for gaseous nitrogen trifluoride (OSHA, 2001b). The American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value (TLV) for nitrogen trifluoride is also 10 ppm. The ACGIH excursion limit recommendation for nitrogen trifluoride allows excursions in worker exposure levels to exceed three times the TLV-TWA for no more than a total of 30 min during a work day. Under no circumstances are the excursion levels allowed to exceed five times the TLV-TWA. The ACGIH biological exposure index (BEI) for nitrogen trifluoride is measured by the level of methemoglobinemia. The BEI is set at methemoglobin in blood comprising 1.5% of total hemoglobin during or at the end of the shift (NLM, 2001a).

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The odor of nitrogen trifluoride is not a good warning property of a release as it cannot be detected at concentrations within the TLV (odor threshold ~1475 mg/m^3) (Airgas, 1999; Committee on Updating of Occupational Exposure Limits, 2001).

Nitrogen trifluoride is classified as an inhalation hazard by the Department of Transportation and is regulated accordingly (Environmental Defense, 2001; NLM, 2001a).

OSHA has included nitrogen trifluoride in its List of Highly Hazardous Chemicals, Toxics and Reactives (29 CFR 1910.119, Appendix A), which contains substances that present a potential for a catastrophic event at or above the threshold quantity. The threshold quantity for nitrogen trifluoride is set at 5000 pounds (57 *FR* 7847, March 4, 1992) (OSHA, 2001a).

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EVIDENCE FOR POSSIBLE CARCINOGENIC ACTIVITY

Human Data: No epidemiological studies or case reports investigating the association of exposure to nitrogen trifluoride and cancer risk in humans were identified in the available literature.

Animal Data:

Carcinogenesis Studies. No two-year carcinogenicity studies of nitrogen trifluoride were found in the available literature.

Acute Studies. The primary acute toxic effect of nitrogen trifluoride is methemoglobinemia, which can lead to anoxia and death (ACGIH, 1991; Haz-Map, 2001; NLM, 2001a).

Dost and co-workers (1968) conducted extensive research on the acute toxicity of nitrogen trifluoride. They found that the hemoglobin of rats intoxicated with nitrogen trifluoride contained up to 0.2 moles of fluoride per mole of oxidized heme, presumably bound to methemoglobin. Such binding did not occur with sodium, chlorine, bromine, or oxygen fluorides, and none of these other compounds caused methemoglobin formation. The investigators noted that nitrogen trifluoride was able to react with hemoglobin despite its very low solubility in water.

Vernot and co-workers (1973) confirmed that the immediate effects of acute exposure to nitrogen trifluoride were caused by methemoglobin formation and resulting anoxia (Table 1). In all species tested, animals that survived the acute intoxication and were held for two weeks or longer showed no gross or histopathologic effects of exposure.

Data on acute toxicity found in the available literature are summarized in Tables 1 and 2.

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Table 1. Acute toxic effects of nitrogen trifluoride.

Species	Dose/route	Effects	References
Rat	8 – 16 ml/kg, single ip injection	Severe cyanosis, spleen darkening and enlargement, slight histologic changes in liver and kidneys; all highest-dose animals died within 2 h.	Torkelson *et al*., 1962
Rat	1,000 – 10,000 ppm for 10 min – 4 h, inhalation	Increase in circulating methemoglobin at 1000 ppm/4 h, but not 3000 ppm/10 min; 87% death at 10,000 ppm/1 h; 60 – 70% methemoglobin concentration at time of death.	Dost *et al*., 1968 Dost *et al*., 1970b NLM, 2001a
Rat	4,018 – 31,200 ppm for 15 – 60 min, inhalation	Most deaths within the first 10 min, 90% – within the first 60 min, some delayed deaths, no deaths after 24 h; eye irritation; gasping; cyanosis.	Vernot *et al*., 1973
Mouse	3,854 – 24,300 ppm for 15 – 60 min, inhalation	Gasping; cyanosis; extensive pneumonia in mice dying after 1 d; 50% died during exposure.	Vernot *et al*., 1973
Rabbit	16 and 20 ml/kg, single ip injection	Slight to moderate cyanosis; no deaths.	Torkelson *et al*., 1962
Dog	7,790 – 53,546 ppm for 15 – 60 min, inhalation	Heinz body-induced hemolysis; anemia; decreased hematocrit, hemoglobin, and erythrocyte count; histotoxic anoxia (lung congestion, edema, focal hemorrhage); ocular irritation; emesis; tachypnea; cyanosis; no deaths after 2 h post-exposure.	Vernot *et al*., 1973
Monkey	7,790 – 32,636 ppm for 15 – 60 min, inhalation	Emesis; ocular irritation; clinical signs of methemoglobinemia-induced anoxia; no deaths after 2 h post-exposure.	Vernot *et al*., 1973

Table 2. Acute inhalation toxicity values for nitrogen trifluoride.*

Species	LC_{50} for 1-h Exposure (ppm)
Mouse	7,500
Rat	6,700
Dog	~ 9,600**
Monkey	~ 10,000**

* Source: Vernot *et al*., 1973.
**Exact value not determined.

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Subacute Studies. Rabbits (4 per group) that had received 7 intraperitoneal (ip) injections of 10 ml nitrogen trifluoride gas in 23 days (sacrificed after additional 6 days) showed enlarged spleens, pathologic changes in the liver, and myocardial degeneration (Torkelson *et al*., 1962).

In a two-week inhalation study, Crl:CD rats (5 males and 5 females per group) were exposed to 0, 20, 100, and 500 ppm of nitrogen trifluoride 6 h/d, 5 d/wk. The animals in the 100- and 500-ppm groups showed signs of mild to severe hemolytic anemia. Microscopic changes were observed in the liver, kidneys, spleen, and bone marrow of the rats in the 100- and 500-ppm groups. These changes were attributed to the effects of the exposure-induced hemolytic anemia (Anon., 1998).

Subchronic Studies. Torkelson and co-workers (1962) conducted an inhalation study of nitrogen trifluoride in rats. Male and female rats (12 per group), exposed to 100 ppm of the test compound 7 h/d, 5 d/wk, for 19 weeks, showed mild to moderate pathologic changes in the liver and kidneys. The average weight of the liver, kidneys, and spleen was increased in male rats. No significant effects on the spleen or on hematologic parameters were observed. There was no evidence of fluorosis in the teeth or bones, although a very slight increase in total fluorine in the urine was detected.

Short-Term Tests: It has been reported that *in vitro* genotoxicity testing of nitrogen trifluoride in the US (1985) and Japan (1989) indicated possible mutagenic activity (Drozdowicz, 1996; Henderson & Woytek, 1994). However, the data cited by these authors were contained in internal toxicology reports, which were not available for review.

In 1995, Air Products and Chemicals conducted short-term studies of nitrogen fluoride. The bacterial mutagenicity study found that nitrogen trifluoride was not mutagenic in Ames *Salmonella typhimurium* strains TA98, TA100, TA102, and TA1535, or in *E. coli* strain WP2 *uvr*A, with or without metabolic activation, at concentrations ranging from 0.1 to 5.0%. In an *in vivo* clastogenicity test, mice were exposed to the test material in nose-

only, "flow-past" exposure chambers at 840, 1274, or 2469 ppm for 4 h; five mice of each sex were sacrificed 24, 48, or 72 h post-exposure; bone marrow smears were prepared from each mouse; and the number of micronucleated polychromatic erythrocytes (PCE) was measured. Although a statistically significant increase in micronucleated PCE was observed in the 72-h, 840-ppm group of male mice, this effect was not observed in the preceding range-finding assay and was not dose-related. No significant increase in micronucleated PCE was found in any other group of animals. The authors concluded that nitrogen trifluoride was neither mutagenic nor clastogenic and attributed prior reports of its mutagenicity to impurities contained in the test sample (Drozdowicz, 1996).

Metabolism: Dost and co-workers (1971) found that 1 mol of nitrogen trifluoride mediated oxidation of 3 heme equivalents both *in vitro* and *in vivo* (in dogs), suggesting that inhaled nitrogen trifluoride reacts only with circulating hemoglobin. The authors speculated that the capillary bed of the lung constituted the sole site of the reaction due to the very low solubility and reactivity of nitrogen trifluoride.

Studies of inorganic fluoride metabolism, conducted by Dost and co-workers, do not suggest existence of any fluoride-bearing degradation products which behave differently from fluoride ion. Rats exposed to 5000 ppm of nitrogen trifluoride for 50 min exhibited a moderate increase in tissue fluoride, which disappeared in one day. However, a high concentration of fluoride persisted in erythrocytes and, in some animals, in spleens for up to 48 h post-exposure. That was not the case in animals exposed to sodium fluoride and certain other inorganic fluorides. Spectral evidence and the apparent stability of the fluorine-hemoglobin/methemoglobin complex suggested that the fluoride was not bound to the oxidized heme, and that methemoglobin was formed by other means. The authors also noted that some nitrogen fluoride may selectively deposit in the thyroid (Dost *et al*., 1970a, b; 1971).

Other Biological Effects: Except for the ocular irritation observed in all species during acute studies, the clinical signs of nitrogen trifluoride intoxication (tachypnea, cyanosis, etc.)

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are believed to be the results of methemoglobin-induced anoxia (Dost *et al*., 1970a,b).

The issue has been raised of tooth mottling and skeletal changes associated with prolonged nitrogen trifluoride exposure (Merck, 2000; Sax & Lewis, 1989), which presumably are linked to the release of fluorine. This information is based on the chronic effects of sodium fluoride. However, specific evidence showing such effects of nitrogen trifluoride was not found in the available literature. As mentioned earlier, no evidence of fluorosis was reported in the subchronic nitrogen trifluoride study in rats (Torkelson *et al*., 1962).

Structure/Activity Relationships: Although structure/activity relationships (SAR) analyses prepared for CSWG consideration generally include carcinogenicity and mutagenicity data, the analysis of nitrogen trifluoride was expanded to address the biological effects associated with fluoride release. Consequently, the SAR discussion includes information on sodium and potassium fluorides and the results subchronic studies, wherever available.

No relevant information was found on two nitrogen trifluoride-related inorganic halides, nitrogen triiodide [13444-85-4] and phosphorus trifluoride [13455-01-1], two nitrogen trifluoride-related inorganic halides. In addition, no relevant information was found on tetrafluorohydrazine [10036-47-2], a structurally related nitrogen trifluoride contaminant.

No carcinogenicity or mutagenicity data were found on nitrogen trichloride [10025-85-1]. However, this compound produced mild histopathological changes in thyroid and kidneys and increased liver enzyme activity in rats in a subchronic study (Nakai *et al*., 2000). It also induced “running fits” in dogs, when administered chronically (Arnold, 1949).

When tested by the NTP in a two-year bioassay, sodium fluoride [7681-49-4] was mostly negative, with the exception of the equivocal results in male rats (NTP, 1990). It was mutagenic in human lymphoid cells, but not in *Salmonella typhimurium*, *E. coli*, or Chinese hamster ovary cells. The compound produced positive results in the mouse

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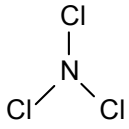
lymphoma clastogenicity assay and sister chromatid exchange test (NLM, 2001b; NTP, 1990; Zeiger *et al*., 1993).

No carcinogenicity information on potassium chloride [7789-23-3] was found in the available literature. The compound was reported to be genotoxic in the mouse lymphoma assay without metabolic activation (NLM, 2001b).

Data available on nitrogen trifluoride and related compounds are summarized in Table 3.

Table 3. Summary of information on nitrogen trifluoride and related compounds.

Compound	Chronic/Subchronic Toxicity Data	Mutagenicity Data
Nitrogen trifluoride 7783-54-2 	Subchronic study in rats (inhalation exposure, 100 ppm, 7 h/d, 5 d/wk, for 19 wk): mild to moderate pathologic changes in liver and kidneys; increased liver, kidney, and spleen weight in males; no evidence of fluorosis; slight increase in total fluorine in urine (Torkelson *et al*., 1962).	Negative in *S. typhimurium* and *E. coli* w/wo S-9; negative in mouse *in vivo* micronucleus assay (Drozdowicz, 1996).
Nitrogen trichloride 10025-85-1 	Subchronic study in rats (0.2 – 90 ppm in drinking water, for 13 wk): increase in relative kidney weight; minimal to mild adaptive histopathological changes in thyroid and kidney; increased hepatic glutathione S-transferase and UPD-glucuronosyl-transferase activities in females (Nakai *et al*., 2000). Chronic study in dogs (50 g/kg bw in diet, 6 d/wk, for 2 yr): animals developed running fits that ceased upon discontinuation of treatment (Arnold, 1949).	ND

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Compound	Chronic/Subchronic Toxicity Data	Mutagenicity Data
Sodium fluoride 7681-49-4 Na^+ F^-	Chronic study in rodents (25 – 175 ppm in drinking water, for 2 yr): equivocal results (osteosarcoma) in male rats; negative in females rats, male mice, and female mice. Non-neoplastic lesions included osteosclerosis (female rats), tooth deformity (rats) and discoloration, dentine dysplasia (NTP, 1990). Subchronic study in rodents (rats: 10 – 300 ppm; mice: 10 – 600 ppm; in drinking water; for 6 months): high-dose rats and mice showed chalky white teeth, chipped or with unusual wear patterns; microscopic focal degeneration of the enamel organ; minimal gastric mucosa hyperplasia (rats); ulcer (1 rat); acute nephrosis and/or liver lesions (in mice that died early); minimal bone growth/remodeling alterations (mice).	Pos. in mouse lymphoma w/wo S-9; neg. in *S. typhimurium* and *E. coli* w/wo S-9; neg. in CHO cells w/wo S-9; pos. in SCE w/wo S-9 and CA wo S-9; mutagenic in human lymphoid cells (NLM, 2001b; NTP, 1990; Zeiger *et al.*, 1993).
Potassium fluoride 7789-23-3 K^+ F^-	ND	Positive in mouse lymphoma wo S-9 (NLM, 2001b).

ND = No data found in the available literature; CHO = Chinese hamster ovary; SCE = sister chromatid exchange; CA = chromosomal aberrations; w/wo = with or without

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