Selected References and Publications

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(3) Meikle et al., 1963. "Drywood termite metabolism of Vikane gas fumigant as shown by labeled pool technique." J. Agric. Food Chem. 11:226-230.

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(5) Thoms, E. M. and Scheffrahn, R.H., 1994. "Control of pests by fumigation with (sulfuryl fluoride)" Down to Earth, Vol. 49, No. 2 pp. 23-30.

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(7) Chambers and Millard, 1995. "Assessing the global use potential of sulfuryl fluoride. 1995 Annual International Research Conference on Methyl Bromide Alternatives and Emissions Reductions." Nov. 6-8, San Diego.

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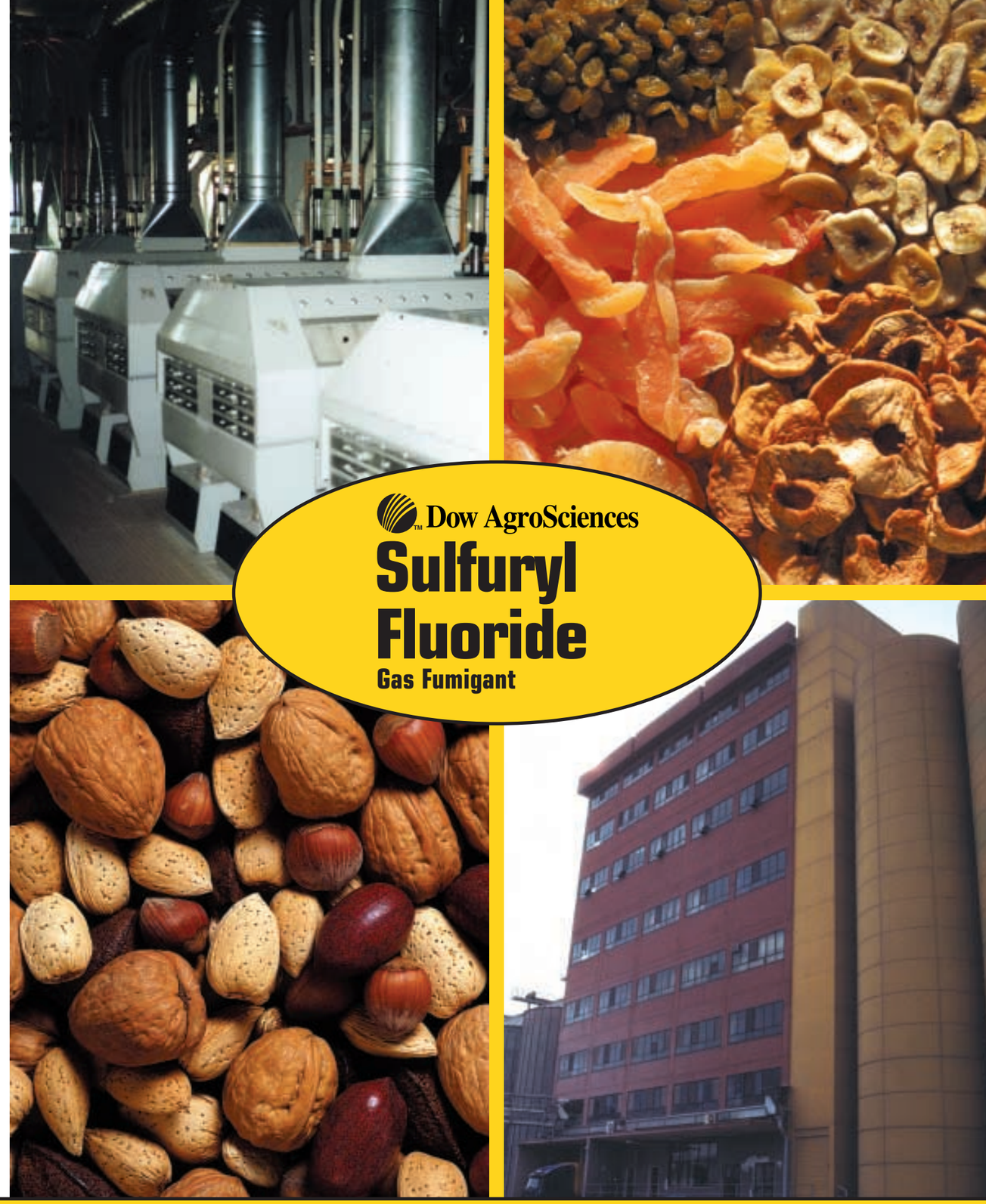
Vikane gas fumigant is registered or authorized for use in the United States, Caribbean, Japan, Germany and Sweden.
ProFume gas fumigant is not available for sale. Registration submissions are being undertaken



Dow AgroSciences
Sulfuryl
Fluoride
Gas Fumigant

Technical Bulletin

This Technical Bulletin for sulfuryl fluoride is provided for reference purposes only.

Dow AgroSciences

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Overview

Dow AgroSciences
Sulfuryl Fluoride
Gas Fumigant

Sulfuryl fluoride is a broad-spectrum postharvest fumigant being developed by Dow AgroSciences, LLC. Fumigation is usually the preferred method of postharvest pest eradication because the pests can be anywhere within the commodity, storage or processing structure, mill or food handling establishment. For many years, methyl bromide has been the fumigant of choice, but its use is being phased out under the Montreal Protocol because of concerns that it depletes the stratospheric ozone layer. The Montreal Protocol is an international agreement ratified by over 160 countries.

Sulfuryl fluoride is a viable alternative to methyl bromide for fumigation of mills, warehouses, storage structures, transportation vehicles, and many commodities and foods within them. The U.S. Department of Agriculture, in a recent article about methyl bromide replacements, stated:

"Though sulfuryl fluoride must undergo rigorous EPA (Environmental Protection Agency) registration procedures, its approval will provide an acceptable alternative to methyl bromide, thus filling a substantial need for postharvest fumigants."(1)

Sulfuryl fluoride, because of its unique mode of action, can also be used as a viable rotation tool to manage and help prevent resistance issues with other fumigants and insecticides.

Dow AgroSciences has and will support the establishment of food tolerances, which will enable the use of sulfuryl fluoride as Sulfuryl fluoride gas fumigant in mills, food processing facilities, warehouses, and transportation vehicles.

Noteworthy Features:

- Broad-spectrum fumigant effective on all life stages of insect and rodent pests
- Flexible for use in long or short exposure fumigations
- Non-flammable, odorless, colorless gas that rapidly vaporizes and distributes quickly
- Non-corrosive gas for use in sensitive areas having equipment and electronic devices
- Very low reactivity as a gas and does not react with materials to form unpleasant odors
- Rapidly penetrates porous materials, rapidly aerates from materials and commodities, and has low sorption on fumigated materials
- Not an ozone depleter and does not interact or cause local ozone formation
- New mode of action can be utilized for resistance management strategies

The Sulfuryl fluoride Story

Red flour beetle
Courtesy of Cereal Research Centre, AAFC

History: Postharvest insect pests that infest grains and dried fruits and tree nuts in mills, warehouses, and food storage facilities cause substantial economic and quality losses. Postharvest losses due to insects in the United States alone were estimated at $5 billion per year in a 1991 study.[2]

With the adoption of the Montreal Protocol, the phase out of methyl bromide in developed countries started, and the search for replacements began. About this time, Dow AgroSciences began reevaluating sulfuryl fluoride for use as a viable methyl bromide alternative for postharvest insect control.

Dow AgroSciences has registered and marketed Sulfuryl fluoride as Vikane* gas fumigant since 1961 in the United States. In Europe it is registered/licensed for use in Germany and Sweden.
It has been successfully used to fumigate more than one million structures including homes, museums, cathedrals, historical landmarks, rare book libraries, and scientific and medical research laboratories to eradicate termites and wood boring beetles.

Research Initiatives: Dow AgroSciences is actively researching and generating data to support tolerances in certain food commodities. When established, these tolerances will allow the use of Sulfuryl fluoride in flour mills, food processing facilities, warehouses, transportation vehicles, and stored grains. Dow AgroSciences is working in cooperation with researchers, food commodity groups, industry consultants and fumigators in Australia, Europe, Japan, and the United States to research and determine optimal dosage and application recommendations. Anticipated registration timelines would allow the use of Sulfuryl fluoride prior to the time when the methyl bromide phase-out is complete.

Pest Control Studies: Efficacy research is underway both in the laboratory and in the field to define dosages and treatment practices to optimize the control of key postharvest insect pests. Laboratory efficacy studies being conducted in cooperation with the USDA-ARS in Fresno, California; the Dried Fruit Association (DFA) of California, Central Science Laboratory in the UK; and Federal Biological Research Center for Agriculture and Forestry in Germany, and the University of Milan in Italy, and Laboratoire National des Denrées Stockées of Cenon-Bordeaux in France are defining the dosages required to control all the life stages of target pests under a range of fumigation conditions.

The laboratory findings are being validated by fumigations at multiple locations within Europe and the United States. These field trials have been designed to further refine fumigant dosages and to optimize fumigation practices. This research will lead to enhanced sealing techniques for increased gas confinement, more efficient fumigant introduction, monitoring, and aeration procedures.

Food Quality: Food quality studies have been conducted on a variety of dried fruits and tree nuts in cooperation with the DFA of California and other commodity groups. Similar studies on cereal grains, flour, and other key commodities have been conducted with food science experts. Protocols have been developed to meet the requirements of the food production industry in the United States and key countries in Europe. Results have shown that under proposed labeled use patterns, Sulfuryl fluoride does not negatively impact taste or quality of tested commodities.

Food Residues: Studies have been completed for cereal grains and dried fruit and tree nuts. Food tolerances are expected to be established on these commodities, which will permit the fumigation of the raw commodity and processed fractions in the United States. Uses of Sulfuryl fluoride for other commodities are in the process of being investigated. In Europe, sulfuryl fluoride will be evaluated under Directive 91/414 EEC.

Stewardship: Dow AgroSciences is committed to the stewardship of all its products and stewardship requirements/programs will be in place for Sulfuryl fluoride. As labels develop, stewardship requirements for authorized users will be specifically defined.

Registration Timelines: Dow AgroSciences is pursuing the following registrations for Sulfuryl fluoride:

- 2002 – Dried fruit and tree nut Experimental Use Permit in California (walnuts and raisins only)
- 2002 – U.S. Section 3 (federal) registration approval and product launch in dried fruit and tree nuts
- 2002 – U.S. Section 3 (federal) registration approval and launch in cereal grains
- 2002/2003 – Registrations will be sort in a number of European countries including France, Germany, Italy, for emptied flour mills and storage facilities, dried fruits and tree nuts
- 2004 – U.S. Section 3 (federal) registration approval and launch in food processing

All registrations are subject to regulatory approval.

Indian meal moth

Biological Activity

Red flour beetles
Courtesy of Cereal Research Centre, AAFC

Introduction:
Efficacy testing in both the laboratory and the field has shown excellent control of a wide spectrum of insect pests. These include important pest species of the coleoptera and lepidoptera orders. Sulfuryl fluoride has been shown to control all life stages of insects, including diapausing stages and eggs.

Targeted Pests: A partial list of targeted pests is shown below:

Common Name	Scientific Name
Indian Meal Moth	*Plodia interpunctella*
Red Flour Beetle	*Tribolium castaneum*
Confused Flour Beetle	*Tribolium confusum*
Warehouse Beetle	*Trogoderma variabile*
Mediterranean Flour Moth	*Ephestia kuehniella*
Sawtoothed Grain Beetle	*Oryzaephilus surinamensis*
Codling Moth	*Cydia pomonella*
Navel Orangeworm	*Amyelois transitella*
Turkish Flat Grain Beetle	*Cryptolestes turcicus*
Yellow Mealworm	*Tenebrio molitor*
Lesser Grain Borer	*Rhyzopertha dominica*
Granary Weevil	*Sitophilus granarius*
Rice Weevil	*Sitophilus oryzae*
Rats	*Rattus spp.*
Mice	*Various spp.*

Warehouse beetle

Commodities: Dow AgroSciences is seeking registration for the use of Sulfuryl fluoride on cereal grains including whole kernels and processed fractions such as wheat (soft red, hard red, durum, and white) rice, corn (field and popcorn), barley and oats; dried fruits such as raisins, prunes, figs, apples, apricots, bananas, and dates; tree nuts including walnuts, almonds, hazelnuts, pecans, and all other tree nuts. Other commodities and processed foods are also being investigated.

Dosage: Fumigation dosage is measured as a product of both concentration (C) and exposure time (T), C x T in g-h/m^3. Because of variables in structures, the environment, pest species to be controlled, and other fumigation factors, each fumigation is different and therefore the amount of Sulfuryl fluoride needed per unit area is variable. The ProFume Fumiguide* calculator, a computer-based program, calculates dosages based on input of a wide range of fumigation variables.

Precision Fumigation: Dow AgroSciences will continue to research, develop, and promote "Precision Fumigation" Techniques. Precision Fumigation can be defined as optimizing fumigant use to maximize efficiency and minimize risk. Precision Fumigation is achieved by integrating all the factors affecting control, such as pest biology, temperature, exposure time, and improved sealing techniques into the fumigation management plan.

Sawtoothed grain beetle
Courtesy of Central Science Laboratory

Mode of Action: Once Sulfuryl fluoride enters an insect or other arthropod through the spiracles in postembryonic life stages, or diffusion through the egg shell, the compound is broken down to the insecticidally active fluoride anion. The fluoride anion disrupts the glycolysis and fatty acid cycles, depriving the insect of necessary cellular energy.

Insecticidal activity results from fluoride inhibition of enzyme systems utilizing magnesium within the glycolysis cycle.[3] After inhibition of the glycolysis and fatty acid cycles, insects attempt to utilize protein and amino acids to maintain a viable energy level, however, these alternative energy producing processes are insufficient to maintain a proper metabolic rate for survival.

Resistance Management: Modeling studies conducted for Indian meal moth (*Plodia interpunctella*) and red flour beetle (*Tribolium castaneum*) indicated that there is a very low probability for resistance development because of high rates of insect immigration, low selection pressure, no existence of resistance, and overlapping generations.

Preliminary results testing Sulfuryl fluoride efficacy on a strain of phosphine resistant red flour beetle indicated no cross-resistance. Further studies will be completed; however, resistance issues with Sulfuryl fluoride are not anticipated because of use patterns, unique mode of action, and lack of known cross-resistance to other fumigants.

Sulfuryl fluoride can also be used as part of an active, planned management program as a rotational treatment to prevent/delay development of insecticide resistance or as a tool to control phosphine resistant insect populations.

Granary weevils
Courtesy of Cereal Research Centre, AAFC

Description of Chemistry

Active Substance Name:

IUPAC Name:	*Sulfuryl fluoride*
CAS Name:	*Sulfuryl fluoride*
CAS Registry Number:	*2699-79-8*
Common Name:	*Sulfuryl fluoride*
Structure and Empirical Formula:	SO_2F_2

Physical Properties:

Molecular Weight:	*102.1 AMU*
Odor:	*Odorless*
Specific Gravity:	*4.18 mg/ml at 25°C and 760 mm Hg*
Melting Point:	*-136.7°C (-93.7°F) at 760 mm Hg*
Boiling Point:	*-55.2°C (-67°F) at 760 mm Hg*
Vapor Pressure:	*1611.467 kPa at 20° C*
Octanol Water Partition Coefficient (log K_{OW}):	*0.14 at 20°C*
Solubility in Water:	*750 mg/kg at 25°C*
Solvent Solubility:	*1-Octanol 14 g/l* *Heptane 22 g/l* *Ethyl Acetate 59 g/l* *1,2 dichloroethane 25 g/l* *Methanol 33 g/l* *Acetone 71 g/l*
Flammability:	*Non-Flammable*

Mammalian Toxicity

Introduction: Sulfuryl fluoride is an odorless, colorless gas and at low concentrations, non-irritating to mucous membranes and gives no warning of its presence. Sulfuryl fluoride is toxic and must be handled carefully in regard to the potential hazards it presents. Therefore, Sulfuryl fluoride presently is, and will continue to be, labeled for use only by trained, professional fumigators. Professional fumigators are trained in proper fumigation techniques.

Acute Toxicity: Oral ingestion of Sulfuryl fluoride is unlikely because of its physical properties and is not toxic dermally. The main route of exposure is through inhalation. Like other fumigants, Sulfuryl fluoride can cause adverse effects after acute exposure, depending on the exposure concentration and duration. A summary of acute toxicology data is provided below:

Study Type	Animal	Sex	Results
Acute Oral	Rat and Guinea Pig	n/a	LD_{50} 100 mg/kg
Acute Dermal	Rat, F-344	Male and Female	LC_{50} > 9599 ppm
Acute Inhalation	Rat, F-344	Male and Female	4-Hr LC_{50} 1122 ppm males 4-Hr LC_{50} 991 ppm females
Acute Inhalation	Rat, F-344	Male and Female	1-Hr LC_{50} 3730 ppm males 1-Hr LC_{50} 3021 ppm females
Acute Inhalation	Mice, B6C3F1	Male and Female	4-Hr LC_{50} 400-600 ppm
Acute Inhalation	Mice, CD1	Male and Female	4-Hr LC_{50} 400-600 ppm

Sub-Chronic Toxicity Studies: A summary of sub-chronic toxicology data is provided below:

Study Type	Animal	Sex	NOEL
Dietary study	Rat	Male and Female	19 ppm
13 wk inhalation	Rat, F-344	Male and Female	30 ppm
13 wk inhalation	Rabbit, NZW	Male and Female	30 ppm
13 wk inhalation	Mice, CD-1	Male and Female	30 ppm
13 wk inhalation	Dog, Beagles	Male and Female	100 ppm

Chronic Toxicity: Lifetime studies with rats and mice indicate that Sulfuryl fluoride is not carcinogenic, nor was there any evidence that it causes birth defects or has the potential to cause adverse reproductive or developmental effects.[4]

Courtesy of USDA

Ecotoxicology and Environmental Fate

Ecotoxicology

Because Sulfuryl fluoride is a gas and applied in closed spaces, the likelihood of exposure to non-target terrestrial and aquatic wildlife species is low. Ecotoxicology studies required for labeling and classification purposes have been conducted and summaries of data are below:

Study Description	Species and Strain	Value
Acute toxicity	Rainbow Trout	96h LC_{50} 0.89 mg/L
Acute toxicity	*Daphnia magna*	48h EC_{50} 0.62 mg/L
Algal growth inhibition	*Selanastrum capricornutum*	72h EC_{50} 0.58 mg/L

Environmental Fate

Dow AgroSciences was recently awarded the 2002 Stratospheric Ozone Protection Award by the U.S. Environmental Protection Agency (EPA) for the development of Sulfuryl fluoride gas fumigant. This award recognizes extraordinary achievements, international leadership, and innovation in preserving the Earth's protective stratospheric ozone layer. Nominated winners have demonstrated a commitment to environmental stewardship through their precedent-setting innovation and leadership.

Fate in Air: Sulfuryl fluoride is not an ozone-depleting chemical.[5][6] It contains no chlorine or bromine and therefore does not contribute to stratospheric ozone depletion. Sulfuryl fluoride is broken down mainly through hydrolysis to release fluorosulfate then fluoride and sulfate. Because it is fully oxidized, it does not interact with or contribute to local ozone formations.[6][7] The relatively small amounts of Sulfuryl fluoride released are calculated to have virtually no impact on the global atmosphere. Standard atmospheric modeling indicates that Sulfuryl fluoride will have an insignificant contribution to global warming because of the low Sulfuryl fluoride/carbon dioxide ratio (<0.0001).

Fate in Soil: Predictive models using the physical properties of Sulfuryl fluoride estimate that less than $1x10^{-5}$ percent of Sulfuryl fluoride will be found in the soil at equilibrium. This is due to the high vapor pressure, which results in rapid dissipation into the atmosphere.

Fate in Water: Sulfuryl fluoride quickly hydrolyzes in water to form fluorosulfate then sulfate and fluoride. Degradation rates increase with increases in aqueous pH. The half-life for Sulfuryl fluoride in water with pH's of 5.9, 8.1, and 9.2 is 3 days, 18 minutes, and 1.8 minutes, respectively.

Food Residues and Worker Exposure

Sulfuryl fluoride and fluoride Residues

- Sulfuryl fluoride residues are transient in fumigated commodities. Sulfuryl fluoride rapidly dissipates following proper aeration procedures. Research on fumigated commodities showed low levels of Sulfuryl fluoride following fumigation and proper aeration. The common residue following fumigation is fluoride.

- Governmental fluoride standards have been set after extensive review of toxicological, medical, and epidemiological data that included consideration of women and children. Reviews were completed by the World Health Organization (WHO) in 1984, the U.S. Public Health Service, Department of Health and Human Services, 1991, and the National Research Council, 1993.

- Dow AgroSciences is working with the EPA and European Authorities to set acceptable residue levels of fluoride in food fumigated with Sulfuryl fluoride.

Worker Exposure

- Like all fumigants, Sulfuryl fluoride can cause adverse effects after acute exposure, depending on the exposure concentration and duration. Therefore, Sulfuryl fluoride is labeled for use only by trained, professional fumigators.

- Exposure Guidelines: Both the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) and Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PEL) are 5 ppm on a Time Weighted Average (TWA). OSHA Short Term Exposure Limit (STEL) is 10 ppm. PEL's are in accord with those recommended by OSHA as in the 1989 revision of PELs.

- A NIOSH or MSHA approved positive-pressure self-contained breathing apparatus (SCBA, not SCUBA) or an air-supplied/SCBA respirator is necessary when entering areas being fumigated where the concentration is unknown or is greater than 3 ppm as measured by a detection device with sufficient sensitivity.

- Eye protection requires wearing goggles or full-face shield during fumigant introduction. No special skin protection is recommended. Skin contact with the liquid may cause freeze damage where the liquid is confined to the skin.

Formulations

Sulfuryl fluoride is formulated as liquid Sulfuryl fluoride (99.8%) packaged under pressure in steel cylinders.