



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES

**MEMORANDUM**

**Date:** 28 May 2009

**SUBJECT:** **Sulfuryl Fluoride.** Human Health Assessment Scoping Document in Support of Registration Review.

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**Petition No.:** N/A  
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**TXR No.:** N/A  
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**40 CFR 180.575**

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**Executive Summary**

Sulfuryl Fluoride (SO<sub>2</sub>F<sub>2</sub>) is an insecticide first registered as Vikane<sup>®</sup> for fumigation of structures in 1959, and has been deemed by EPA (both OPP and OAR) to be a methyl bromide alternative. A Reregistration Eligibility Decision (RED) for sulfuryl fluoride (SF) was completed by the Agency in September 1993. In 2000 the Agency was petitioned to grant an experimental use permit for the fumigation of raisins and walnuts with ProFume<sup>®</sup>, which contains 98% SF. Since that time, subsequent petitions have resulted in numerous food-use registrations of SF associated with treatment of food storage and processing facilities as well as direct treatment of foodstuffs.

SF and its breakdown product, fluoride, are residues of concern for both tolerance and risk-assessment purposes, and OPP has conducted separate assessments addressing the risks associated with each. The toxicological database for SF is currently considered to be complete, with the exception of an immunotoxicity study which is newly required due to changes in 40 CFR Part 158. The available toxicology data for SF show that the primary effect is vacuolation of the white matter of the brain (a neurotoxic effect). Based on the use pattern for sulfuryl fluoride and several reported incidences of human poisonings in the RED (September, 1993) and elsewhere in the general toxicological literature, the Agency has classified sulfuryl fluoride as Toxicity Category I for acute inhalation toxicity. The acute dermal toxicity study (assumed Toxicity Category of IV), the primary skin irritation study (assumed Toxicity Category of IV), the primary eye irritation study (assumed Toxicity Category of I), and the dermal sensitization study (assumed to be a non-sensitizer) have been waived. In a non-guideline study in which rats were dermally exposed (with no inhalation exposure) to vapors of SF gas at an exposure concentration of 9599 ppm for 4 hours, no treatment-related adverse effects were observed. Risk assessments for SF are currently based on the vacuolation effects. Although the Agency has waived the need for an inhalation developmental neurotoxicity study for SF, a 10-fold database uncertainty factor has been retained due to uncertainty regarding the regulatory endpoints.

Based on the currently available toxicological data, use pattern information, and risk assessment strategies, residential and occupational acute-, short-, intermediate-, and long-term quantitative risk estimates are below HED's level of concern. Occupational risks assume SF concentrations are below 1 ppm prior to reentry of fumigated spaces, as per the use label. Dietary and aggregate risk estimates for chronic exposure to SF are below HED's level of concern based on average residue values from fumigations at the maximum treatment rate.

For fluoride, OPP has relied on the Office of Water regarding toxicological effects and points of departure. Currently, the effect of concern is skeletal fluorosis with a maximum allowable intake of 8 mg/day (0.114 mg/kg/day for a 70-kg adult). The Office of Water is currently re-examining the toxicological database for fluoride and may derive a new RfD based on recommendations from a recent National Academy of Sciences' review of fluoride (March 2006).

OPP risk assessments for fluoride have taken into account exposure from the uses of SF and cryolite (another insecticide that forms fluoride upon breakdown), from fluoride in drinking water, from background levels of fluoride in foods, from incidental ingestion of toothpaste, and from inhalation of fluoride-contaminated air (as may occur near smelting operations). Residue estimates for these sources are mid- to high-end values. The resulting aggregate risk estimates for skeletal fluorosis are below HED's level of concern for all population subgroups.

During registration review, the following items need to be addressed:

- Lack of an immunotoxicity study (OPPTS 870.7800);
- Obtain and evaluate an inhalation developmental neurotoxicity study (OPPTS 870.6300);
- Evaluate the points of departure for risk assessment as well as associated uncertainty factors in accordance with current guidance;
- Evaluation of inhalation toxicity for humans via development of a human-equivalent concentration (HEC) for different durations of exposure;

- Develop risk assessments in accordance with fumigant guidelines currently under development;
- Evaluate the potential for bystander exposure and incorporate these exposure estimates into an aggregate risk assessment, as appropriate;
- Complete a new occupational exposure assessment to incorporate newly submitted data (not yet reviewed) as well as requested data (via the DCI process) regarding worker exposures;
- Conduct additional occupational exposure scenarios to ensure that all the appropriate worker populations and job tasks are included in the analysis (including activities being conducted near fumigation operations);
- Evaluate available worker exposure data for ethical compliance;
- Incorporate information regarding the fluoride analytical method and transfer of fluoride to livestock, as deemed necessary;
- To the extent possible, harmonize SF tolerances; and
- Reexamine the fluoride risk assessment as necessary based on the forthcoming hazard and relative source contribution assessments being developed by the Office of Water.

## **Introduction**

The HED SF Registration Review Team has evaluated the human health risk assessments and the available information for SF and fluoride to determine what new data and risk assessments may be needed for registration review. The most recent aggregate risk assessment for SF and fluoride (M. Doherty *et al.*, 18 January 2006, D312659) was completed as part of the Agency's review of a petition to establish uses of SF on various foods and in food processing facilities. A comprehensive listing of the documents that were consulted is provided in the reference section below.

Technical grade SF (99.8% active ingredient) is marketed as a liquefied gas in pressurized steel cylinders. Sulfuryl fluoride, as Vikane<sup>®</sup>, is registered for fumigation of closed structures such as domestic dwellings, garages, barns, storage buildings, commercial warehouses, ships in port, and railroad cars. It is primarily used in the southeast and southwest U.S. and in Hawaii to control drywood termites; however, it is also used to control powder post beetles, old house borers, bedbugs, carpet beetles, clothes moths and cockroaches as well as mice and rats. As Profume<sup>®</sup>, SF may be used to fumigate warehouses, mills, and other structures/containers containing food as well as for the fumigation of foods directly. Tolerances associated with these food uses range from 0.01 ppm to 15 ppm for SF [40 CFR 180.575], and from 3 ppm to 900 ppm for fluoride [40 CFR 180.145].

The primary sources for determining the status of the SF database were the RED for Vikane and the assessments prepared by OPP to evaluate the requested food uses of SF as ProFume. A comprehensive open-literature search was not completed. Screening-level searches (Google Scholar, Science Direct) indicate a lack of new information since the 2006 assessment that would impact the aggregate human health risk assessment for SF. As previously noted, the Agency's Office of Water is currently examining the hazard information that is available for fluoride; hence, an open-literature search for fluoride was not conducted.

## Hazard Identification/Toxicology

The toxicological profile of SF is presented in Tables D1 and D2. Sulfuryl fluoride is acute to moderately toxic via oral exposure (Toxicity Category II). Based on rodent toxicity, the use pattern for SF and several reported incidences of human poisonings in the general toxicological literature, the Agency has classified SF as Toxicity Category I for acute inhalation toxicity. When released from pressurized steel cylinders, SF causes freezing of skin and eye tissues on contact. Therefore, no dermal studies or eye irritation studies have been required to be submitted. The acute dermal and primary skin irritation study (assumed Toxicity Category IV), primary eye irritation study (assumed Toxicity Category I) and the dermal sensitization studies (assumed to be a non-sensitizer) have been waived.

In 2-week inhalation studies in rats, dogs and rabbits, different target organs were affected. In rats, the primary target organ was the kidney, in which severe histopathological lesions were observed. In dogs, the primary target organ was the upper respiratory tract, in which minimal inflammation was observed. Intermittent tremors and tetany were also noted in dogs. In rabbits, the primary target organ was the brain, in which malacia (necrosis) and vacuolation were observed in the cerebrum. Inflammation of the upper respiratory tract was also noted in rabbits.

In subchronic (90-day) and chronic (1-2 year) inhalation studies in rats, mice, dogs and rabbits, the brain was the major target organ. Malacia and/or vacuolation were observed in the white matter of the brain in all four species. In dogs and rabbits, clinical signs of neurotoxicity were also observed. Inflammation of the nasal passages and histiocytosis of the lungs were observed in rats and rabbits, but not in dogs, in which species inflammation of the upper respiratory tract was more prominent in the 2-week study. In mice, follicular cell hypertrophy was noted in the thyroid gland. Decreased body weights and body weight gains were also observed in rats, dogs and mice. In many subchronic and chronic inhalation studies in rats, dogs, and rabbits, dental fluorosis was the most sensitive effect observed. SF is classified as “Not likely to be carcinogenic to humans” based on carcinogenicity studies in rats and mice. There was no evidence for mutagenicity in both *in vivo* and *in vitro* assays.

SF did not produce any developmental toxicity in rats despite severe maternal toxicity. Pup and offspring body weights were reduced in developmental rabbit and rat reproduction studies, respectively. In all studies, maternal and parental NOAELs were lower than or equivalent to the developmental offspring NOAELs. No reproductive toxic effects were observed in rats following exposure to SF.

In April 2004, the Health Effects Division granted a waiver for the DNT based on the lack of chronic dietary exposure, minimal short-term exposure, animal welfare concerns, and a rat metabolism study which shows that SF is rapidly metabolized to fluoride. However, there remains uncertainty in the absence of a DNT; therefore, EPA has retained the FQPA 10X factor in assessing the risk posed by SF. Recent advances in study technique have made inhalation DNTs appropriate for endpoint consideration (e.g. methyl bromide); therefore, HED is requesting that an inhalation DNT be completed for sulfuryl fluoride.

The endpoints used for risk assessment purposes from the most recent Human Health Risk Assessment (HED memo of 1/18/2006, M. Doherty, D312659) are shown in Table D3. An acute RfD was not determined because no toxicological endpoints attributable to a single exposure were identified in the available toxicology studies. The chronic RfD of 0.003 mg/kg/day was based on a NOAEL of 8.5 mg/kg/day (brain necrosis, decreased body and liver weights, and dental fluorosis) in a 90-Day subchronic inhalation toxicity study in rabbits. Applied uncertainty factors included 10x for intraspecies variation, 10x for interspecies extrapolation, 10x for database uncertainty for the lack of a DNT study, and 3x for using a subchronic study for chronic assessment. Chronic dog and chronic rat studies were available but were not selected as the basis for the RfD because the effects from the rabbit study are considered to be more severe and the chronic RfD based on the effects in the 90-day study would be protective of the effects (e.g., dental fluorosis) seen following chronic exposure.

Endpoints were not selected for incidental oral and dermal scenarios due to the low potential for exposure.

Endpoints were selected for occupational short-, intermediate-, and long-term inhalation risk assessment. The short-term inhalation dose and endpoint for risk assessment are the NOAEL of 30 mg/kg/day based on brain necrosis and inflammation of the respiratory tissues observed at the LOAEL of 90 mg/kg/day in a 2-week inhalation study in rabbits. The intermediate- and long-term inhalation dose and endpoint for risk assessment are the NOAEL of 8.5 mg/kg/day based on brain necrosis observed at the LOAEL of 28 mg/kg/day in a 90-day subchronic inhalation study in rabbits.

For fumigants and other active ingredients for which inhalation toxicity is the primary concern, HED is currently calculating human equivalent concentrations (HECs) based on the available inhalation animal studies for fumigants. Physiological differences between human and the study animal respiratory pathways are considered during the calculation of the HEC. Therefore, the pharmacokinetic portion of the  $UF_{\text{animal}}$  is removed. While not required, comprehensive histological evaluations of the respiratory tract, preferably 6 levels of the nasal passages is suggested. Study duration should be appropriate for anticipated exposure scenarios. The absence of these data may result in increased uncertainty around the endpoints.

To support registration review, a search of the open literature was conducted for toxicity studies involving SF using a database of the National Library of Medicine's TOXNET System and the Google scholar search. No additional studies relevant to HED's human health risk assessments were found.

As specified in the revised 40 CFR Part 158 data requirements, an immunotoxicity study on SF should be conducted (Table D4).

### ***Conclusions for Hazard Identification/Toxicology***

As specified in the revised 40 CFR Part 158 data requirements, an immunotoxicity study on SF should be conducted. The endpoints and safety factors used for risk assessment purposes from the most recent Human Health Risk Assessment are still appropriate; however, it may be

appropriate to calculate an HEC to evaluate risk via the inhalation route. While not required by the Agency, the absence of an inhalation toxicity study with comprehensive evaluations of the respiratory tract may result in increased uncertainty around the endpoints. A 3X uncertainty factor to address the use of a subchronic study to establish a chronic endpoint is currently in place for SF. This uncertainty factor will need to be reconsidered during registration review. In addition, HED is now requesting that an inhalation DNT be completed for sulfuryl fluoride. Although this study was previously waived due to the technical difficulties associated with this type of study, recent progress in study techniques have made an inhalation DNT a viable study for consideration in risk assessment.

## **Dietary Exposure**

The Dietary Exposure Evaluation Model (DEEM) incorporating the 1989-1992 Continuing Surveys of Food Intakes by Individuals (CSFII) was used to estimate dietary exposure for the most recent SF risk assessment. The dietary assessments for both SF and fluoride assumed average residues from fumigations conducted at the maximum rate and incorporated percent crop treated estimates from the Biological and Economics Analysis Division (BEAD, 2005). Risk estimates for SF and fluoride are below HED's level of concern for all population subgroups (Attachment E). Refinements to the dietary assessment for fluoride have been submitted by Dow AgroSciences and the document is currently under review by HED. If found to be acceptable, some of the refinements for fluoride may be suitable for refining the SF exposure as well (e.g., % crop treated estimates). Revisions to the hazard assessment for fluoride by OW may necessitate a new dietary risk assessment.

The most recent risk assessment requested data pertaining to use of a total fluoride analytical method as well as information on the transfer of fluoride to livestock commodities. Those data have been submitted and are currently in need of review by OPP.

### ***Conclusions for Dietary Exposure***

During registration review a new dietary exposure assessment for SF may be needed to incorporate new % crop treated information. A new fluoride dietary assessment may be needed to incorporate % crop treated information as well as revised residue estimates based on total fluoride and use pattern information recently submitted by Dow AgroSciences.

## **Residential Exposure**

No residential scenarios have been assessed for sulfuryl fluoride. The Agency has historically assumed that, provided adequate aeration of dwellings is completed prior to re-entry, exposure to owners of fumigated structures is expected to be negligible given proper aeration procedures are in place; however, there is the potential for bystander exposures which can occur from emissions during treatment and aeration of commodities and structures. For registration review and as per other fumigants, these exposures will need to be characterized, including the use of computer modeling analyses (e.g., PERFUM) and estimation of potential buffer zones (J. Dawson and C. Smith, D353906, 6 November 2008).

There is sufficient information to complete such analyses for SF. However, more refined analyses are possible. If desired, a sampling strategy should be developed for field studies to be used as a source of additional empirical data. The following factors need to be considered in order for OPP to use the collected data to further characterize the potential risks from sulfuryl fluoride: site selection, building structure, volume, emissions related to specific aeration methods, application rate, release height and air exchange rates, historical emissions data, storage stability, analytical method used to analyze the ambient concentration samples, quality control data, flow rate, and sampling scheme, among others. To the extent that these data show potential for bystander exposure, residential assessments may be needed during registration review.

### ***Conclusions for Residential Exposure***

Revisiting the residential risk assessment during registration review is recommended. As per prior fumigant risk assessments, bystander risk to SF emissions from treated commodities and structures may need to be evaluated based on SF emissions, the label prescribed use conditions, and the durations of the applicable HECs.

### **Aggregate Risk Assessment**

Based on OPP's current understanding, the aggregate exposure and risk estimates for SF are equivalent to the dietary exposure and risk estimates and are currently below HED's level of concern.

### ***Conclusions for Aggregate Risk***

Dietary exposure estimates for both SF and fluoride are likely to be revised during registration review; therefore, new aggregate risk estimates will need to be calculated. In addition, bystander exposure estimates may need to be incorporated into the evaluation of aggregate risk.

### **Occupational Exposure**

ProFume is dispensed as a gas from a steel cylinder through a hose into the interior of an enclosed, sealed structure. People must be evacuated from the structure before it is treated. After treatment, the structure remains closed for a period of time after which aeration begins. The label prohibits people not wearing a NIOSH-approved self contained breathing apparatus (SCBA) from entering the treated areas until air levels of sulfuryl fluoride have declined to 1 part per million (ppm) or less. Because sulfuryl fluoride is a Restricted Use Pesticide, it may only be applied by or under the direct supervision of a trained, certified applicator.

### **Occupational Handlers**

No data regarding the number of exposure days per year for occupational workers were provided. Inhalation exposures were assessed for short-, intermediate-, and long-term durations. The use rates and aeration restrictions for sulfuryl fluoride are the same for both the Vikane<sup>®</sup> and Profume<sup>®</sup> products; therefore, occupational assessment of the food uses associated with Profume<sup>®</sup> are applicable to the non-food, structural uses of Vikane<sup>®</sup>. Since no dermal endpoint

was selected, HED has not estimated occupational risks associated with dermal exposures.

No worker exposure data were submitted to the Agency regarding the fumigation of food commodities. Although HED has not finalized its guidance on data requirements and risk assessment approaches for commodity/structural fumigations, it is likely that data regarding potential worker exposure associated with commodity fumigation will be required. As part of the registration review, data used to refine emission rates for bystander exposure calculations could be used to refine current approaches for model parameterization for this use pattern.

HED previously reviewed worker exposure data from the fumigation of numerous tarped structures with sulfuryl fluoride. Currently, MOEs are at or greater than HED's LOCs (Attachment F).

Since sulfuryl fluoride has been deemed by EPA to be a methyl bromide alternative and due to the similarities of these chemicals, the data requirements used by the Agency to assess exposures to MeBr should be the standard when assessing sulfuryl fluoride. As noted below, in the course of preparing the scoping document, HED is gathering additional information related to data requirements and new policies, and this information should be used to conduct updated occupational exposure assessments during registration review.

Furthermore, HED notes that forthcoming fumigant assessment guidelines will need to be taken into consideration when evaluating the quality and completeness of future data submissions (Dawson J. and Smith C.; D353724, July 2008 and D306857, 9 June 2008).

A number of studies were submitted to the Agency since the RED was completed (Appendix G), and will need to be evaluated during registration review; these studies provide air monitoring data at a variety of fumigation sites. These data will be used for refining the current occupational risk assessments. Emerging approaches such as the use of real-time monitoring devices, modeling emissions from fumigated commodities, and forthcoming guidelines will be included in the Agency's evaluation of SF.

#### Occupational Post-Application Workers

Further consideration may be given to post-application exposures pending future evaluation of the air monitoring data submitted. As part of registration review, tasks for workers near fumigation facilities/operations need to be defined to properly assess post-application activities (i.e. aerators, fork-lift operators, etc.). Potential exposures due to off-gassing will be assessed for workers conducting post-application activities near treatment operations.

#### ***Conclusions for Occupational Exposure***

The Agency believes that most applicator exposures are likely to be of a shorter duration (i.e., acute or short-term by agency definition). A much smaller percentage of the overall user population is expected to have longer duration exposures (i.e., intermediate-term or chronic). A new occupational handler risk reassessment should be completed during registration review to incorporate recently submitted data that have not yet been reviewed as well as data requested under the data call-in process, a human equivalent concentration calculated for workers (based

on 8 hours of exposure), and to the extent that they are available, policies currently under development regarding assessment of fumigant chemicals. The existing data for workers' exposure to sulfur fluoride are limited in terms of the variety of post-application activities. Emission-rate data for potential exposures due to off-gassing from treated facilities/commodities for workers conducting post-application activities need to be submitted to the Agency.

### **Public Health and Pesticide Epidemiology Data**

A summary report listing incidents for SF reported to the OPP Incident Data System (IDS) has been provided for the docket (Memo, M. Hawkins, 3 February 2009). Seventy-one incidents are reported for the United States from 2002 to the present for the single chemical only. All incidents are associated with structural fumigation (Vikane<sup>®</sup>). The reported incidents will be screened in more detail during the development of the Final Work Plan (FWP) for SF.

### **Tolerance Assessment and International Harmonization**

Tolerances associated with the food uses of SF range from 0.01 ppm to 15 ppm for SF [40 CFR 180.575], and from 3 ppm to 900 ppm for fluoride [40 CFR 180.145]. Tolerances/MRLs are not harmonized for a number of commodities. Differences are generally small, and harmonization may be possible. An evaluation of residues, with the goal of determining the feasibility of harmonization should be undertaken during registration review.

### **Environmental Justice**

There do not appear to be any particular socioeconomic subgroups that may experience a higher degree of exposure to SF. There may be identifiable populations that experience higher degrees of exposure to fluoride. Such elevated exposures are generally associated with increased water consumption and the use of SF has little, if any, impact to those groups. Potential areas of environmental justice concerns, to the extent possible, will be considered in future human health risk assessments for SF and fluoride, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," [http://www.epa.gov/compliance/resources/policies/ej/exec\\_order\\_12898.pdf](http://www.epa.gov/compliance/resources/policies/ej/exec_order_12898.pdf). The Office of Pesticide Programs (OPP) typically considers the highest potential exposures from the legal use of a pesticide when conducting human health risk assessments, including, but not limited to, people who obtain drinking water from sources near agricultural areas, the variability of diets within the U.S., and people who may be exposed when harvesting crops. Should these highest exposures indicate potential risks of concern, OPP further refines the risk assessments to ensure that the risk estimates are based on the best available information.

### **Cumulative**

The Agency has not determined whether SF shares a common mechanism of toxicity with other chemical substances. Prior to a final Registration review decision for SF, the Agency will determine if there is any new information, such as new hazard or exposure data or information on changes to the use pattern, which would affect the need for a cumulative risk assessment. Should the Agency determine that new information on SF is available that could potentially

trigger the need for a cumulative risk assessment and result in a risk of concern, the Agency will revisit the cumulative risk assessment. Risk estimates for fluoride are evaluated through a separate risk assessment.

## **Human Studies**

Sulfuryl fluoride occupational risk assessments relied in part on data from a study in which adult human subjects were involved (Jaquith, D., D229345, 12 December 2000). This study appears to be an “observational” study and, therefore, not subject to the need for Human Studies Review Board (HSRB) evaluation. Registration review should include an ethics evaluation of this study as well as other similar studies that have been submitted to the Agency (see Appendix G).

## **Data Requirements**

### Toxicology (See Table D4)

*870.6300 Developmental Neurotoxicity.* OPP had waived this study for reasons of technical difficulty. Recent advances in study technique have made inhalation DNTs appropriate for endpoint consideration (e.g. methyl bromide); therefore, HED is requesting that an inhalation DNT be completed.

*870.7800 Immunotoxicity in rats.* This study is required as per the recently revised pesticide registration data requirements (40 CFR Part 158).

### Residue Chemistry

None.

### Occupational/Residential Exposure (See Table G2)

*875.1400 Inhalation Exposure Study for Applicators.* These studies are required to assess exposures for applicators involved in fumigating commodities/materials and/or structural facilities.

*875.1700 Product Use Information.* This study is required to assess product use information parameters by major use region, frequency, and application equipment.

*875.2500 Post-Application Inhalation Exposure Study.* This study is required to assess post-application exposures for workers near fumigation facilities/operations or who work directly with previously treated commodities/materials.

*875.2500 Post-Application Inhalation Exposure Study.* This study is required to assess post-application exposure levels from indoor air in residences that are in proximity to fumigation activities.

875.2500 *Post-Application Inhalation Exposure Study*. This study is required to assess ambient air concentrations for communities in proximity to treated facilities.

*Special Studies - Monitoring data on fumigated commodities*. Special studies are required to evaluate emission rates for sulfuryl fluoride from treated commodities/materials and the potential for occupational exposure due to those emissions in the channels of trade after fumigation activities are complete.

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National Research Council of the National Academy of Sciences. Fluoride in Drinking Water: A Scientific Review of EPA's Standards. The National Academies Press. March 2006.

## Attachments

### A. Chemical Identity

Sulfuryl fluoride ( $\text{SO}_2\text{F}_2$ ) is a gas at standard temperature and pressure. It has a melting point of  $-136^\circ\text{C}$ , a boiling point of  $-55^\circ\text{C}$ , and a vapor pressure of 11552 mm Hg (Torr) at  $20^\circ\text{C}$ . At  $20^\circ\text{C}$ , sulfuryl fluoride has a vapor density of 4.3 g/L (heavier than air) and is both colorless and odorless. The log  $K_{\text{OW}}$  is estimated to be 0.41. Sulfuryl fluoride has a very low solubility in water (0.075 g/100 g). Solubilities in other solvents are 0.78 g/100 g in Wesson oil, 1.74 g/100 g in acetone, and 2.12 g/100 g in chloroform. Sulfuryl fluoride rapidly breaks down to form sulfate and fluoride anion. As ProFume<sup>®</sup> and Vikane<sup>®</sup>, sulfuryl fluoride constitutes 99% of the product and there are no known impurities of toxicological concern.

Fluorine has an atomic mass of 18.99, is extremely electronegative and reactive, and occurs as the diatomic  $\text{F}_2$  in its elemental form. Due to its high reactivity, fluorine does not typically exist outside of the laboratory. In the environment, fluorine readily reacts with all other elements except nitrogen, oxygen, and the lighter noble gases to form various fluoride complexes. It is these fluoride complexes that govern the behavior and bioavailability of fluoride. Due to fluorine's ability to readily react with other elements and molecules, fluoride has the potential to occur in food, water, and air, and exposure to humans may occur through any of these media.

B. Products and Use Patterns

The fumigation rate for sulfuryl fluoride is the product of the fumigant concentration and exposure time. The maximum target rate is 1500 mg·hr/L for normal atmospheric fumigations and 200 mg·hr/L for vacuum fumigations. Double fumigations are recommended for insect infestations where eggs may be present, with the second fumigation timed to control newly hatched, immature stages. The proposed label specifies that all food commodities be aerated for a minimum of 24 hours prior to the foods entering commerce. All structures must be aerated to a sulfuryl fluoride level of no more than 1 ppm prior to re-entry unless SCBA is worn.

<b>Table B.1. Summary of Directions for the Use of Sulfuryl Fluoride from the Proposed Label</b>						
Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Max. per Applic. Rate (mg·hr/L)	Max. No. Applic. per Batch	Max. Cumulative Applic. Rate (mgAhr/L)	Aeration (hours)	Use Directions and Limitations
Fumigation of foods and sealed food processing facilities	ProFume [62719-376]	1500 (ambient pressure) 200 (vacuum fumigation)	2	1500 (ambient pressure) 200 (vacuum fumigation)	24	Food commodities must be aerated for 24 hours prior to entering commerce.
Fumigation of structures	Vikane [62719-4]	1500	Not Applicable	Not Applicable	24	Workers must wear SCBA while levels of sulfuryl fluoride are in excess of 1 ppm.

### C. Residue Chemistry

Summary of US and International Tolerances and Maximum Residue Limits for Sulfuryl Fluoride [40 CFR 180.575]			
Commodity	Tolerances or MRLs (ppm)		
	US	Codex <sup>1</sup>	Canada <sup>2</sup>
All processed food commodities not otherwise listed	2.0	-	
Barley, bran, postharvest	0.05	0.1 (cereal) Po	
Barley, flour, postharvest	0.05		
Barley, grain, postharvest	0.1	0.05 (cereal) Po	
Barley, pearled barley, postharvest	0.05		
Cacao bean, roasted bean, postharvest	0.2		
Cattle, meat, dried	0.01		
Cheese	2.0		
Coconut, postharvest	1.0		
Coffee, bean, roasted bean, postharvest	1.0		
Corn, field, flour, postharvest	0.01	0.1 Po	
Corn, field, grain, postharvest	0.05	0.05 (cereal) Po	0.03
Corn, field, grits, postharvest	15.0		
Corn, field, meal, postharvest	0.01	0.1 Po	
Corn, pop. grain, postharvest	0.05	0.05 (cereal) Po	
Cotton, undelinted seed, postharvest	0.5		
Egg, dried	1.0		
Fruit, dried, postharvest	0.05	0.06 Po	0.05 (dried figs) 0.03 (dried prune plum) 0.01 (raisins, proposed 01/12/09)
Ginger, postharvest	0.5		
Grain, aspirated fractions, postharvest	0.05		
Herbs and spices group 19, postharvest	0.5		
Hog, meat	0.02		
Milk, powdered	2.0	0.05 (cream) Po	
Millet, grain, postharvest	0.1	0.05 (cereal) Po	
Nut, pine, postharvest	0.2		
Nut, tree, Group 14, postharvest	3.0	3 Po	3.0 (pecans) 0.04 (almonds, proposed 01/12/09)
Oat, flour, postharvest	0.05		
Oat, grain, postharvest	0.1	0.05 (cereal) Po	
Oat, groats/rolled oats, postharvest	0.1		
Peanut, postharvest	0.5		
Pistachio, postharvest	3.0		0.3
Rice, bran, postharvest	0.01	0.1 (cereal) Po	
Rice, flour, postharvest	0.05		
Rice, grain, postharvest	0.04	0.05 (cereal) Po	0.03
Rice, hulls, postharvest	0.1		
Rice, polished rice, postharvest	0.01	0.1 Po	
Rice, wild, grain, postharvest	0.05		
Sorghum, grain, grain, postharvest	0.1	0.05 (cereal) Po	
Triticale, grain, postharvest	0.1	0.05 (cereal) Po	
Vegetable, legume, group 6, postharvest	0.5		
Wheat, bran, postharvest	0.05	0.1 (cereal bran) Po	
Wheat, flour, postharvest	0.05	0.1 Po	
Wheat, germ, postharvest	0.02	0.1 Po	
Wheat, grain, postharvest	0.1	0.05 (cereal) Po	0.1
Wheat, milled byproducts, postharvest	0.05		
Wheat, shorts, postharvest	0.05		
Wheat, wholemeal	-	0.1 Po	
Rye flour	-	0.1 Po	
Rye wholemeal	-	0.1 Po	
Dates	-	-	0.01

<sup>1</sup> Residue definition for enforcement = sulfuryl fluoride. Po = postharvest

<sup>2</sup> Residue definition for enforcement = sulfuryl fluoride

D. Toxicology

Guideline No.	Study Type	MRID	Results	Tox Category
870.11	Acute Oral Rats	43314	M: LD <sub>50</sub> = 100 mg/kg F: LD <sub>50</sub> = 100 mg/kg	II*
870.12	Acute Dermal	-----	Study Waived *	IV**
870.13	Acute Inhalation Mice (4 hour exposure)	41769101	M: LC <sub>50</sub> = 660 ppm (2.56 mg/L) F: LC <sub>50</sub> = 642 ppm (2.49 mg/L)	I*
870.13	Acute Inhalation Rats (1 hour exposure)	238663	LC <sub>50</sub> = 4512 ppm ( 17.5 mg/L)	I*
870.24	Primary Eye Irritation	-----	Study Waived *	I**
870.25	Primary Skin Irritation	-----	Study Waived *	IV**
870.26	Dermal Sensitization	-----	Study Waived *	Non-Sensitizer **
-----	Dermal Vapor Rats (4 hour dermal exposure)	41712001	No adverse effects at 9600 ppm (40.3 mg/L)	N/A

\* Memorandum by M. Lewis (SRRD) to V. Dutch (SRRD), 11/17/99, HED Doc. No. 078003.

\*\* Assumed Toxicity Category. See memorandum by M. Lewis (above).

N/A Not applicable

Guideline No.	Study Type	Results
-----  (inhalation study)	2-Week inhalation toxicity, rats  0, 100, 300, 600 ppm (0/0, 83/89, 249/267, 498/534 mg/kg/day) (M/F)	<b>NOAEL:</b> 83/89 mg/kg/day (M/F) <b>LOAEL:</b> 249/267 mg/kg/day (M/F): M&F = slightly increased kidney weights, minimal histopathology in kidney. <u>At 498/534 mg/kg/day (M/F):</u> M&F = high mortality, decreased body weights, severe histopathology in kidney, gross and histopathology in many tissues/organs (secondary to kidney effects); severe inflammation of respiratory tissues in 1 survivor. No treatment-related neurotoxicity.
-----  (inhalation study)	2-Week inhalation toxicity, dogs  0, 30, 100, 300 ppm (0/0, 7.9/8.0, 26/27, 79/80 mg/kg/day) (M/F)	<b>NOAEL:</b> 26/27 mg/kg/day (M/F) <b>LOAEL:</b> 79/80 mg/kg/day (M/F): M&F = intermittent tremors and tetany during exposures, minimal inflammatory changes in upper respiratory tract, decreased body weight (F only). <u>Note</u> Bincreased serum fluoride at ≥26/27 mg/kg/day.

**Table D.2. Toxicity Profile of Technical Grade Sulfuryl Fluoride (99.8% active ingredient)**

Guideline No.	Study Type	Results
-----  (inhalation study)	2-Week inhalation toxicity, rabbits  0, 100, 300, 600 ppm (0/0, 30/30, 90/90, 180/180 mg/kg/day) (M/F)	<b>NOAEL:</b> 30/30 mg/kg/day (M/F) <b>LOAEL:</b> 90/90 mg/kg/day (M/F): M&F = malacia (necrosis) in cerebrum, vacuolation of cerebrum, moderate inflammation of respiratory tissues. <u>At 180/180 mg/kg/day (M/F):</u> M&F = convulsions, hyperactivity, malacia (necrosis) in cerebrum, vacuolation of cerebrum, moderate inflammation of respiratory tissues.
(870.3100)  (inhalation study)	90-Day inhalation toxicity, rats  0, 30, 100, 300 ppm (0/0, 24/25, 80/83, 240/250 mg/kg/day) (M/F)	<b>NOAEL:</b> 24/25 mg/kg/day (M/F) <b>LOAEL:</b> 80/83 mg/kg/day (M/F): M&F = dental fluorosis. <u>At 240/250 mg/kg/day (M/F):</u> M&F = vacuolation of caudate-putamen nucleus and white fiber tracts of the internal capsule of the brain, decreased body weight, inflammation of nasal passages, alveolar histiocytosis; slight hyperplasia of renal collecting ducts (F only).
(870.3100)  (inhalation study)	90-Day inhalation toxicity, mice  0, 10, 30, 100 ppm (0/0, 12.5/12.1, 38/36, 125/121 mg/kg/day) (M/F)	<b>NOAEL:</b> 38/36 mg/kg/day (M/F) <b>LOAEL:</b> 125/121 mg/kg/day (M/F): M&F = microscopic lesions in caudate-putamen nucleus and external capsule, decreased body weight, decreased body weight gain, follicular cell hypertrophy in thyroid. <u>Note</u> Bincreased serum fluoride at $\geq 38/36$ mg/kg/day.
(870.3150)  (inhalation study)	90-Day inhalation toxicity, dogs  0, 30, 100, 200 ppm (0/0, 7.5/7.6, 25/26, 50/51 mg/kg/day) (M/F)	<b>NOAEL:</b> 25/26 mg/kg/day (M/F) <b>LOAEL:</b> 50/51 mg/kg/day (M/F): M&F = slight histopathology of the caudate nucleus of the basal ganglia, decreased bodyweight, decreased body weight gain, transient neurological signs (lateral recumbancy, tremors, incoordination, salivation, tetany, inactivity) starting at day 19 in 1 M.
(870.3150)  (inhalation study)	90-Day inhalation toxicity, rabbits  0, 30, 100, 600/300* ppm (0/0, 8.6/8.5, 29/28, 86/85 mg/kg/day) (M/F)  * 600 ppm reduced to 300 ppm after 9 exposures due to convulsions and hind leg paralysis .	<b>NOAEL:</b> 8.6/8.5 mg/kg/day (M/F) <b>LOAEL:</b> 29/28 mg/kg/day (M/F): M&F = decreased body weight, decreased liver weight, dental fluorosis, vaculoation of white matter of the brain (F only). <u>At 86/85 mg/kg/day (M/F):</u> M&F = malacia (necrosis) and vacuolation of putamen, globus pallidus and internal & external capsules in brain, decreased body weight gain, alveolar histiocytosis, histopathology in nasal epithelium. <u>Note</u> Bincreased serum fluoride at all dose levels ( $\geq 8.6/8.5$ mg/kg/day).
(870.3700)  (inhalation study)	Developmental toxicity inhalation study, rats  0, 25, 75, 225 ppm (0, 27, 81, 243 mg/kg/day)(F)	<b>Maternal NOAEL:</b> 243 mg/kg/day (F): highest dose tested. <b>Maternal LOAEL:</b> >243 mg/kg/day (F). <u>Note</u> -significant maternal toxicity observed in range-finding study at 300 ppm. <b>Developmental NOAEL:</b> 243 mg/kg/day (F): highest dose tested. <b>Developmental LOAEL:</b> >243 mg/kg/day (F)

<b>Table D.2. Toxicity Profile of Technical Grade Sulfuryl Fluoride (99.8% active ingredient)</b>		
Guideline No.	Study Type	Results
(870.3700)  (inhalation study)	Developmental toxicity inhalation study , rabbits  0, 25, 75, 225 ppm (0, 9.5, 29, 86 mg/kg/day)(F)	<b>Maternal NOAEL:</b> 29 mg/kg/day (F) <b>Maternal LOAEL:</b> 86 mg/kg/day (F): F = decreased body weight and decreased body weight gain during treatment. <u>Note</u> -significant maternal toxicity observed in range-finding study at 300 ppm. <b>Developmental NOAEL:</b> 29 mg/kg/day (F) <b>Developmental LOAEL:</b> 86 mg/kg/day (F): F = decreased fetal body weight, decreased crown-rump length, possibly increased fetal liver pathology (pale liver).
(870.3800)  (inhalation study)	2-Generation reproduction inhalation study, rats  0, 5, 20, 150 ppm (0/0, 3.6/3.6, 14/14, 108/108 mg/kg/day ) (M/F)	<b>Parental NOAEL:</b> 3.6/3.6 mg/kg/day (M/F) <b>Parental LOAEL:</b> 14/14 mg/kg/day (M/F): M&F = pale foci in lungs, increased alveolar macrophages in lungs. <u>At 108/108 mg/kg/day (M/F):</u> M&F = vacuolation of caudate putamen tracts in brain, decreased body weight, histopathology in lungs, dental fluorosis. <b>Offspring NOAEL:</b> 14/14 mg/kg/day (M/F) <b>Offspring LOAEL:</b> 108/108 (M/F): Decreased pup weights in F1 and F2 generations (probably secondary to maternal body weight loss).
870.41	Chronic toxicity, rats	See (870.4300)
(870.4100)  (inhalation study)	1-Year chronic inhalation toxicity, dogs  0, 20, 80, 200 ppm (0/0, 5.0/5.1, 20/20, 50/51 mg/kg/day) (M/F)	<b>NOAEL:</b> 5.0/5.1 mg/kg/day (M/F) <b>LOAEL:</b> 20/20 mg/kg/day (M/F): M&F = decreased body weight gain, increased alveolar macrophages in lungs, dental fluorosis. <u>At 50/51 mg/kg/day (M/F):</u> M&F = increased mortality, malacia (necrosis) in caudate nucleus of brain, follicular cell hypertrophy in thyroid, histopathology in lung.
870.42	Carcinogenicity, rats	See (870.4300)
(870.4200)  (inhalation study)	18-Month carcinogenicity inhalation study, mice  0, 5, 20, 80 ppm (0/0, 5.3/6.3, 25/25, 101/101 mg/kg/day) (M/F)	<b>NOAEL:</b> 25/25 mg/kg/day (M/F) <b>LOAEL:</b> 101/101 mg/kg/day (M/F): M&F = cerebral vacuolation in brain, decreased body weight gain; follicular cell hypertrophy in thyroid (M only); increased mortality (F only), heart thrombus (F only), lung congestion (F only).  No evidence of carcinogenicity in M and F.
(870.4300)  (inhalation study)	2-Year combined chronic toxicity/ carcinogenicity inhalation study, rats  0, 5, 20, 80 ppm (0/0, 3.5/3.9, 14/16, 56/62 mg/kg/day) (M/F)	<b>NOAEL (M):</b> 3.5 mg/kg/day <b>LOAEL (M):</b> 14 mg/kg/day: M = dental fluorosis. <u>At 56 mg/kg/day (M):</u> M = effects similar to those in F at 62 mg/kg/day. <b>NOAEL (F):</b> 16 mg/kg/day <b>LOAEL (F):</b> 62 mg/kg/day: F = greatly increased mortality (due mostly to severe kidney toxicity which led to kidney failure); histopathology in brain (vacuolation in cerebrum and thalamus/hypothalamus), adrenal cortex, eyes, liver, nasal tissue, and respiratory tract; dental fluorosis.  No evidence of carcinogenicity in M and F.
870.5100	Mutagenicity - Reverse gene mutation (S. typhimurium)	Negative without and with S-9 activation.
870.5395	Mutagenicity - <i>in vivo</i> micronucleus assay, mice (bone marrow cells)	Negative.

<b>Table D.2. Toxicity Profile of Technical Grade Sulfuryl Fluoride (99.8% active ingredient)</b>		
Guideline No.	Study Type	Results
870.5500	Mutagenicity - unscheduled DNA synthesis (primary rat hepatocytes)	Negative.
(870.6200)  (inhalation study)	Acute inhalation neurotoxicity study, rats (special design)  0, 100, 300 ppm ( 0, 118, 354 mg/kg/day) (F only)	<b>Systemic NOAEL:</b> 354 mg/kg/day (F): highest dose tested. <b>Systemic LOAEL:</b> >354 mg/kg/day (F). <b>Neurotoxic NOAEL:</b> 354 mg/kg/day (F): highest dose tested. <b>Neurotoxic LOAEL:</b> >354 mg/kg/day (F). <u>Note</u> -study included electrophysiological parameters, but no microscopic pathology.
(870.6200)  (inhalation study)	90-Day inhalation neurotoxicity study, rats (special design)  0, 30, 100, 300 ppm ( 0/0, 24/25, 80/83, 240/250 mg/kg/day) (M/F)	<b>Systemic NOAEL:</b> 24/25 mg/kg/day (M/F) <b>Systemic LOAEL:</b> 80/83 mg/kg/day (M/F): M&F = pale foci in pleura and macrophages in lungs, dental fluorosis <u>At 240/250 mg/kg/day (M/F):</u> M&F = decreased body weight, excessive salivation, poor grooming. <b>Neurotoxic NOAEL:</b> 24/25 mg/kg/day (M/F) <b>Neurotoxic LOAEL:</b> 80/83 mg/kg/day (M/F): M&F = disturbances in electrophysiologic parameters (slowing of VER and SER waveforms in F and ABR waveforms in M). <u>At 240/250 mg/kg/day (M/F):</u> M&F = slowing of all waveforms except CNAP, vacuolation of white matter in caudate putamen in cerebrum.  <u>Note</u> -study included electrophysiological parameters.
(870.6200)  (inhalation study)	1-Year inhalation neurotoxicity study, rats (special design)  0, 5, 20, 80 ppm ( 0/0, 3.5/3.9, 14/16, 56/62 mg/kg/day) (M/F)	<b>Systemic NOAEL:</b> 3.5/3.9 mg/kg/day (M/F) <b>Systemic LOAEL:</b> 14/16 mg/kg/day (M/F): M&F = dental fluorosis. <u>At 56/62 mg/kg/day (M/F):</u> M&F = increased kidney and liver weights, progressive kidney disease, histopathology in lung. <b>Neurotoxic NOAEL:</b> 56/62 mg/kg/day (M/F): highest dose tested. <b>Neurotoxic LOAEL:</b> >56/>62 mg/kg/day (M/F).  <u>Note</u> -study did <u>not</u> include electrophysiological parameters.
870.6300	Developmental neurotoxicity, rats	Study waived.
870.7485	Metabolism and pharmacokinetics, rats	Study waived in Reregistration Eligibility Document (RED) published by EPA in 1993.
870.7600	Dermal Penetration, rats	No study available. Not required.

<b>Table D.3. Summary of Dose and Endpoint Selection for use in Human Health Risk Assessments for Sulfuryl Fluoride</b>			
Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary	None UF = N/A	Not applicable	No toxicological endpoint attributable to a single exposure was identified in the available toxicology studies on sulfuryl fluoride.
Chronic Dietary (All populations)	NOAEL= 8.5 mg/kg/day UF = 3000* Chronic RfD = 0.003 mg/kg/day	FQPA SF = 1X cPAD = <u>chronic RfD</u> FQPA SF = 0.003 mg/kg/day	90-Day Inhalation - Rabbit LOAEL = 28 mg/kg/day based on vacuolation of white matter in the brain of females.
Incidental Oral (All durations)	None	Not applicable	Due to sulfuryl fluoride being a gas, no significant incidental oral exposure is anticipated. No quantification is required.
Dermal (All durations)	None	Not applicable	Due to sulfuryl fluoride being a gas and label restrictions, no significant dermal exposure is anticipated. Furthermore, no hazard was identified; therefore, no quantification is required.
Short-Term Inhalation (1 to 30 days)	Inhalation study NOAEL= 30 mg/kg/day (100 ppm; 0.42 mg/L)	Residential LOC = 1000** Occupational LOC = 100	2-Week Inhalation - Rabbit LOAEL = 90 mg/kg/day (300 ppm; 1.25 mg/L) based on malacia (necrosis) and vacuolation in brain, inflammation of nasal tissues and trachea.
Intermediate-Term Inhalation (1 to 6 months)	Inhalation study NOAEL = 8.5 mg/kg/day (30 ppm; 0.13 mg/L)	Residential LOC = 1000** Occupational LOC = 100	90-Day Inhalation - Rabbit LOAEL = 28 mg/kg/day (100 ppm; 0.42 mg/L) based on vacuolation of white matter in the brain of females.
Long-Term Inhalation (>6 months)	Inhalation study NOAEL = 8.5 mg/kg/day (30 ppm; 0.13 mg/L)	Residential LOC = 3000* Occupational LOC = 300	90-Day Inhalation - Rabbit LOAEL = 28 mg/kg/day (100 ppm; 0.42 mg/L) based on vacuolation of white matter in the brain of females.
Cancer (oral, dermal, inhalation)	Classified as "Not likely to be carcinogenic to humans"		

UF = uncertainty factor, FQPA SF = FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

\* Includes the conventional UF of 100 and a 10X FQPA safety factor and a 3X uncertainty factor for the use of a short-term study to assessing long-term risk.

\*\* Includes the conventional UF of 100 and a 10X FQPA safety factor.

<b>Table D.4. Toxicology Data Requirements</b>
<b>Guideline Number: 870.7800</b>
<b>Study Title: Immunotoxicity</b>
<b>Rationale for Requiring the Data</b>
<p>The immunotoxicity study is a new data requirement under 40 CFR Part 158 as a part of the data requirements for registration of a pesticide (food and non-food uses).</p> <p>The Immunotoxicity Test Guideline (OPPTS 870.7800) prescribes functional immunotoxicity testing and is designed to evaluate the potential of a repeated chemical exposure to produce adverse effects (i.e., suppression) on the immune system. Immunosuppression is a deficit in the ability of the immune system to respond to a challenge of bacterial or viral infections such as tuberculosis (TB), Severe Acquired Respiratory Syndrome (SARS), or neoplasia. Because the immune system is highly complex, studies not specifically conducted to assess immunotoxic endpoints are inadequate to characterize a pesticide's potential immunotoxicity. While data from hematology, lymphoid organ weights, and histopathology in routine chronic or subchronic toxicity studies may offer useful information on potential immunotoxic effects, these endpoints alone are insufficient to predict immunotoxicity.</p>
<b>Practical Utility of the Data</b>
<p><b>How will the data be used?</b></p> <p>Immunotoxicity studies provide critical scientific information needed to characterize potential hazard to the human population on the immune system from pesticide exposure. Since epidemiologic data on the effects of chemical exposures on immune parameters are limited and are inadequate to characterize a pesticide's potential immunotoxicity in humans, animal studies are used as the most sensitive endpoint for risk assessment. These animal studies can be used to select endpoints and doses for use in risk assessment of all exposure scenarios and are considered a primary data source for reliable reference dose calculation. For example, animal studies have demonstrated that immunotoxicity in rodents is one of the more sensitive manifestations of TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) among developmental, reproductive, and endocrinologic toxicities. Additionally, the EPA has established an oral reference dose (RfD) for tributyltin oxide (TBTO) based on observed immunotoxicity in animal studies (IRIS, 1997).</p> <p><b>How could the data impact the Agency's future decision-making?</b></p> <p>If the immunotoxicity study shows that the test material poses either a greater or a diminished risk than that given in the interim decision's conclusion, the risk assessments for the test material may need to be revised to reflect the magnitude of potential risk derived from the new data.</p> <p>If the Agency does not have these data, a 10X database uncertainty factor may be applied for conducting a risk assessment from the available studies.</p>

E. Dietary Exposure and Risk Estimates.

Table E1. Sulfuryl Fluoride Chronic Dietary Exposure and Risk Estimates for Fumigation of Food and Food Processing Facilities with Sulfuryl Fluoride. The cPAD for sulfuryl fluoride is 0.003 mg/kg/day for all population subgroups.

Population Subgroup	Food Fumigations		Space Fumigations		Food + Space	
	Exposure Estimate, mg/kg/day	% cPAD	Exposure Estimate, mg/kg/day	% cPAD	Exposure Estimate, mg/kg/day	% cPAD
U.S. Pop. (total)	0.000064	2	0.000018	1	0.000082	3
All infants (< 1 year)	0.000041	1	0.000097	3	0.000138	5
Children 1-2 yrs	0.000189	6	0.000036	1	0.000225	8
Children 3-5 yrs	0.000177	6	0.000036	1	0.000213	7
Children 6-12 yrs	0.000100	3	0.000026	1	0.000126	4
Youth 13-19 yrs	0.000058	2	0.000017	1	0.000075	3
Adults 20-49 yrs	0.000047	2	0.000014	<1	0.000061	2
Adults 50+ yrs	0.000045	2	0.000011	<1	0.000056	2
Females 13-49 yrs	0.000046	2	0.000013	<1	0.000059	2

Table E2. Fluoride Chronic Dietary Exposure and Risk Estimates for Fumigation of Food and Food Processing Facilities with Sulfuryl Fluoride. The RfD for fluoride is 8 mg/day for all population subgroups.

Population Subgroup	NHANES Estimated Body Weight, kg*	Food Fumigations			Space Fumigations			Food + Space	
		Exposure Estimate		% RfD	Exposure Estimate		% RfD	Exposure Estimate, mg/day	% RfD
		mg/kg/day	mg/day		mg/kg/day	mg/day			
U.S. Pop. (total)	70	0.008701	0.6091	8	0.000820	0.0574	1	0.6665	8
All infants (< 1 year)	7	0.010972	0.0768	1	0.000876	0.0061	<1	0.0829	1
Children 1-2 yrs	13	0.017980	0.2337	3	0.002052	0.0267	<1	0.2604	3
Children 3-5 yrs	22	0.019274	0.4240	5	0.002009	0.0442	1	0.4682	6
Children 6-12 yrs	40	0.012879	0.5152	6	0.001361	0.0544	1	0.5696	7
Youth 13-19 yrs	60	0.008014	0.4808	6	0.000795	0.0477	1	0.5285	7
Adults 20-49 yrs	70	0.007212	0.5048	6	0.000660	0.0462	1	0.5510	7
Adults 50+ yrs	70	0.006670	0.4669	6	0.000516	0.0361	<1	0.5030	6
Females 13-49 yrs	61	0.006398	0.3903	5	0.000603	0.0368	<1	0.4271	5

\*U.S. EPA. 2000. Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health. Office of Science and Technology, Office of Water EPA-822-B-00-004. Washington, DC.

F. Occupational Exposure

Table F1. Occupational Exposure MOEs for ProFume. MOEs assume one fifth the geometric mean exposure concentrations of 0.08 ppm (fumigators) and 0.17 ppm (tent workers) determined from structural fumigation studies with Vikane, and an Activity Factor of 2. The 5-fold reduction factor is due to differences in reentry concentrations (5 ppm for Vikane vs. 1 ppm for ProFume) at the time of the assessments (Vikane reentry is now 1 ppm). MOEs are rounded down to 2 significant figures.

Work Activity	Short-Term (NOAEL = 100 ppm)		Intermediate-Term (NOAEL = 30 ppm)		Long-Term (NOAEL = 30 ppm)	
	LOC	MOE	LOC	MOE	LOC	MOE
Fumigator	100	2100	100	650	300	650
Tent/Structural Worker	100	1000	100	300	300	300

MOE = [NOAEL × Animal Exposure Duration (6 hrs/day) × Animal Activity Factor (1)] ÷ [ Human Exposure Concentration × Human Exposure Duration (8.6 hrs/day) × Human Activity Factor (2)]

## G. Occupational Exposure Studies

Table G1. Occupational Exposure Studies for Review for Sulfuryl Fluoride. The following studies need to be scientifically and/or ethically reviewed during the registration review process.		
MRID No.	Study Name	Date
46278004	Determination of Atmospheric Concentrations of Sulfuryl Fluoride following fumigation of Mills using ProFume-North America 2001	Dec 20, 2001
46278003	Determination of Atmospheric Concentrations of Sulfuryl Fluoride following fumigation of Mills using ProFume-North America 2000	Feb 11, 2002
46278002	Sulfuryl Fluoride Exposure Potential to Workers Involved in the Fumigation and Aeration of Mills Using ProFume - North America	March 1, 2002
46278001	Evaluation of the Extraction Efficiency of the Direct Diffusion Fluoride-Ion Selective Probe Analysis Method by Direct Comparison to the Total Fluoride Neutron Activation Analysis	June 10, 2002
46278010	Summary Report - Determination of Atmospheric Concentration of Sulfuryl Fluoride Following Fumigation of a Mill using	May 13, 2004
46278006	Summary Report - Determination of Atmospheric Concentration of Sulfuryl Fluoride Following Fumigation of a Mill using ProFume-Germany 2000	May 13, 2004
46278007	Summary Report - Determination of Atmospheric Concentration of Sulfuryl Fluoride and Occupational Exposure of Fumigators during Structural Fumigation of a Mill using ProFume-Germany 2002	May 13, 2004
46278008	Summary Report - Determination of Atmospheric Concentration of Sulfuryl Fluoride Following Fumigation of a Mill using ProFume-Italy 2001	May 13, 2004
46278012	Summary of Workers, Re-entry Workers and Bystander Potential Exposure to Sulfuryl Fluoride Following Following of Structure with ProFume Gas Fumigant	May 18, 2004
46278005	Determination of Exposure Potential to Workers and Atmospheric Concentration of Sulfuryl Fluoride During and Following Fumigation of a Mill using ProFume-North America 2002	May 17, 2004
46605601	Report for the Air Monitoring Around a Structural Application of Sulfuryl Fluoride in Loomis, CA-Summer 2004	June 9, 2005
47164501	The dispersal of fumigants around ocean shipping containers	2007
47594702	Comparison of Total Fluoride and Soluble Fluoride Anion Residue Analysis in Various Commodities Fumigated with Sulfuryl Fluoride	Nov 6, 2008
47686401	An Observational Study for the Determination of Exposure Potential to Workers and Atmospheric Concentrations of Sulfuryl Fluoride During and Following Fumigation of Dry Commodities Using ProFume Gas Fumigant	June 30, 2008
47686402	Summary of the Dow Chemical Company HSRB Approval of the Observational Worker Study 020071	Feb 20, 2009

Table G2. Occupational/Residential Exposure Data Requirements
<b>Guideline Number: 875.1400</b>
<b>Study Title: Inhalation Exposure Study for Applicators</b>
<b>Rationale for Requiring the Data</b>
<p>The inhalation exposure route is very important for exposure scenarios such as fumigation activities where gases will be generated. However, very limited worker exposure monitoring data are available for workers involved in the fumigation of commodities, other materials, and/or structural facilities. These data do not address the breadth of possible activities associated with sulfuryl fluoride uses that are of potential risk concern. Traditional sources of worker exposure information (e.g., Pesticide Handlers Exposure Database or PHED) have not been used to supplement the existing data and do not apply because of the highly volatile nature of sulfuryl fluoride.</p> <p>To protect workers from inhalation exposure to pesticides, the Agency requires inhalation exposure monitoring data. These data will ensure that the Agency has the most accurate information possible to assess exposures for those involved in the fumigation process. In addition, these data will be used during registration review to evaluate the potential for sulfuryl fluoride occupational exposure to fumigators who treat structural facilities, commodities, and other materials, and will inform the Agency as to how to manage any risks which may be identified based on these data which will reflect the current use practices for sulfuryl fluoride.</p>
<b>Practical Utility of the Data</b>
<p><b>How will the data be used?</b></p> <p>The inhalation exposure data will be used to assess occupational risks for workers involved in fumigation activities during treatment of commodities, materials and/or structural facilities.</p> <p><b>How could the data impact the Agency’s future decision-making?</b></p> <p>The inhalation exposure data will be used to determine the accuracy of the inhalation risks to occupational applicators during fumigation activities based on modern fumigation practices. If future risk assessments are performed without these data, the Agency will have to factor a significant degree of uncertainty into its regulatory decision-making process and that the current mitigation measures (i.e., personal protective equipment) may not provide adequate protection for workers applying sulfuryl fluoride in structural facilities and/or during the treatment of commodities and other materials.</p> <p>The lack of these data will limit the flexibility of the Agency and registrants with respect to the ability to evaluate risks associated with the modern use practices associated with sulfuryl fluoride. It will also allow the Agency to refine its previous risk assessment and could be used to defend challenges to the sulfuryl fluoride decision and to consider additional sources of exposure to those involved in the fumigation process.</p>

**Guideline Number: 875.1700**

**Study Title: Product Usage Information**

**Rationale for Requiring the Data**

The Agency's understanding of sulfuryl fluoride products and usage is limited to the directions found on pesticide labels and estimates of the amounts used to treat certain commodities or structures. The Agency, believes that the current understanding of the sulfuryl fluoride usage pattern is not sufficient to assess the full range of potential exposure associated with its use because how it is applied, how much is applied, and associated fumigation practices (e.g., aeration methods) can impact exposures and these data are not available in a systematic manner.

Additional data are necessary to understand sulfuryl fluoride usage in terms of both commodity and facility fumigations and the potential exposures as a result of these uses. These data will ensure that the Agency has the most accurate information possible to assess product usage parameters by major use region, frequency, season, maximum and typical rates, and application equipment/procedures. In addition, these data will be used during registration review to evaluate the potential exposure for workers and the general public.

**Practical Utility of the Data**

**How will the data be used?**

This information will be used to confirm the end-use products, use patterns, usage assumptions and parameters to determine exposures to sulfuryl fluoride for humans or provide the basis for possible refinements to the process based on a more thorough understanding of modern fumigation practices.

**How could the data change the Agency's decision?**

Additional precautions and/or restrictions may be necessary to protect workers and the general public from exposures to sulfuryl fluoride as a consequence of commodity/material fumigations and/or fumigation of structural facilities. These data will allow the Agency to refine its previous risk assessment and could be used to defend challenges to the sulfuryl fluoride decision.

**Guideline Number: 875.2500**

**Study Title: Post-Application Inhalation Exposure Study**

**Rationale for Requiring the Data**

Postapplication inhalation exposure to sulfuryl fluoride is predicted to occur as a result of the registered uses of sulfuryl fluoride, including commodity/material fumigation and/or structural fumigations. The existing data for exposure to sulfuryl fluoride are limited in terms of the variety of post-application activities and the potential exposures due to off-gassing from treated structural facilities and commodities.

The original data requirements were not broad enough to assess risks to occupational workers near fumigated facilities treated with sulfuryl fluoride or who have to work directly with sulfuryl fluoride treated commodities/materials that could result in post-application exposures which may be a concern. These data will ensure that the Agency has the most accurate information possible to assess post-application exposures for workers near fumigation structural facilities/operations or who work with treated commodities/materials. In addition, these data will be used in registration review to determine if the potential for postapplication occupational exposure for workers near fumigation facilities/operations is below the Agency's level of concern or establish further risk management needs that would apply to the use of sulfuryl fluoride.

**Practical Utility of the Data**

**How will the data be used?**

These data will be used to determine inhalation exposure to sulfuryl fluoride for workers conducting a variety of post-application activities near fumigated facilities/commodities or who work directly with treated commodities/materials.

**How could the data impact the Agency's future decision-making?**

The post-application inhalation exposure study will provide data to support and fully characterize and quantify the exposure and risks of workers exposed to this pesticide. Due to the lack of data, the Agency has used assumptions in developing the risk assessment. These data will allow the Agency to refine its previous risk assessment and could be used to defend challenges to the sulfuryl fluoride decision.

**Guideline Number: 875.2500**

**Study Title: Post-Application Inhalation Exposure Study**

**Rationale for Requiring the Data**

Post-application inhalation exposure to sulfuryl fluoride in the general population can occur as a result of the registered use of sulfuryl fluoride on fumigated structures and/or commodities/materials. This inhalation exposure may not be limited to occupational workers, but may occur for bystanders who may be located close to treated facilities or facilities where commodity fumigations occur. The existing data for such emissions from specific treatments are limited because they evaluate emissions from treated residences (i.e., emissions into adjacent neighborhoods and within treated houses themselves) and emissions from treated structures. However, these data do not quantify the impacts that a residence would have on exposure levels. This is important because individuals would spend much of their time indoors near a fumigation event and be negatively impacted. Available data capture only outdoor measurements of such exposures.

In other words, the Agency has no measured data to estimate concentrations inside homes located near fumigation sites and will assume that the indoor and outdoor concentrations of sulfuryl fluoride in residential settings are identical. This assumption could possibly lead to an overestimate or underestimate of exposure to sulfuryl fluoride. The required data will ensure that the Agency has the most accurate information possible to protect residents (i.e., bystanders) living in proximity to treated facilities. In addition, these data will be used during registration review to determine if the potential for postapplication exposure for residences near fumigation facilities/operations is below the Agency's level of concern.

**Practical Utility of the Data**

**How will the data be used?**

These data will be used to characterize the concentrations inside residences versus outside concentrations, and confirm that bystander buffer zone distances are protective.

**How could the data impact the Agency's future decision-making?**

The post-application inhalation exposure study will provide data to support and fully characterize and quantify the exposure and risk to bystanders exposed to this pesticide. These data will allow the Agency to: (1) evaluate whether the mitigation measures, including buffer zones, have effectively reduced ambient air concentrations of sulfuryl fluoride for residences near fumigated facilities/commodities, (2) refine its previous risk assessment, and (3) defend challenges to the sulfuryl fluoride decision.

**Guideline Number: 875.2500**

**Study Title: Post-Application Inhalation Exposure Study**

**Rationale for Requiring the Data**

Postapplication inhalation exposure from ambient air to sulfuryl fluoride is predicted to occur as a result of the registered use of sulfuryl fluoride on multiple fumigated structures and/or commodities during the season of use in high areas of use which can result in community based exposures from multiple sources. The existing data for ambient air concentrations are limited for communities in proximity to areas where commodity/material fumigations may occur, as well as where facilities themselves may be treated.

These data will ensure that the Agency has the most accurate information possible to protect communities near fumigation facilities/operations. In addition, these data will be used to determine if the potential for postapplication exposure for communities near commodity fumigation facilities and treated structures is below the Agency's level of concern.

**Practical Utility of the Data**

**How will the data be used?**

These data will be used to evaluate: (1) postapplication inhalation exposure to sulfuryl fluoride for communities near fumigated facilities/commodities, (2) potential maximum peak air concentrations in areas of high seasonal use, and (3) potential community-level air concentrations in areas of high sulfuryl fluoride use.

**How could the data impact the Agency's future decision-making?**

The post-application inhalation exposure study will provide data to support and fully characterize and quantify the exposure and risks of communities exposed to this pesticide. These data will allow the Agency to: (1) evaluate whether the mitigation measures such as good agricultural practices can effectively reduce ambient air concentrations, (2) determine postapplication inhalation exposure to sulfuryl fluoride for communities near fumigated facilities/commodities, (3) refine its previous risk assessment, and (4) to defend challenges to the sulfuryl fluoride decision.

**Special Study: Monitoring data on fumigated commodities with Sulfuryl Fluoride.**

**Rationale for Requiring the Data**

The potential postapplication exposures associated with commodity fumigation were not quantitatively assessed when these uses were established. The Agency did not have monitoring data to directly measure emissions of sulfuryl fluoride from fumigated commodities/materials.

These data will ensure that the Agency has the most accurate information possible on exposure to evaluate emission rates from treated commodities. Postapplication risks estimates will be calculated for workers exposed to sulfuryl fluoride and will be used to determine if the potential for occupational exposure due to those emissions (i.e., for postapplication workers who must handle or receive treated commodities) is below the Agency's level of concern.

**Practical Utility of the Data**

**How will the data be used?**

These data will be used to determine if the exposure to sulfuryl fluoride from handling treated commodities/materials is below the Agency's level of concern. In addition, these data will be used to inform emissions factors and buffer zone estimates during the treatment and aeration phases of the fumigations for sulfuryl fluoride commodity uses.

**How could the data impact the Agency's future decision-making?**

These monitoring data are needed to fully characterize emissions from fumigated commodities. These data will allow the Agency to refine its previous risk assessment in terms of model parameterization (i.e., buffer zones, emissions and other factors). In addition, more precise information appropriate for parameterization of the exposure models could be used to refine the previous risk assessment and to defend challenges to the sulfuryl fluoride decision.