UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF PREVENTION, PESTICIDE AND TOXIC SUBSTANCES

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
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MEMORANDUM

Date: 27 January 2010

SUBJECT: Sulfuryl Fluoride – Human Health Risk Assessment for the Requested Soil Fumigation Experimental Use Permit

PC Code: 078003
MRID No.: NA
Petition No.: 62719-EUP-AE
Assessment Type: Single Chemical, Aggregate
TXR No.: NA
Decision No.: 408474

DP Barcode: D364353
Registration No.: 62719-EUP-AE
Regulatory Action: EUP
Registration Case No.: NA
CAS No.: 2699-79-8
40 CFR 180.575

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1.0 Executive Summary

Dow AgroSciences has petitioned the Agency for an experimental use permit for the fumigation of soil with sulfuryl fluoride. The proposal is for a 3-year program designed to evaluate this methyl bromide replacement in terms of residues, efficacy, and plant-back intervals. Application would be shank injected, at least 10 inches from the nearest soil-air interface, to soil beds at a maximum rate of 500 lb a.i./A. The beds would be tarped with Blockade® film immediately after application and seeding/transplanting would occur 2-3 weeks following application.

HED has evaluated the first year of the proposed program and has no objection to RD granting this portion of the experimental use permit. Typically, a quantitative risk assessment would be required to fully evaluate a soil fumigant EUP; however, the proposed program entails treatment of a very small area (approximately 1.5 acres total) in the first year, making a qualitative assessment sufficient at this time. HED has numerous recommendations regarding data to be collected during the conduct of the program and notes that the EUP label should be revised with respect to the buffer zone stipulation (see below) prior to granting the permit. The proposal specifies that any crops grown on treated fields be destroyed after harvest; therefore, there are no dietary exposure concerns that result from this EUP. HED believes that for purposes of this EUP, the label directions mitigate potential risks to workers to levels that have already been evaluated and deemed safe in previous, food-fumigation assessments. Currently the label specifies that applications "...shall not be made within 100 feet of an occupied structure such as a school, hospital, business or residence." Given the scope of this EUP, the available information regarding airborne concentrations of SF on and nearby treated fields, and buffer zone calculations for methyl bromide, HED is satisfied with the 100-foot buffer zone EXCEPT for locations in proximity to schools, hospitals, residences, and other difficult-to-evacuate buildings. HED recommends that the label be revised to specify a 1/4-mile (1320-foot) buffer zone between treated fields and any such structure. Such buffer zones are in keeping with those specified for other soil fumigants. HED also notes that the small acreages being proposed for the program are not of sufficient area to conduct full-field flux studies. Flux data will be required for the Agency to evaluate a Section 3 registration request. Also needed to evaluate a Section 3 registration request will be data depicting residues of fluoride in crops grown on fumigated and control plots, full characterization of the good agricultural practices (GAPs) associated with use of sulfuryl fluoride including soil preparation activities, and appropriate data for assessing risks to workers performing fumigation and post-fumigation activities.

2.0 Ingredient Profile

Sulfuryl fluoride (SO_2F_2) is a fumigant that is being considered as a methyl bromide replacement for the control of nematodes and other soil-borne pests. Sulfuryl fluoride is a gas at standard temperature and pressure. It has a melting point of -136°C, a boiling point of -55°C, and a vapor pressure of 11552 mm Hg (Torr) at 20°C. Sulfuryl fluoride rapidly breaks down to form sulfate and fluoride anion. As XRM-5162®, 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 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.

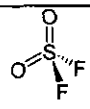
2.1 Summary of Registered/Proposed Uses

Table 2.1. Summary of Directions for Use of Sulfuryl Fluoride as a Soil Fumigant

Applic. Timing, Type, and Equip.	Formulation EPA Reg. No.	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Chisel injection, pre-plant	XRM-5162 62719-EUP-AE	400-500	1	500	NA	Cover w/ Blockade film immediately after application. Allow 2-3 weeks before seeding or transplanting

2.2 Structure and Nomenclature

Table 2.2. Test Compound Nomenclature.

Chemical Structure		F^-
Common name	Sulfuryl fluoride	Fluoride
Company experimental name	Sulfuryl fluoride	Fluoride
IUPAC name	Sulfuryl fluoride	Fluoride
CAS name	Sulfuryl fluoride	Fluoride
CAS #	2699-79-8	16984-48-8
Molecular Formula	F_2O_2S	F^-
Molecular weight	102.056	19.0
End-use product/EP	XRM-5162 (gas fumigant)	

2.3 Physical and Chemical Properties

Table 2.3. Physicochemical Properties of the Technical Sulfuryl Fluoride.

Parameter	Value	Reference
Melting point/range	-136°C	Vikane MSDS
Boiling point	-55°C	Vikane MSDS
pH	Not Provided	
Density (20°C)	4.3 g/L	Vikane MSDS
Water solubility	1.67 g/L	Vikane MSDS
Solvent solubility	Vegetable oil: 0.78 g/100g Acetone: 1.74 g/100 g Chloroform: 2.2 g/100 g	Vikane Chemical Fact Sheet
Vapor pressure (20°C)	11552 mm Hg (Torr)	Vikane MSDS
Dissociation constant (pK_a)	Not Provided	

Table 2.3. Physicochemical Properties of the Technical Sulfuryl Fluoride.		
Parameter	Value	Reference
Octanol/water partition coefficient $Log(K_{OW})$	Not Provided	
UV/visible absorption spectrum	Not Provided	

3.0 Hazard Characterization/Assessment

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 Reregistration Eligibility Decision (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 an inhalation developmental neurotoxicity (DNT) 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. A 10-fold database uncertainty factor has been retained due to uncertainty regarding the regulatory endpoints.

As previously noted, risks associated with this EUP request are not being evaluated quantitatively. Should the registrant wish to pursue a Section 3 registration for the soil-fumigation use of sulfuryl fluoride, then a quantitative assessment will be conducted and the inhalation DNT will be required. To date, Dow has conducted only limited histopathology on the lung and nasal cavities based upon the lack of irritation caused by SF. To be consistent with current HED policy for fumigant registrations, microscopic examination of the larynx, nasal tissues, and trachea following acute exposures is necessary. Nasal sectioning must be performed using the method of Morgan (1991)[1], in which 6 nasal sections are produced using specifically defined landmarks (Mery et. al., 1994)[2]. Prior to initiating any studies, HED is strongly encouraging Dow to consult with OPP regarding experimental design and data needs.

In addition to assessing sulfuryl fluoride, an evaluation of the risks associated with fluoride exposure from the soil-fumigation use will need to be evaluated. Such an evaluation will be based on the hazard assessment currently being developed by the Agency's Office of Water.

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1 Morgan, K.T. 1991. Approaches to the identification and recording of nasal lesions in toxicology studies. *Toxicologic Pathology* 19 (4; Part 1), 337-351.

2 Mery, S.; Gross, E.A., Joyner, D.R.; Godo, M.; and Morgan, K.T. 1994. Nasal diagrams: a tool for recording the distribution of nasal lesions in rats and mice. *Toxicologic Pathology* 22 (4), 353-372.

The doses and endpoints currently being used to assess exposure to sulfuryl fluoride are summarized in Tables 3.1 and 3.2, below. For a complete hazard characterization of sulfuryl fluoride, see M. Doherty, D312659, 18 January, 2006. Note that for all risk assessments a database uncertainty factor has been retained at 10X due to the lack of a developmental neurotoxicity study. In addition, a 3X safety factor has been included for chronic dietary assessment due to use of a subchronic study (90-day) for assessing long-term exposure.

Table 3.1. Summary of Dose and Endpoint Selection for use in Dietary and Non-occupational Human Health Risk Assessments for Sulfuryl Fluoride.

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** = chronic RfD / 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 and based on its use pattern, no significant incidental oral exposure is anticipated.
Dermal (All durations)	None	Not applicable	Due to sulfuryl fluoride being a gas and based on its use pattern, no significant dermal exposure is anticipated. No hazard 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 for MOE = **1000**	**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 for MOE = **1000**	**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 for MOE = **3000**	**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

Table 3.2. Summary of Dose and Endpoint Selection for use in Occupational Human Health Risk Assessments for Sulfuryl Fluoride.

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Level of Concern for Risk Assessment	Study and Toxicological Effects
Dermal (All durations)	None	Not applicable	Due to sulfuryl fluoride being a gas and based on its use pattern, no significant dermal exposure is anticipated. No hazard 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)	**Occupational** LOC for MOE = **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)	**Occupational** LOC for MOE = **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)	**Occupational** LOC for MOE = **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

4.0 Public Health and Pesticide Epidemiology Data

No incident reports or epidemiological data were used directly in the development of this risk assessment. However, as noted in the hazard characterization, reported incidences of human poisonings contributed to the Agency's classification of sulfuryl fluoride acute inhalation toxicity as Toxicity Category I.

5.0 Dietary Exposure/Risk Characterization

This is a "crop-destruct" EUP and, as such, there are no dietary risk issues associated with it.

Given the proposed use as well as the reactivity and short life of the sulfuryl fluoride molecule, HED does not have any concerns about a pre-plant soil fumigation use resulting in residues of parent compound in the mature, edible crop parts. However, HED is requesting that fluoride residue data from crops grown in treated and untreated plots be collected to determine the impact that the requested use may have on fluoride exposure if a Section 3 registration is ultimately sought. Furthermore, as this is a multi-year program, HED encourages Dow to conduct multiple fumigations on the same site in order to evaluate the potential for fluoride to accumulate in treated soils and any impact this may have on residue levels in crops.

6.0 Residential (Non-Occupational) Exposure/Risk Characterization

As mentioned previously, potential inhalation risks are of concern for bystander exposures from the proposed EUP use for sulfuryl fluoride. To evaluate these potential risks the registrant has submitted a summary of data collected from two XRM-5162 (sulfuryl fluoride) field studies. A qualitative preliminary review of the summary results for field flux data and soil gas measurements was conducted.

As stated by the registrant, concentrations of SF from air samples collected 100 m off the treated field were below the limit of quantification (LOQ) and decline rapidly during the first 24 hours (sample timing and LOQ not specified). On-field air measurements show maximum concentrations of 0.27 ppm (Georgia) and 0.077 ppm (Florida). HED notes that the Environmental Fate and Effects Division (EFED) has determined that these concentrations are from applications at approximately ½ of the maximum application rate.

Since sulfuryl fluoride has been deemed by EPA to be a methyl bromide (MeBr) alternative and due to the similarities of these chemicals, the data required by the Agency to assess exposures to MeBr will also be needed for assessing sulfuryl fluoride. The amended MeBr RED established tarped broadcast buffer zones distances by application rate and block size (9 July 2008, EPA 738-R-08-005). Based on the proposed total acres (about 1.5A in year one) treated for this EUP, HED believes that buffer zones derived for MeBr in the amended RED would be protective and should be used during the proposed SF EUP study.

Based on this information, HED concludes that the proposed 100-foot buffer zone for the proposed sulfuryl fluoride EUP study is adequate; except for those sites adjacent to schools, hospitals, residences, and/or other difficult-to-evacuate structures, for which a ¼-mile (1320-foot) buffer should be established. Provided the EUP label is modified regarding the ¼-mile buffer zone, HED has no concerns about non-occupational exposures resulting from this EUP.

As mentioned above, the size of buffer zones around treated field is dependent, in part, on the size of the field being treated. Therefore, a complete assessment for bystander exposure will be conducted if a Section 3 registration is sought. Appropriate flux data will be required to support such a registration.

7.0 Aggregate Risk Assessments and Risk Characterization

Provided the above-specified label modifications are made, HED believes that this proposed EUP will not result in dietary or non-dietary exposure to the U.S. population or any identifiable population subgroups. Aggregate risks are, therefore, not of concern.

8.0 Cumulative Risk Characterization/Assessment

The Agency has not determined whether SF shares a common mechanism of toxicity with other chemical substances. 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 and include the contribution of fluoride coming from other chemicals.

9.0 Occupational Exposure/Risk Pathway

As with the dietary, residential, and aggregate risk evaluations, HED has not completed a quantitative assessment of occupational risks associated with the proposed EUP. The proposed EUP label specifies that if the concentration of sulfuryl fluoride in the fumigation area and/or breathing zone of workers is in excess of 1 ppm, then a positive-pressure self-contained breathing apparatus (SCBA) must be worn. No respiratory protection is required if the concentration of sulfuryl fluoride is equal to or less than 1 ppm. This restriction is in keeping with the label and risk assessments previously conducted by OPP. For those assessments, risks to workers were not of concern.

The proposed label for the EUP states that, "During fumigation, it is essential that concentrations of XRM-5162 in the breathing zone inside the cab of the application equipment be monitored. ...The concentration of XRM-5162 must be monitored in the breathing zone as defined by where the worker stands or sits while performing these tasks." HED is requesting that SF concentration data from the monitoring devices be captured and submitted to the Agency to confirm compliance with the permit and as part of the industrial hygiene (IH) monitoring plan to ensure: 1) the best recognized IH practices are implemented during the application and post-application process, and 2) no significant worker exposures were identified as a result of this EUP. Activities determined to have no significant exposure potential should be appropriately documented for historical purposes following the proposed label protocol. This documentation can serve as a valuable information resource to evaluate the accuracy of worker exposure estimates in future risk assessments and ensure the adequacy of the proposed label safety measures.

Furthermore, the existing data for workers' 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 soil. Emission-rate monitoring data for potential exposures due to off-gassing from treated soil for workers conducting post-application activities near or in fumigated areas or who have to work directly with sulfuryl-fluoride-treated soil should be submitted to the Agency.

10.0 Data Needs and Label Recommendations

No data are needed at this time to support the EUP request. HED is requesting that some data be collected during conduct of the EUP and that supporting data will be required if the registrant wishes to pursue a future Section 3 registration for this use. In addition to the specific items listed below, complete details and characterization of good agricultural practices should be provided. The registrant is directed to the fumigant reregistration web site (http://www.epa.gov/oppsrrd1/reregistration/soil_fumigants/) for more information. Given the complexity of assessing fumigant uses, HED strongly encourages the petitioner to consult with the Agency to ensure that experimental designs and the resulting data are appropriate for conducting a human health risk assessment for the soil fumigation use of sulfuryl fluoride.

10.1 Toxicology

There are no toxicology needs at this time. In the event that the registrant wishes to pursue a Section 3 registration for this use of sulfuryl fluoride, an immunotoxicity study as well as an inhalation developmental neurotoxicity study will be required.

10.2 Residue Chemistry

HED is requesting that residue data for total fluoride be collected from crops grown in treated and control soil. Such data will be required to determine the food-use status of the proposed soil fumigation use pattern and to conduct a risk assessment if one is deemed appropriate. To the extent possible, data depicting fluoride residues in soil and crops following multiple fumigations should be collected to evaluate the potential for accumulation of fluoride and subsequent uptake into plants.

10.3 Occupational and Residential Exposure

Prior to granting this EUP, HED is recommending that the label be modified to provide for a ¼-mile buffer zone between treated fields and occupied structures (schools, hospitals, residences, and/or other difficult-to-evacuate structures). The 100-foot buffer zone currently on the label is adequate for situations without a nearby occupied structure.

HED is requesting that data from devices used to monitor the concentration of SF in the breathing zone of applicators be captured and submitted to the Agency. These monitoring devices are required for compliance with the permit and are an integral part of the industrial hygiene plan.

Flux data will be required to properly evaluate worker and bystander risks resulting from the soil fumigation use of sulfuryl fluoride. HED understands that some flux data have been collected. Initial review indicates that the studies are not adequate to support a future Section 3 registration. HED is requesting that monitoring data suitable for evaluating the emission of sulfuryl fluoride from treated soils during fumigation and post-fumigation activities be collected and submitted as part of the experimental program.

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R180633

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