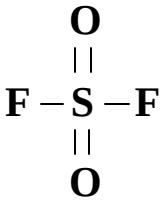
SULFURYL FLUORIDE (Vikane®)

RISK CHARACTERIZATION DOCUMENT

Executive Summary



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LIST OF CONTRIBUTORS AND ACKNOWLEDGEMENT

The Risk Characterization Document (RCD) for sulfuryl fluoride as Vikane® addresses the risk associated with human inhalation exposure when used in structural fumigation and non-food commodity fumigation. It is consisted of five documents: Executive Summary, Volume I. Health Risk Assessment, Volume II. Occupational and Residential Exposure Assessment, Volume III. Environmental Fate, and Volume IV. DPR Responses to Comments.

Executive Summary

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Introduction

The Department of Pesticide Regulation (DPR) conducts risk assessments for pesticides used in California to determine whether the use poses a present or potential human health hazard in California. Risk assessment is the systematic scientific characterization of potential adverse health effects resulting from human exposures to hazardous agents or situations. This type of assessment includes a quantitative assessment of the exposure and the potential magnitude of the risks, and a description of the uncertainties in the conclusions and estimates. After the completion of the risk assessment, the risk management phase takes place at DPR. Risk management refers to the process by which policy actions are chosen to deal with hazards identified in the risk assessment process. Risk managers consider scientific evidence and risk estimates, along with statutory, engineering, economic, social, and political factors, in evaluating alternative regulatory options and choosing among those options.

Risk assessments are mandated by Senate Bill (SB) 950, the Birth Defect Prevention Act, and Assembly Bills (AB) 1807 and 3219. Under SB 950, the risk assessment is comprehensive and considers the potential exposures of various population groups, which may include workers, residents, and bystanders, depending on how the pesticide is used. Bystander is defined as any person not directly involved with the fumigation process, but is in the vicinity of the fumigation site. For each group, multiple routes of exposure, when appropriate, are assessed. These include inhalation via the air, absorption through the skin, and consumption of treated food. In comparison, AB 1807 and 3219 establish a procedure for identification and control of toxic air contaminants (TACs) in California. The statutes define toxic air contaminants as air pollutants that may cause or contribute to an increase in mortality or in serious illness, or that may pose a present or potential hazard to human health. DPR TAC program focuses on the evaluation and control of pesticides in ambient community air.

This report describes the risk assessment for the inhalation exposure to sulfuryl fluoride in the product Vikane®, under both SB 950 and AB 1807 mandates. In preparing this report, DPR staff reviewed pertinent scientific literature and reports through Spring 2005. Based on the results of this comprehensive evaluation, the Director of DPR will determine whether sulfuryl fluoride is a TAC, and whether mitigation measures are needed to reduce the exposure by workers and the general population in California. If sulfuryl fluoride is designated a TAC, the risk management provisions of the law mandate the DPR to determine the need for and develop appropriate control measures for sulfuryl fluoride uses, in consultation with the Office of Environmental Health Hazard Assessment (OEHHA), the Air Resources Board (ARB), the air pollution districts, air quality management districts, and county agricultural commissioners of the affected counties.

What is contained in this report?

This report evaluates the potential for sulfuryl fluoride exposure and includes:

- A review of the available scientific evidence on sulfuryl fluoride and fluoride regarding their physical properties, sources in the environment, and fates in the environment;

- Summary of toxicology studies conducted with sulfuryl fluoride and fluoride;
- Estimates of human exposure to sulfuryl fluoride in the air at work sites and surroundings; and
- An assessment of the risk to humans resulting from current or anticipated exposures to airborne sulfuryl fluoride.

What is sulfuryl fluoride, what are the primary sources of sulfuryl fluoride in the environment, and how is it used?

Sulfuryl fluoride is a colorless, odorless gas. The molecular formula is F_2O_2S and the molecular weight is 102.1 g/mole. It is highly volatile with a vapor pressure of 1.16×10^4 mmHg at 25 °C and a Henry's Law Constant of 3.28×10^{-2} atm·m^3/mol. It is soluble in water at 750 ppm (at 25 °C, pH 7), and readily soluble in most organic solvents.

The primary source of sulfuryl fluoride in the environment is from its use as a fumigant. Sulfuryl fluoride, marketed as Vikane®, is used to fumigate sealed structures and their contents (construction materials, furnishings, and household effects) such as dwellings (including mobile homes), buildings, barns, vehicles, fumigation chambers, rail cars, and surface ships in port. It controls existing infestations of insects and related pests such as drywood termites, powder post beetles, old house borers, death-watch beetles, bedbugs, cockroaches, clothes moths, rats, and mice.

In the preparation of a building for fumigation, the structure is evacuated and edible items are placed in airtight sealed containers. With windows and doors opened, the unoccupied building is covered with a tarpaulin (tarp) and sealed at the base to contain the fumigant. Since Vikane® is odorless and colorless, chloropicrin is added as a warning agent. On the next day, the tarpaulin is removed and the inside is actively aerated with fans for at least 1 hour, and later passively to disperse and release the fumigant into the atmosphere. After a minimum aeration of 8 hours, the sulfuryl fluoride air concentration at the breathing zone inside the building is measured. The building is approved or "cleared" when the concentration is 5 ppm or less, a level considered safe for residents and workers to reoccupy the buildings. Sulfuryl fluoride is also used in the fumigation of non-food commodities such as pallets, furniture, bags, beds, and mattresses. In this type of fumigation, sulfuryl fluoride is introduced into containers or chambers with the commodity to be fumigated. After fumigation, these chambers are aerated, with the release of sulfuryl fluoride via a stack into the atmosphere. For both types of fumigation, posting of a sign with information on the fumigation is required from application until the treated site air concentration is 5 ppm or less.

In California, Vikane® is used in all counties throughout the year. The total poundage used was 1.5 million pounds in 1993, and increased to almost 3.3 million pounds in 2004. The increase is attributed to its use in the fumigation of structures, as a replacement for methyl bromide, which use has declined significantly in the last few years. For the fumigation of commodities already harvested (dried fruits, nuts, and grains) with ProFume®, which was approved in 2005, use data are not yet available.

What are the fates of sulfuryl fluoride in the environment?

After fumigation, sulfuryl fluoride in the air of treated structures is immediately released into the atmosphere in the gaseous state. Once in the atmosphere, the fate of sulfuryl fluoride is unclear since there are no available studies on this subject. Sulfuryl fluoride is expected to have a long atmospheric lifetime with respect to photolysis, reaction with hydroxyl radicals, nitrate radicals and ozone in the atmosphere, and dissolution and/or degradation in sea water. Sulfuryl fluoride is, therefore, expected to be transported throughout the global atmosphere. The potential for sulfuryl fluoride to contribute to the greenhouse effect is a subject for future research. However, for lack of any data to suggest otherwise, its ability to absorb infrared radiation and, expected long atmospheric lifetime make sulfuryl fluoride a good candidate for a greenhouse gas.

There is a slower release of sulfuryl fluoride, which had adsorbed into structural material and household commodities (non-food). The rate of release depends on the type of material. Studies showed that sulfuryl fluoride is retained longer in synthetic material such as polystyrene insulation, latex baby bottle nipples, and polyester cushion fibers, compared to other materials.

Who will be exposed to sulfuryl fluoride, and what are the exposure levels?

There are three population subgroups, which may be exposed to sulfuryl fluoride: workers, residents, and bystanders. A bystander is any one who is not involved with the application of the fumigant, but who may be exposed as a consequence of its use. He/she can be at the outdoors or indoors since the air concentrations are assumed to be the same for both places. In this report, the exposures of these groups are estimated based on the assumption that the applications followed label directions. They are expressed as absorbed doses, which accounts for differences in the age-related inhalation rate, and in the exposure duration under the various scenarios. For workers, their exposure durations are acute, short-term, intermediate-term, long-term, and lifetime. For residents and bystanders, the exposures are primarily acute and short-term durations. For each group, the highest exposure occurs with acute duration. The sulfuryl fluoride concentration experienced by bystanders varies and depends on many factors including the weather (*i.e.*, wind, temperature), distance from application site, and application rate. The high-end values from monitoring data are selected to estimate their exposures in this document.

For structural fumigation, the workers are designated as fumigators and tent crew. The fumigators introduce the fumigant into the structure, start aeration, and clear the building for reentry. They may have additional exposure when they perform tent crew activities. The tent crew seals the structure to prevent fumigant leakage during fumigation, and dismantles the tarp to aerate the structure after fumigation. The exposures of these workers were determined by monitoring studies that measured the air concentrations in the environment and breathing zones during typical fumigation of California homes using application rate lower than the maximum allowed on the label (submaximal rate). Under acute exposures, the range of estimated exposures was 1.17 mg/kg/day (fumigator doing both fumigator and tent crew activities) to 0.000006 mg/kg/day (fumigator checking structure after the first hour of aeration). The estimated acute exposures for the maximal rate application ranged from 16.85 mg/kg/day (fumigator doing both

fumigator and tent crew activities) to 0.00009 mg/kg/day (fumigator checking structure after the first hour of aeration). The intermediate, annual, and lifetime exposures were also estimated.

Non-food commodity fumigation involves the fumigators, and another category of workers, handlers. The handlers transfer commodities from the treatment site to a storage site or to the market. Currently there are no air monitoring data for non-food commodity handlers. The estimated exposures of these workers were based on an assumed exposure to a maximal sulfuryl fluoride air concentration of 5 ppm (0.43 mg/kg/day) because levels greater than this would required the use of self-contained breathing apparatus, according to the Vikane® label.

Residents of treated homes are exposed to sulfuryl fluoride after their houses have been treated because the current label permits reentry when the air concentration is no higher than 5 ppm. Data from a monitoring study involving 7 California homes were used to estimate these exposures. The data show that indoor air concentrations did not go to zero in 24 hours after aeration. During the first 24 hours after potential reentry, the mean sulfuryl fluoride air concentrations in these houses range from 0.01 ppm to 1.58 ppm. This would be equivalent to an absorbed dose ranging from 0.20 mg/kg/day for 15-18 year olds to 0.57 mg/kg/day for infants <1 year old. At 40-48 hours after aeration, sulfuryl fluoride was still detected, ranging from 0.02 ppm to 0.48 ppm.

When fumigation or aeration occurs in a fumigated structure, bystanders, i.e., adult and child residents living nearby, have the potential for short-term exposure during their normal outdoor activities. As there are no data on the amount of sulfuryl fluoride, which may enter adjacent homes, indoor and outdoor air levels are assumed to be the same. Therefore, in addition to potential exposure during routine outdoor activities, bystanders may also be exposed while indoors. The estimated bystander exposures were derived from monitoring studies using a submaximal rate of application. For acute exposure during the first 12-hours of the application phase, the range of estimated absorbed doses ranged from 0.14 mg/kg/day (15 to 18 years old) to 0.36 mg/kg/day (infants <1 years old). At the maximal rate of application for the same time period, the range of estimated absorbed doses ranged from 1.4 mg/kg/day (15 to 18 years old) to 3.6 mg/kg/day (infants <1 years old).

The estimated acute absorbed doses during aeration using the Tarpaulin Removal and Aeration Plan method, currently used in California, ranged from 0.36 mg/kg/day (15 to 18 years old) to 0.90 mg/kg/day (infants <1 years old) for the submaximal rate application. The calculated exposures during application and aeration were 14.5 times higher if maximal rate application was used. At this maximal rate, the acute exposures ranged from 5.2 mg/kg/day (15 to 18 years old) to 13.1 mg/kg/day (infants <1 years old).

Bystanders near a non-food commodity fumigation facility may experience exposures during the application and aeration phases of the fumigation. As sulfuryl fluoride is rarely used to fumigate non-food commodities, only acute exposures are expected. As with structural fumigation, these bystanders are assumed to be exposed to sulfuryl fluoride while both outdoors and indoors at a maximum ambient air level of 5 ppm. For acute exposure, the range of estimated absorbed doses was 0.9 mg/kg/day (15 to 18 years old) to 2.3 mg/kg/day (infants <1 years old).

What are the potential health effects from acute or repeated exposures to sulfuryl fluoride and fluoride?

Neurotoxicity and respiratory effects were observed in humans and laboratory animals. In humans, acute inhalation exposure to high concentrations of sulfuryl fluoride resulted in respiratory irritation, lung damage, central nervous system depression, and death. These high exposures occurred when people entered structures under fumigation illegally or after insufficient aeration. Epidemiological studies reported that fumigation workers who used sulfuryl fluoride showed neurological effects, which included reduced performance on cognitive tests and pattern memory tests, and reduced olfactory function. Unfortunately, the actual exposure levels and duration of these workers were not known, and some of them were also exposed to methyl bromide, another neurotoxicant.

In laboratory animals, sulfuryl fluoride is acutely toxic at high concentrations. The concentrations for 50% lethality (LC_{50}) in rats are 3020-3730 ppm for 1-hour exposure and 991-1500 ppm for 4-hour exposure. The 4-hour LC_{50} in mice is >400 ppm to 660 ppm. At non-lethal concentrations, neurotoxicity is observed in rats, mice, rabbits, and dogs.

With repeated exposures, the primary target tissues for sulfuryl fluoride inhalation toxicity in laboratory animals were the brain, respiratory system, and teeth. With up to two-weeks of exposure, clinical signs observed included tremors, lethargy, respiratory effects, incapacitation, tetany, and convulsion. Animals treated with sulfuryl fluoride for two weeks showed tissue damage in the kidney (rats), brain (rabbits, mice), and respiratory tract (rabbits and dogs). After 13 weeks of inhalation exposure, the brain was the primary target for sulfuryl fluoride toxicity in all species studied (rats, mice, rabbits, and dogs). The most common lesion was vacuoles in the cerebral tissues. Other effects reported were nasal tissue inflammation (rats and rabbits), kidney hyperplasia (rats), lung histiocytosis (rats), thyroid hypertrophy (mice), and fluorosis (rats). The significant finding from reproductive and developmental toxicity studies was reduced body weight of fetuses (rabbits), pups (rat), and dams (rats). There were no teratogenic effects in rats or rabbits exposed to sulfuryl fluoride during gestation.

With chronic exposure, the primary target tissue for sulfuryl fluoride was the brain and the respiratory tract in rats, mice, and dogs. As with subchronic exposure, brain vacuoles were observed in the cerebrum. The sites of lesions in the respiratory tract included nasal tissues, trachea, larynx, and lungs. Dental fluorosis was observed in both rats and dogs. Progressive glomerulonephropathy was considered the cause of death in sulfuryl fluoride treated rats.

Of the metabolites identified in the rat, fluoride likely caused the dental fluorosis in laboratory animals after repeated exposures. Fluoride as well as other metabolites, fluorosulfate and sulfate, may be involved in other effects reported.

Is there any potential cancer risk from exposure to sulfuryl fluoride?

Sulfuryl fluoride did not cause tumors in rats and mice after lifetime exposures. Sulfuryl fluoride also did not cause any damage to the genetic material in laboratory studies. However, hyperplasia of kidneys and nasal tissues, and hypertrophy of the thyroid were reported in laboratory animals after repeated exposures. These could be indication of pre-neoplastic effects due to exposure.

Does the concentration of sulfuryl fluoride in the air pose a potential health hazard for humans?

While the current label limited the exposure to no higher than 5 ppm, this report shows that human exposures under some scenarios are higher than 5 ppm. One way to quantify the potential health hazard of human exposure is by comparing the No-Observed-Effect Level (NOEL), a dose does not cause toxicity in laboratory animals, and the human exposure levels under different scenarios. This comparison yields a numerical term, known as a margin of exposure (MOE), the ratio of the NOEL in animals to the estimated exposure in humans. For sulfuryl fluoride, the NOELs (as absorbed doses) for acute, 1-2 weeks, subchronic (13-weeks) exposures are 54 mg/kg/day, 7.2 mg/kg/day, 2.2 mg/kg/day, and 0.72 mg/kg/day. Based on the uncertainty in the toxicology database, scenarios with MOEs lower than 100 and 1000 for occupational and residential/bystander exposures, respectively, are considered to pose a health hazard for humans.

The hazard can also be quantified by comparing with the reference concentration, which is an estimate of a daily inhalation exposure concentration for the human population that is likely to be without an appreciable risk of deleterious non-carcinogenic effects. This term includes the consideration of the toxicity and uncertainties in its determination. The reference concentrations (and exposure durations) for workers are 2.57 ppm (acute), 0.48 ppm (1-2 weeks), 0.14 ppm (subchronic), and 0.04 ppm (chronic). For infants, the highest exposed group in the general population, the reference concentrations (and exposure durations) are 0.12 ppm (acute), 0.023 ppm (1-2 weeks), 0.007 ppm (subchronic), and 0.002 ppm (chronic). For the listing of a pesticide as a TAC under AB 1807, the exposure of bystanders is compared with the reference concentration. Exposures exceeding 1/10 of the reference concentration would be considered for listing as a TAC. This criterion is equivalent to a MOE of less than 10,000 for bystander exposures.

The risk assessment recommends that sulfuryl fluoride should be listed a TAC. Furthermore, the exposures of workers, residents, and bystanders under many scenarios pose health hazards and need to be reduced.

Does fluoride ion, as a degradation product of sulfuryl fluoride, pose a potential health hazard?

The sources of human exposure to fluoride are drinking water (major source), food, dental products, and use of fluoride-containing pesticides such as sulfuryl fluoride and cryolite. Human exposure to fluoride from the use of sulfuryl fluoride in Vikane® is not evaluated in this report

due to lack of exposure data. This report provides estimates of fluoride exposure, which show a wide range depending on the assumptions. The inhalation and dietary exposures to fluoride will be evaluated when the risk assessment for ProFume® is conducted.

The primary effect of fluoride, a metabolite of sulfuryl fluoride, is dental fluorosis. With low-level chronic exposures to fluoride, there is some evidence, though not conclusive, that suggests fluoride may cause cancer, in particular osteosarcoma, in the bone tissue. Fluoride is known to concentrate in calcified tissues. Sodium fluoride caused damage to the genetic material under some laboratory conditions. Chronic toxicity studies with sodium fluoride in the drinking water showed low incidence of a type of bone cancer (osteosarcoma) in male rats, but not in female rats or either gender of mice. Another study with sodium fluoride in the diet showed increased incidences of osteomas (benign bone tumors) in mice, but not rats. A case-control study found a positive association between exposure to fluoride in drinking water and the incidence of osteosarcoma in 6 to 8 year old boys, but not girls. Additional research is needed to clarify these findings and to determine the oncogenicity of fluoride.

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DATE: July 1, 2005

SUBJECT: FINDINGS ON THE HEALTH EFFECTS OF THE ACTIVE INGREDIENT: SULFURYL FLUORIDE

Enclosed please find a copy of the Office of Environmental Health Hazard Assessment's (OEHHA) findings for the active ingredient sulfuryl fluoride. These findings, which supercede our previous draft findings (dated December 23, 2004), were prepared in response to the final draft risk characterization document (RCD Volumes I and II, dated June 1, 2005) for sulfuryl fluoride prepared by the Department of Pesticide Regulation (DPR). The information contained in these documents served to identify sulfuryl fluoride as a candidate toxic air contaminant (TAC).

Pursuant to Food and Agricultural Code sections 14022 and 14023, OEHHA provides review, consultation and comments to DPR on the evaluation of the health effects of candidate toxic air contaminants (TAC) included in the TAC documents. As part of its statutory responsibility, OEHHA also prepares findings on the health effects of the candidate toxic air contaminants. This documentation is to be included as part of the DPR report.

Should you have any questions regarding OEHHA's draft findings on the health effects of sulfuryl fluoride, please contact Dr. David Rice at (916) 324-1277 (primary reviewer), Mr. Robert Schlag at (916) 323-2624, or Dr. Anna M. Fan at (510) 622-3165.

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Draft Final
July 1, 2005

Office of Environmental Health Hazard Assessment's Findings On the Health Effects of Sulfuryl Fluoride

Pursuant to Food and Agricultural Code Sections 14022 and 14023, the Office of Environmental Health Assessment (OEHHA) of the California Environmental Protection Agency provides consultation and technical assistance to the Department of Pesticide Regulation (DPR) on the evaluation of health effects of candidate toxic air contaminants (TAC) and prepares health-based findings. OEHHA previously reviewed and commented on the draft documents prepared by DPR on the evaluation of human health risks associated with potential exposure to sulfuryl fluoride. These documents are used by DPR in considering listing sulfuryl fluoride as a TAC. As part of its statutory responsibility, OEHHA has also prepared these findings on the health effects of sulfuryl fluoride which are to be included as part of DPR's Risk Characterization / Toxic Air Contaminant (RCD/TAC) documents.

Environmental Fate and Exposure

1. Sulfuryl fluoride (sulfuric oxyfluoride) is a fumigant used for structural and non-food commodity fumigations. Vikane is the registered trade name for the product that is used to control a variety of pests such as drywood termites, powder post beetles, old house borers, bedbugs, clothes moths, rodents, and cockroaches in dwellings, buildings, construction materials, furnishings, and vehicles. Use of sulfuryl fluoride increased from 1.7 million pounds in 1994 to 3 million pounds in 2002. The major use (>99%) is for structural pest control and the increase in use is attributed to the decline in the use of methyl bromide for the same purpose.

2. Relatively little is known about the environmental fate of sulfuryl fluoride. The chemical is hydrolyzed in water to fluorosulfuric acid and fluoride ion. Under neutral conditions, the reaction proceeds slowly, while under alkaline conditions the hydrolysis is rapid. Data addressing the fate of sulfuryl fluoride in soil and biota is unavailable.

3. Exposure was estimated for residents re-occupying fumigated dwellings (postclearance), and for bystanders during active structural fumigation and during the aeration phase using two different aeration techniques. Exposure was also estimated for bystanders during non-food commodity fumigations. Ambient air exposures for the general population other than bystanders were not estimated since they were assumed to be negligible.

4. Exposure to residents entering cleared, fumigated houses was based on the results of a 48-hour postclearance air monitoring study of seven homes (Shurdut, 1995). The 48-hour

data were used to estimate 24-hour sulfuryl fluoride air concentrations, which were then used to calculate the 24-hour acute absorbed daily dose (ADD). Since no longer-term data existed, the air concentration data was also used to generate dissipation curves, which provided air concentrations to estimate the short term (7-day) ADD, the annual ADD (AADD) and the lifetime average ADD (LADD). Ninety-fifth percentile upper bound air concentrations were used to derive acute, short-term and annual ADDs. An estimate of the average 7-day air concentration was used to calculate the lifetime ADD. Seven-day exposures, assumed as the dissipation curves for all residences in the study, show that air concentrations of sulfuryl fluoride were negligible at 7-days post clearance. Predicted air concentrations for sulfuryl fluoride of 1.78 ppm (7.42 mg/m^3), 0.42 ppm (1.75 mg/m^3), and 0.095 ppm (0.40 mg/m^3) were used to calculate acute ADDs, short-term/annual ADDs, and LADDs, respectively.

5. Bystander exposure during structural fumigations was estimated based on a study by Wright and co-workers (Wright et al., 2003) who monitored air levels of sulfuryl fluoride during an application of sulfuryl fluoride at the submaximal application rate of 16 g/m^3 and the structures' subsequent aeration. Data collected during the application phase was used to estimate acute 12 and 24-hour ADD (using upper 95^{th} percentile air concentrations), AADD (using upper 95^{th} percentile air concentrations) and the LADD (using average air concentration). Estimated air concentrations for sulfuryl fluoride of 1.60 ppm (6.67 mg/m^3), 1.12 ppm (4.67 mg/m^3), and 0.69 ppm (2.88 mg/m^3) were used to calculate 12-hour ADDs, 24-hour/annual ADDs, and LADDs, respectively. Estimates of air concentrations following use of sulfuryl fluoride at the maximum application rate of 160 g/m^3 were estimated by multiplying the estimated submaximal air concentrations by ten.

6. Wright et al.(2003) monitored air levels of sulfuryl fluoride following a structural fumigation during the aeration phase using the "Stack" method of aeration. Briefly, the stack method involves 12 hours of active ventilation via an exhaust stack with tarpaulin in place; the structure is then tested for clearance after the ventilation period. Data collected during this monitoring study was used to estimate acute 1 and 4-hour ADD (using upper 95^{th} percentile air concentrations), AADD (using upper 95^{th} percentile air concentrations) and the LAADD (using average air concentrations). Estimated air concentrations for sulfuryl fluoride of 7.99 ppm (33.32 mg/m^3), 1.97 ppm (8.21 mg/m^3), and 0.60 ppm (2.50 mg/m^3) were used to calculate 1-hour ADDs, 4-hour/annual ADDs, and LADDs, respectively. Estimates of air concentrations following use of sulfuryl fluoride at the maximum application rate of 160 g/m^3 were estimated by multiplying the estimated submaximal air concentrations by ten.

7. Bystander exposure during aeration using an alternate clearance method known as "TRAP", which involves 10 minutes active ventilation followed by tarpaulin removal, and then 60 minutes of active aeration, was estimated by using air concentrations of

sulfuryl fluoride calculated for worker exposure during general detarping activities. Estimated air concentrations for sulfuryl fluoride of 24 ppm (100 mg/m^3) and 6.2 ppm (26.7 mg/m^3) were used to calculate 2-hour ADDs/AADDs and LADDs, respectively. These estimates were made from air morning data following a sulfuryl fluoride application at the average application rate of 11 g/m^3. Estimates of air concentrations following use of sulfuryl fluoride at the maximum application rate of 160 g/m^3 were estimated by multiplying the estimated submaximal concentrations by 14.5.

8. No air monitoring data is available to estimate bystander exposures associated with nonfood commodity fumigation. Exposures were estimated assuming a maximum ambient air level of 5 ppm (20.9 mg/m^3), which is the maximum allowed by the Vikane label. Exposure over a 24-hour period was assumed.

9. Based on the results of a pharmacokinetic analysis in Fisher rats by Mendrala and co-workers (2002), inhalation absorption was estimated at 18%. Absorbed doses were calculated taking into consideration air concentration, inhalation rate (specific for age group and activity), the absorption factor (18%), and body weight. Exposure was estimated for several age groups (in years): <1, 1-2, 3-5, 6-8, 9-11, 12-14, 15-18, and > 18 (adults). Because of children's high breathing rate to body weight ratio, exposures were greatest for children less than one-year of age.

10. Human exposure to atmospheric sulfuryl fluoride can occur by both inhalation and dermal routes, but the predominant route for systemic exposure is inhalation. Dermal uptake of sulfuryl fluoride has not been quantitatively estimated in these studies but it is expected to provide less than 1 percent of the systemic dose received by inhalation.

Health Effects Studies

Humans

11. Several unintentional cases of human poisoning with sulfuryl fluoride have been reported in the literature. A number of these cases were fatalities, nearly all of which were cases associated with entering structures that were either undergoing active fumigation, were still tarped and not yet cleared for reentry, or were cleared for reentry and sulfuryl fluoride levels not yet measured. Symptoms included coughing, chest discomfort, hypotension, hyperexcitability, hyperventilation, tachycardia, and seizures. Post mortem evaluations typically reveal severe pulmonary edema, respiratory and lung mucosa and brain edema. A single non-lethal case has also been reported. In the latter case, reddened conjunctiva, pharyngeal and nasal mucosa and reversible paresthesia of the right leg was reported.

12. Sulfuryl fluoride exposure has resulted in serious illness in California. Between 1997 and 2001, a total of 32 incidents were reported to DPR associated with either sulfuryl

fluoride, chloropicrin or both and were due to spillage, drift or chemical residues. Short-term exposure typically resulted in irritation of the eyes, nose and throat along with respiratory symptoms of difficulty in breathing and shortness of breath. Nausea, dizziness, paresthesia, disorientation, headache, confusion and memory loss have also been reported. In a cross-sectional epidemiological study of 1234 structural fumigation workers, reduced performance on the pattern memory test and reduced olfactory function was noted in workers exposed with "high sulfuryl fluoride exposure."

Animals

13. The acute toxicity of sulfuryl fluoride has been evaluated in a variety of animal species including rats, mice, dogs, rabbits, and guinea pigs. Neurotoxiciy was observed in rats, mice, rabbits and dogs at non-lethal concentrations. With exposures up to two weeks, signs observed in these species included tremors, lethargy, respiratory effects, incapacitation, tetany, and convulsions. Renal effects (papillary necrosis, degeneration and regeneration of the collecting and proximal tubules) in rats, cerebral lesions (vacuolation, malacia, demyelination) in rabbits and mice and respiratory effects (tissue inflammation in nasal, trachea and bronchi/bronchioles) in rabbits and dogs were observed at the LOAELs in the two-week exposure studies. One-hour LC_{50}s were 3730 ppm and 3020 ppm in male and female rats, respectively. Four-hour LC_{50}s ranged from approximately 600 ppm in mice to 1500 ppm in rats. An acute NOAEL of 300 mg/kg/day (300 ppm; 6 hr/d x 2d) was observed in rats exposed for 6-hours/day over the course of two days, based on no effects observed in the FOB or electrodiagnostic tests at this, the highest dose tested. The lowest two-week NOAEL, 40 mg/kg/day (100 ppm; 6 hr/d x 5d/w x 2w), was established in rabbits based on brain and respiratory tract lesions at the next higher dose of 121 mg/kg/day (300 ppm; 6 hr/d x 5d/w x 2w).

14. Subchronic toxicity studies in laboratory animals provide information on adverse effects following inhalation exposure of rats, mice, rabbits and dogs to sulfuryl fluoride. The brain was the primary target for sulfuryl fluoride toxicity in all species studied and the most common lesion following subchronic exposure was vacuolation of the cerebrum. Other effects reported were nasal tissue inflammation in rats and rabbits, renal hyperplasia, pulmonary histocytosis and fluorosis in rats, and thyroid hypertrophy in mice. A NOAEL of 12 mg/kg/day (30 ppm; 6hr/d x 5d/w x 13w) was established in rabbits based on cerebral vacuolation and nasal inflammation at the next higher dose of 40 mg/kg/day (100 ppm).

15. Three chronic toxicity/oncogenicity inhalation studies are available for sulfuryl fluoride, one each in rats, mice and dogs. In all species tested, the brain and the respiratory tract were the primary target organs for sulfuryl fluoride toxicity. Similar to subchronic exposures, cerebral vacuoles were observed in the brains of treated animals. Respiratory tract lesions consisted of inflammation of the nasal passages, trachea, larynx, and lungs

and lung congestion. Dental fluorosis was also observed in rats and dogs. Progressive glomerular nephropathy was also observed in rats and was considered the cause of early mortality in the high dose groups (57 mg/kg/day, 80 ppm; 6hr/d x 5d/w x 2y) of both sexes. A NOAEL of 4 mg/kg/day (6hr/d x 5d/w x 2y) was identified in male rats based on dental fluorosis in the next higher dosed group, 14 mg/kg/day. No oncogenic responses were observed in any of the three species tested.

16. Reproductive toxicity of sulfuryl fluoride was tested in rats in a two-generation study. Maternal effects consisted of lung inflammation and alveolar macrophage aggregates and the formation of cerebral vacuoles. Effects on pups occurred at doses that were maternally toxic and consisted solely of reduced body weight. The maternal NOAEL was 4 mg/kg/day (5 ppm; 6 hr/d x 5d/w x 2generations) based on the effects on the lungs observed at the next higher dose of 14 mg/kg/day (20 ppm); the latter dose was the NOAEL for the brain lesions). The reproductive NOAEL was 14 mg/kg/day (20 ppm; 6 hr/d x 5d/w x 2generations), based on reduced body weight of pups at the next higher dose of 107 mg/kg/day (150 ppm).

17. Developmental toxicity studies have been conducted in rats and rabbits. No teratogenic effects were observed in either species. In rats, maternal toxicity was observed at 100 ppm (100 mg/kg/day) in a range finding study based on a decrease in body weight and body weight gain and decreases in food and water consumption at the highest dose of 300 mg/kg/day (300 ppm; 6 hr/dx10d; gestational days 6 to 15). No fetal effects were observed in the study. A NOAEL of > 225 mg/kg/day (the highest dose tested, 225 ppm; 6 hr/dx10d; gestational days 6 to 15) was established in the definitive rat study for maternal and fetal effects based on the absence of effects at this dose. In rabbits, a maternal and developmental NOAEL of 42 mg/kg/day (75 ppm; 6 hr/d x 13d; gestational days 6 to 18) was observed based on reduced body weights and body weight gain in the dams and reduced fetal body weights at the highest dose of 127 mg/kg/day (225 ppm) (Hanley et al., 1981, 1989). No histological examination of either maternal or pup brains was performed in either species.

Basis, Potency, and Range of Health Risks to Humans

18. Human health risks for acute exposures to sulfuryl fluoride are estimated in the RCD/TAC document using an NOAEL of 300 mg/kg/day (300 ppm; 6 hr/dx2d) based on no effects observed in rats in the FOB or electrodiagnostic tests at this highest dose level in the study. A short-term (2 week) NOAEL of 40 mg/kg/day (6 hr/d x 5d/w x 2w) based on lesions in the brain and respiratory tract in rabbits at the next higher dose of 121 mg/kg/day (300 ppm) was used for evaluating human exposures longer than acute, but shorter than subchronic durations.

19. Human health risks from subchronic exposure to sulfuryl fluoride are estimated in the RCD/TAC document based on a subchronic NOAEL of 12 mg/kg-day (30 ppm; 6 hr/d x 5d/w x 13w) identified in 13 week rabbit study and was based on brain lesions (cerebral vacuoles) and nasal inflammation at the next higher dose of 40 mg/kg-day (100 ppm).

20. Chronic exposure to airborne sulfuryl fluoride was evaluated in the RCD/TAC based on a NOAEL of 4 mg/kg-day (5 ppm; 6 hr/d x 5d/w x 2generations) from a two-generation reproduction study in rats based on lung inflammation and alveolar macrophage aggregates observed in the dams at the next higher dose of 14 mg/kg-day (20 ppm).

21. OEHHA agrees with the selection of the critical studies and identification of the endpoints and NOAELs found in the RCD/TAC document.

22. Margins of exposure (MOEs) were calculated in the RCD/TAC document for the various age groups and scenarios by dividing the NOAEL by the estimated exposure. Only variants of acute exposures were actually evaluated in the RCD/TAC, even though exposures for longer durations were estimated. Acute (24 hour) exposure was assessed for residents entering cleared, fumigated homes. Acute (12 and 24 hour) exposures were assessed for bystanders at structural fumigation sites during the application phase. For bystanders at structural fumigation sites during the aeration phase, two-hour exposures were evaluated for the TRAP aeration procedure while 1-hour and 4-hour exposures were evaluated for bystanders near structures aerated by the Stack method. Acute (24-hopur) exposures were evaluated for bystanders at or near a non-food commodity fumigation site.

23. MOEs exceeding 100 when based on NOAELs from animal studies are typically considered by DPR to be sufficiently protective of human health. In the case of sulfuryl fluoride, however, a higher benchmark of 1,000 was adopted for residential and bystander exposures because of a data gap resulting from the lack of a suitable developmental neurotoxicity study. In addition, DPR Regulations (Title 3, CCR Section 6890) specifies that a pesticide shall be listed as a toxic air contaminant if the ambient air concentrations are greater than: 1) 10-fold below the reference concentration for pesticides with threshold effects, or 2) 10-fold below the negligible risk concentration. Because of the relationship between MOEs and reference concentrations, MOEs lower than 10,000 meet the criterion #1, above.

24. MOEs presented in the RCD/TAC for acute (24 hour) exposure of residents entering cleared, fumigated homes range from 104 for children <1 year of age to 270 for 15-18 year-old children. We note that all MOEs for residents of fumigated homes are less than 1,000 and are therefore of potential human health concern.

25. For fumigations conducted at the submaximal application rate of 16 g/m3, MOEs presented in the RCD/TAC for acute (12 hour) exposure of bystanders at a structural fumigation site during the application phase were all less than 1,000 and ranged from 150 for infants <1year of age to 386 for 15-18 year-old children. MOEs presented for acute (24 hour) exposure were also all less than 1,000 and ranged from 108 for infants <1year of age to 270 for 15-18 year-old children. For fumigations occurring at the maximum application rate (160 g/m3), MOEs for acute (12 hour) exposure of bystanders at a structural fumigation site during the application phase were all less than 100 and ranged from 15 for infants <1 year of age to 39 for 15-18 year-old children. MOEs presented for acute (24 hour) exposure were also all significantly less than 100 and ranged from 11 for infants <1year of age to 27 for 15-18 year-old children. We note that all MOEs for bystanders under all scenarios near an active structural fumigation site are extremely low, and are therefore of potential human health concern.

26. For fumigations conducted at the submaximal application rate of 16 g/m3, MOEs presented in the RCD/TAC for acute (2 hour) exposure of bystanders at a structural fumigation site during the aeration phase utilizing the TRAP method were all less than 1,000 and ranged from 64 for infants <1year of age to 150 for 15-18 year-old children. Using the Stack aeration technique, MOEs presented for acute (1 hour) exposure were also all 1,000 or less and ranged from 386 for infants <1year of age to 1080 for 15-18 year-old children. Acute, 4-hour MOEs with Stack aeration ranged from 360 for infants <1year of age to 900 for 15-18 year old children. For fumigations occurring at the maximum application rate (160 g/m3), MOEs for acute (2 hour) exposure of bystanders during the aeration phase utilizing the TRAP method also all significantly less than 100 and ranged from 4 for infants <1year of age to 10 for 15-18 year-old children. Using the Stack aeration technique, MOEs presented for acute (1 hour) exposure also were all less than 100 and ranged from 39 for infants <1year of age to 108 for 15-18 year-old children. Acute, 4-hour MOEs with Stack aeration ranged from 36 for infants <1year of age to 90 for 15-18 year old children. We note that all MOEs for bystanders near structural fumigation sites utilizing either TRAP or Stack methodology for aeration were all under 1,000 and many were less than 100 and are therefore of potential human health concern. We are particularly concerned with bystander exposure at the maximum application rate using the TRAP aeration technique, where all MOEs were 10 or less.

27. MOEs presented in the RCD/TAC for acute (24 hour) exposure of bystanders at or near a non-food commodity fumigation site were all significantly less than 1,000 and ranged from 23 for infants <1year of age to 60 for 15-18 year-old children. We note that all MOEs for all age groups under this scenario are less than 100 and are therefore of potential human health concern.

28. Continuous and or repeated exposures to sulfuryl fluoride are considered unlikely; accordingly only acute exposures were evaluated in the RCD/TAC. Annual exposures

based on 1 – 7 day exposures were not evaluated in the document because they were considered acute exposures. Lifetime risks of sulfuryl fluoride exposure were also not evaluated since sulfuryl fluoride exposure is considered acute, there are no toxic endpoints unique to chronic exposure and there is no evidence that sulfuryl fluoride is oncogenic.

29. Reference concentrations (RfCs) are calculated in the RCD/TAC for acute (24-hour), short duration (up to two-weeks), subchronic (13-weeks) and chronic exposures to sulfuryl fluoride in ambient air. The RfC is calculated by dividing the oral NOAEL (in mg/kg-day) by the appropriate human breathing rate (in m^3/kg-day) and uncertainty factor (unitless). RfCs were calculated based on breathing rats of infants (0.59 m^3/kg-day) since that provided the most health-protective value. An uncertainty factor of 1000 was applied to each NOAEL in consideration of the variability between and within species (100) and for the lack of a developmental neurotoxicity study (10). RfCs presented in the RCD/TAC, along with the corresponding NOAELs and assumptions made in the calculations can be seen in Table 1.

Other Relevant Findings

30. U.S. EPA's Food Quality Protection Safety Factor Committee has recommended that the ten-fold safety factor be retained in the calculation of RfCs for chronic and dietary residential exposures. This is due to the lack of a suitable developmental neurotoxicity study for sulfuryl fluoride and concern regarding brain vacuolation observed in adult animals. Accordingly, an additional 10-fold uncertainty is applied when interpreting MOEs and in the RfC calculations presented in the RCD/TAC document.

31. Limited information is available regarding any potential environmental breakdown products of sulfuryl fluoride. The extent of or any toxicological significance of co-exposure to possible breakdown products cannot be evaluated.

32. Estimates of the contribution to total chronic fluoride exposure from all sources (drinking water, dietary and cryolite) from occupational fluoride sources ranged from a low of 5% to a high of 92%. A value of 46% contribution from occupational sources (0.05 mg/kg/day of a total 0.11 mg/kg/day) was proposed in the RCD as probably reflecting current exposures.

33. Cumulative exposure to other chemicals with similar mechanisms of action is possible. The extent of or any toxicological significance of cumulative exposure to these compounds has not and should be evaluated.

Table 1. Reference Concentrations (RfCs) Calculated in the RCD/TAC for Acute, Short Duration (1-2 weeks), Subchronic (13 weeks), and Chronic Exposures to Sulfuryl Fluoride

Exposure Duration	NOAEL[1] (mg/kg-day)	RfC[2] (mg/m^3)	Air Concentrations[3] (mg/m^3)
Acute (1 day)	54[4]	0.51	7.42
Short-term (1-2 weeks)	7.2[5]	0.10	1.75
Subchronic (13 weeks)	2.2[6]	0.03	n.a.[8]
Chronic	0.72[7]	0.01	n.a.[8]

1. Absorbed dose NOAELs, inhalation absorption was assumed to be 18%.
2. A breathing rate (infants) of 0.59 m^3/kg-day was used for the calculations. An uncertainty factor of 1000 was applied to all calculations.
3. Estimated concentrations of sulfuryl fluoride in indoor air following clearance of fumigated homes. Estimates based on the exposure study by Shurdut, 1995. See also Finding #4.
4. Albee et al., 1993a, NOAEL of 300 mg/kg-day based on no effect in the FOB or electrophysiological tests in rats at this, the highest dose tested.
5. Eisenbrandt et al., 1985, NOAEL of 40 mg/kg-day based on brain lesions in rabbits at the next higher dose of 121 mg/kg-day.
6. Nitschke et al., 1987b, NOAEL of 12 mg/kg-day based on brain lesions in rabbits observed at the next higher dose of 40 mg/kg-day.
7. Breslin et al., 1992, NOAEL of 4 mg/kg-day based on pulmonary effects observed in rats at the next higher dose of 14 mg/kg-day.
8. n.a. = not applicable as continuous exposure exceeding 7 days is not expected.

CENTER FOR OCCUPATIONAL AND ENVIRONMENTAL HEALTH

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August 29, 2006

Ms. Mary-Ann Warmerdam
Director
Department of Pesticide Regulation
1001 I Street
P.O. Box 4015
Sacramento, California 95812-4015

Dear Ms. Warmerdam:

With this letter I am pleased to transmit the Scientific Review Panel on Toxic Air Contaminants' Findings on sulfuryl fluoride. The findings were based on the Panel's review of the Department of Pesticide Regulation's draft report titled "Sulfuryl Fluoride (Vikane®) Risk Characterization Document" prepared by the Department of Pesticide Regulation and reviewed by the Office of Environmental Health Hazard Assessment.

The Panel reviewed the draft report as well as the scientific data on which the report is based, the scientific procedures and methods used to support the data, and the conclusions and assessments on which the report is based, as required by state law. The Panel also reviewed comments received and responses to those comments. In approving the report, it is the Panel's conclusion that the report, with the revisions requested by the Panel, is based on sound scientific knowledge.

The Panel recommends that you take the necessary steps to list sulfuryl fluoride as a toxic air contaminant. Sulfuryl fluoride is a broad spectrum insecticide and rodenticide used to fumigate sealed structures and their contents. Upon review of the toxicity of sulfuryl fluoride it is apparent that the available information supports the finding of its being listed as a Toxic Air Contaminant.

It was noted during the discussion that fluoride is a toxic metabolite of sulfuryl fluoride. There is a developing literature on the toxicity of fluoride and the Panel recommends that the Department review that developing literature over time to ensure the information is up-to-date. For example, a committee of the National

Academy of Sciences (NAS) reviewed the literature on the potential of fluoride to cause cancer, in particular bone, and concluded the data was tentative and mixed. Therefore, it will be important to follow developments in this area since it is currently a focus of attention. Further research on the toxicity of this compound for a range of endpoints is indicated.

Let me also take this opportunity to thank the Department of Pesticide Regulation staff for their efforts in completing this report. The Panel appreciates the time and work that were put into the report as well as responding to further questions from the Panel.

Lastly, we ask that the Panel's findings and this letter be made a part of the final report.

Sincerely,

John R. Froines

John R. Froines, Ph.D.
Chairman
Scientific Review Panel

cc: Scientific Review Panel members

Joan E. Denton, Ph.D.
Director
Office of Environmental Health Hazard Assessment

Robert F. Sawyer, Ph.D.
Chairman
Air Resources Board

Jim Behrmann
Liaison, Scientific Review Panel

Enclosure: **Findings of the Scientific Review Panel on the Proposed Identification of Sulfuryl Fluoride as a Toxic Air Contaminant**

Findings of the Scientific Review Panel on the Proposed Identification of Sulfuryl Fluoride as a Toxic Air Contaminant as adopted at the Panel's June 26, 2006 Meeting

The Scientific Review Panel on Toxic Air Contaminants (Panel) reviewed the report, *Sulfuryl Fluoride (Vikane®) Risk Characterization Document*, June 2005, prepared by the Department of Pesticide Regulation (DPR). The Panel reviewed and discussed the report in its July 8, 2005 and December 13, 2005 meetings, along with findings prepared by the Office of Environmental Health Hazard Assessment (OEHHA) dated July 1, 2005.

This report was written to meet the statutory requirements of the state's toxic air contaminant statute (AB 1807) which addresses releases into the ambient air, and also DPR's SB950 requirements (addressing both occupational and general population exposures).

A public review draft was released in August 2004 for public comment and review by the Air Resources Board, OEHHA and by the Panel lead members for this report, Drs. Atkinson and Byus. A subsequent draft was prepared in April 2005, and a final draft was sent to the Panel for its consideration in June 2005. Additional revisions were incorporated into the report based on comments from the Panel in its July and December 2005 meetings, and a revised final draft was sent to the Panel in June 2006. Based on its discussion at the July 8, 2005, December 13, 2005 and June 26, 2006 meetings, the Panel's review of the draft report and information submitted through the public comment process, the Panel makes the following findings pursuant to Food and Agricultural Code section 14023:

(1) Sulfuryl fluoride is a broad spectrum insecticide and rodenticide used to fumigate sealed structures and their contents. There are two registered products approved for use in California, Vikane® and ProFume®. Vikane® is the registered trade name for the sulfuryl fluoride product that is used to control existing infestations of insects and related pests such as drywood termites, powder post beetles, old house borers, death-watch beetles, bedbugs, clothes moths, rodents, and cockroaches in dwellings (including mobile homes), buildings, barns, vehicles, fumigation chambers, rail cars, and surface ships in port and their contents such as construction materials, furnishings, and household effects. ProFume® is the registered trade name for the sulfuryl fluoride product approved in 2005 for use in food commodity fumigations; this relatively new use was not evaluated in this report.

(2) Use of sulfuryl fluoride increased from 1.5 million pounds in 1993 to almost 3.3 million pounds in 2004. In 2004 almost 1.2 million pounds were used in Los Angeles County alone. The major use (>99%) is for

structural pest control and the increase in use is attributed to the decline in the use of methyl bromide for the same purpose.

(3) After fumigation of a tented structure, sulfuryl fluoride in the air of treated structure is immediately released through clearance or aeration of the structure using a variety of procedures, including the Tarpaulin removal and aeration plan ("TRAP") method. The TRAP method, which is used in California, involves 10 minutes of active ventilation followed by tarpaulin removal, and then additional aeration. Essentially, all of the applied sulfuryl fluoride is released into the atmosphere as a gas.

(4) Once in the atmosphere, the fate of sulfuryl fluoride is unclear since there are no available studies specifically on this subject. Based on limited relevant data, sulfuryl fluoride appears to have a long atmospheric lifetime with respect to photolysis, reaction with hydroxyl radicals, nitrate radicals and ozone in the atmosphere, and dissolution and/or degradation in sea water. Sulfuryl fluoride is therefore expected to be transported throughout the global atmosphere. The potential for sulfuryl fluoride to contribute to the greenhouse effect needs to be further investigated by DPR. Specifically, the Global Warming Potential of sulfuryl fluoride needs to be calculated.

(5) For residents and neighbors (referred to in the report as "bystanders"), exposures are primarily acute and of short-term duration. Ambient air exposures for the general population other than neighbors were not estimated since they were assumed to be negligible. The likelihood of community-wide exposures is very low because there are a limited number of application sites. All exposure estimates are predicated on appropriate use practices; in scenarios of misuse these estimates would not apply.

(6) Sulfuryl fluoride is a colorless, odorless gas, highly toxic to human beings as well as other mammals. The applied concentrations of sulfuryl fluoride sufficient to kill insects and rodents in tented buildings and containers are lethal to human beings. Unintentional cases of human poisoning and fatalities due to entering homes being fumigated, and other exposures due to spills or drift have been reported. Signs and symptoms included coughing, chest discomfort, hypotension, hyperventilation, tachycardia, and seizures. Postmortem evaluations typically revealed severe pulmonary and brain edema. Nonfatal exposure usually resulted in irritation of the eyes, nose and throat along with respiratory symptoms of difficulty in breathing and shortness of breath. Nausea, dizziness, paresthesia, disorientation, headache, confusion and memory loss have also been reported.

(7) At non-lethal concentrations of sulfuryl fluoride, neurotoxicity was observed in exposed rats, mice, rabbits, and dogs. With repeated exposures, the primary target tissues for sulfuryl fluoride inhalation toxicity in experimental animals were the brain and respiratory system. With up to two weeks of exposure, clinical signs observed included tremors, lethargy, respiratory effects, incapacitation, tetany, and convulsion. Animals treated for two weeks showed tissue damage in the kidney (rats), brain (rabbits, mice), and respiratory tract (rabbits and dogs). After 13 weeks of inhalation exposure, the brain was the primary target for sulfuryl fluoride toxicity in all species studied (rats, mice, rabbits, and dogs). The most common lesion was vacuoles in the cerebral tissues. Other effects reported were nasal tissue inflammation (rats and rabbits), kidney hyperplasia (rats), lung histiocytosis (rats), thyroid hypertrophy (mice), and fluorosis (rats). The significant finding from reproductive and developmental toxicity studies was reduced body weight of fetuses (rats), pups (rats), and dams (rats).

(8) In animals, the following were identified as critical NOELs: acute – 300 ppm; short-term (1-2 weeks) – 100 ppm; subchronic (13 weeks) – 30 ppm; and chronic (annual) – 5 ppm (See Summary Table 1 from the DPR report attached).

(9) Appendix B of Volume I of the report provides a review on fluoride in general. Fluoride is a toxic metabolite of sulfuryl fluoride. There are many natural sources of fluorides including fluorine, volcanic emissions, weathering and dissolution of fluoride-containing minerals, marine aerosols, including anthropogenic sources used in industry and chemical productions, as well as fluoride being added to the water supply. The total human exposure to fluoride varies due to multiple sources of exposure. These sources include air, drinking water, food, and consumer products. Thus, any current and future use of sulfuryl fluoride (Vikane®, or from ProFume®, the product name used in food-commodity fumigation) must be considered within the context of the total fluoride burden experienced by people in the State of California.

(10) A committee of the National Academy of Sciences (NAS) completed its review of the U.S. EPA's Maximum Contaminant Level Goal of 4 mg fluoride/L in drinking water. The NAS committee summarized all available data from animals and humans, genotoxicity assays, and studies of mechanisms of action relating to oncogenicity. The committee's conclusion was that the evidence on the potential of fluoride to cause cancer, in particular in bone, was "tentative and mixed." Fluoride, a metabolite of sulfuryl fluoride, is clastogenic and can induce osteosarcomas in male rats. There is conflicting evidence

whether fluoride in the drinking water may be associated with an increased incidence of osteosarcomas in male humans.

(11) It is anticipated by DPR that there will be increased approved use of sulfuryl fluoride (as ProFume®) in food commodity fumigation. Such use is predicted to result in increased total exposures. This increased use was not evaluated in this report. Additional monitoring will be necessary to better define the resulting concentrations and to be able to consider the risks to the numbers of people exposed.

(12) Based on the available toxicity studies and the resulting NOELs, the reference concentrations for sulfuryl fluoride determined by DPR for residents/bystanders (infants) are 0.002 ppm for chronic long-term exposure; 0.007 ppm for sub-chronic (13 week) exposure; 0.023 ppm for 1-2 week exposure; and 0.12 ppm for an acute, 1-day exposure.

(13) Residents of treated homes may be exposed to sulfuryl fluoride after their houses have been treated. Residents' exposure was estimated based on results from a 48-hour post-clearance monitoring study of seven homes. During the first 24 hours after residents are allowed to reenter the houses, the mean sulfuryl fluoride air concentrations in these houses ranged from 0.01 ppm to 1.78 ppm. At 40-48 hours after aeration, sulfuryl fluoride was still detected, ranging from 0.02 ppm to 0.48 ppm. The predicted sulfuryl fluoride concentration rapidly decreases during the first two days following clearance, and tends toward zero around day 6 or 7.

(14) Neighbors and other persons in the vicinity are at risk for exposure to sulfuryl fluoride during any phase of a structural fumigation, from application through clearance, with the greatest potential for exposure likely during aeration.

(15) The estimated acute exposure for bystanders during the fumigation procedure exceeded 1/10th of the reference concentrations, and thus would meet the criteria established by DPR for listing under the AB1807 Toxic Air Contaminant Program. For the following scenarios and exposure duration the exposures exceeded 1/100 (occupational adult exposure) or 1/1000* (residential and bystander exposure) of the no-effect levels based on laboratory animal studies: 1. *Structural fumigation*: a. Workers and any non-residential intruders at both submaximal and maximal application rates; b. Residents of all age groups following clearance; c. Bystanders of all age groups during the application stage and during the TRAP method of aeration; and 2. *Non-food commodity fumigation*: all bystanders.

Table 1 below summarizes the critical no-observed-levels (NOELs) and reference concentrations, and Table 2 compares infant bystander exposures with the acute reference concentrations.

* A higher benchmark margin of exposure of 1000 was used for sulfuryl fluoride residential and bystander exposures in this RCD because of the lack of a study to fulfill the requirement for a developmental neurotoxicity study by the U.S. Environmental Protection Agency.

(16) As required by law, the Panel has reviewed the scientific data on which the report is based, the scientific procedures and methods used to support the data, and the conclusions and assessments on which the report is based. The Panel concludes that the report, with the revisions specified by the Panel, is based on sound scientific knowledge, and represents a balanced assessment of our current scientific understanding.

(17) The Panel recommends that the Director of DPR initiate regulatory steps to list sulfuryl fluoride as a toxic air contaminant pursuant to Food and Agricultural Code section 14023.

I certify that the above is a true and correct copy of the findings adopted by the Scientific Review Panel on June 26, 2006.

Original signed by

_____

John R. Froines, Ph.D.
Chairman, Scientific Review Panel

Attachments:
Summary Table 1: Critical no-observed-effect levels (NOELs) and reference concentrations for the risk characterization of sulfuryl fluoride.
Table 2: Comparison of infant bystander exposures with the acute reference concentration.

Summary Table 1. Critical no-observed-effect levels (NOELs) and reference concentrations for the risk characterization of sulfuryl fluoride.[a]

Duration	NOEL (ppm)	NOEL (mg/kg/day)	NOEL in absorbed dose (mg/kg/day)	Reference concentration		Critical Endpoint
				Workers (Adult) UF=100	Residents/ Bystanders (Infants) UF=1000	
Acute 1 day	300	300	54	2.57 ppm 10.7 mg/m^3	0.12 ppm 0.51 mg/m^3	No effect in FOB and electro-physiological tests in rats
1-2 weeks	100	40	7.2	0.48 ppm 2.01 mg/m^3	0.023 ppm 0.10 mg/m^3	Brain lesion (malacia and vacuoles) in rabbits
Sub-chronic (13-week)	30	12	2.2	0.14 ppm 0.60 mg/m^3	0.007 ppm 0.03 mg/m^3	Brain lesion (vacuoles) in rabbits
Chronic	5	4	0.72	0.04 ppm 0.18 mg/m^3	0.002 ppm 0.01 mg/m^3	Lung inflam-mation, alveolar macrophage aggregates in rats

a/ From Table 18 of this volume.

Source: DPR, "Sulfuryl Fluoride (Vikane®) Risk Characterization Document, Volume I, Health Risk Assessment, June 2006, at page 6.

Table 2. Comparison of infant bystander exposures with the acute reference concentration.*

Scenario	Air level[a]	Hours exposed[a]	Air level as 24-hour time-weighed average	% RfC[b]	MOE[c]
Structural Fumigation at Submaximal Rate					
Application phase					
First 12-hours	1.6 ppm	12	0.8 ppm	667%	150
24 hours	1.12 ppm	24	1.12 ppm	933%	108
Aeration phase TRAP method					
2 hours	24 ppm	2	2 ppm	1,667%	60
Non-food Commodity Fumigation					
24 hours	5 ppm	24	5 ppm	4,167%	24

* adapted from Table 31 in Volume 1.

a/ Based on information in Tables 14a, 15a, 16a, and 17 in **Volume II**.
b/ The reference concentration for infants was 0.12 ppm (Table 18).
c/ The MOEs were those shown in Tables 28-30.

Source: DPR, "Sulfuryl Fluoride (Vikane®) Risk Characterization Document, Volume I, Health Risk Assessment, June 2006, at page 86.

Department of Pesticide Regulation

Mary-Ann Warmerdam
Director

Arnold Schwarzenegger
Governor

M E M O R A N D U M

TO: Paul H. Gosselin
Chief Deputy Director

FROM: Mary-Ann Warmerdam
Director
(916) 445-4000

DATE: September 18, 2006

SUBJECT: DIRECTOR'S PROPOSED DECISION CONCERNING SULFURYL FLUORIDE AS A TOXIC AIR CONTAMINANT

Attached is a public notice of the proposed decision concerning my response to the Scientific Review Panel's (SRP's) findings on sulfuryl fluoride as a toxic air contaminant. My response has been made in accordance with all authorities and requirements stipulated in the Food and Agricultural Code and California Code of Regulations[1] that mandate this determination.

Thanks to you, our staff, and all the members of the SRP for the excellent work.

Attachment

cc: Robert Sawyer, Chair (w/Attachment)
Air Resources Board

Joan E. Denton, Ph.D., Director (w/Attachment)
Office of Environmental Health Hazard Assessment

Jim Behrmann, Scientific Review Panel, Air Resources Board Liaison (w/Attachment)

Scientific Review Panel (w/Attachment)

[1] The SRP's findings were transmitted on September 8, 2006. The Food and Agricultural Code and California Code of Regulations mandate that the DPR Director must respond within ten working days.

bcc: Tobi Jones, Ph.D., DPR Assistant Director (w/Attachment)
Jerry Campbell, DPR Assistant Director (w/Attachment)
Chuck Andrews, Chief, DPR Worker Health and Safety Branch (w/Attachment)
Barry Cortez, Chief, DPR Pesticide Registration Branch (w/Attachment)
David Duncan, Chief, DPR Pest Management and Licensing Branch (w/Attachment)
Gary Patterson, Chief, DPR Medical Toxicology Branch (w/Attachment)
Scott T. Paulsen, Chief, DPR Pesticide Enforcement Branch (w/Attachment)
John S. Sanders, Ph.D., Chief, DPR Environmental Monitoring Branch (w/Attachment)
Randy Segawa, DPR Environmental Monitoring Branch (w/Attachment)
Shifang Fan (1807 files), DPR Environmental Monitoring Branch (w/Attachment)
Linda Irokawa-Otani, DPR Regulations Coordinator (w/Attachment)
Segawa Surname File (w/Attachment)

Post Until
October 27, 2006

NOTICE OF PROPOSED DECISION CONCERNING THE DIRECTOR'S DECLARATION OF SULFURYL FLUORIDE AS A TOXIC AIR CONTAMINANT

Section 14023 of the Food and Agricultural Code requires the Director of the Department of Pesticide Regulation (DPR) to determine if a pesticide is a toxic air contaminant (TAC) after receiving the findings of the Scientific Review Panel (SRP), a panel of experts representing a range of scientific disciplines. Based on the findings of SRP's assessment of the report entitled "Final Draft Sulfuryl Fluoride (Vikane) Risk Characterization Document" and the criteria given in Title 3, California Code of Regulations (3 CCR) section 6890(b), DPR's Director proposes to declare sulfuryl fluoride as a TAC.

Background

With the enactment of California's TAC Act (Assembly Bill 1807, Tanner, Chapter 1047, Statutes of 1983; amended by Tanner, Chapter 1380, Statutes of 1984), the Legislature created the statutory framework for the evaluation and control of chemicals as TACs. The statute defines TACs as air pollutants that may cause or contribute to increases in serious illness or death, or that may pose a present or potential hazard to human health. DPR is responsible for the evaluation of pesticides as TACs.

In general, the law focuses on the evaluation and control of pesticides in ambient community air. In implementing the law, DPR must: (1) conduct a review of the physical properties, environmental fate, and human health effects of the candidate pesticide; (2) determine the levels of human exposure in the environment; and (3) estimate the potential human health risk from those exposures. The law requires DPR to list in regulation those pesticides that meet the criteria to be TACs.

For each pesticide, the law requires the preparation of a report that includes: the environmental fate and use of the pesticide, an assessment of exposure of the public to air concentrations of the pesticide, and a health assessment. The report is reviewed by the Office of Environmental Health Hazard Assessment and the Air Resources Board, and is made available for public review. Based on the results of these reviews, the draft report is revised as appropriate. The draft undergoes a rigorous peer review for scientific soundness by SRP. Based on the results of this comprehensive evaluation, DPR's Director determines whether the candidate is a TAC. If DPR's Director determines the pesticide meets the criteria to be a TAC, DPR declares the pesticide a TAC in regulation, and adds it to the TAC list. For more information describing how DPR prioritizes pesticides for evaluation and risk assessment see the document entitled "Process for Human Health Risk Assessment Prioritization and Initiation" on DPR's Web site at <http://www.cdpr.ca.gov/docs/risk/raprocess.pdf>.

Once a candidate pesticide has been declared a TAC, it enters phase two of the program–the mitigation, or control, phase. In the mitigation phase, DPR investigates the need for, and appropriate degree of, control for the TAC. If reductions in exposure are needed, DPR must develop control measures to reduce emissions to levels that adequately protect public health.

Conclusions

Title 3 CCR section 6890 states, "A pesticide shall be identified as a toxic air contaminant if its concentrations in ambient air are greater than the following levels (for the purposes of this section, a threshold is defined as the dose of a chemical below which no adverse effect occurs):

> (a) For pesticides which have thresholds for adverse health effects, this level shall be ten-fold below the air concentration which has been determined by DPR's Director to be adequately protective of human health.
>
> (b) For pesticides which do not have thresholds for adverse health effects, this level shall be equivalent to the air concentration which would result in a ten-fold lower risk than that which has been determined by DPR's Director to be a negligible risk."

The reference concentration is the estimate of daily human exposure that is not likely to result in health concerns. It is calculated from the no observed effect levels from toxicity studies in experimental animals and applicable uncertainty factors. The reference concentrations for sulfuryl fluoride included an uncertainty factor of 1000 to account for the extrapolation of data from laboratory animal study, variation in response between individuals, and the lack of a developmental neurotoxicity study. The no observed effect levels for acute, 1-2 weeks, subchronic (13-weeks), and chronic exposures were 300, 100, 30, and 5 parts per million (ppm), respectively. The reference concentrations (and exposure durations) for infants, the highest exposed group in the general population, are 0.12 ppm (acute), 0.023 ppm (1-2 weeks), 0.007 ppm (subchronic), and 0.002 ppm (chronic). As described above, air concentrations exceeding one-tenth (10 percent) of the reference concentrations meet the criteria for listing as a TAC. Therefore, sulfuryl fluoride air concentrations exceeding 0.012 ppm (acute), 0.0023 ppm (1-2 weeks), 0.0007 ppm (subchronic), and 0.0002 ppm (chronic) would meet the criteria for listing as a TAC.

Human exposures were estimated using the monitoring data for structural fumigation during application and aeration phases, and the label limit of 5 ppm for nonfood commodity fumigation. Infant bystander acute exposures (air level as 24-hour time weighed average) ranged from 0.31 to 5 ppm. These were 255 percent to 4,167 percent of the acute reference concentration of 0.12 ppm, meeting the criteria for identifying sulfuryl fluoride as a TAC.

SRP agrees with the science presented in the risk characterization document and recommends that DPR's Director identify sulfuryl fluoride as a TAC.

Actions

DPR proposes to adopt a regulation designating sulfuryl fluoride as a TAC. DPR proposes to add sulfuryl fluoride to the list of pesticides in 3 CCR section 6860(a).

DPR will conduct a public hearing concerning the proposed regulation.

APPROVED BY: _____ Date: September 18, 2006____
Mary-Ann Warmerdam, Director