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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

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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 24 hours	 1.6 ppm 1.12 ppm	 12 24	 0.8 ppm 1.12 ppm	 667% 933%	 150 108
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.