SULFURYL FLUORIDE (Vikane®)

RISK CHARACTERIZATION DOCUMENT

Volume IV

DPR Responses to Comments

Medical Toxicology Branch
Worker Health and Safety Branch
Environmental Monitoring Branch
Department of Pesticide Regulation
California Environmental Protection Agency

Responses to Comments on the March 2004 Draft

1. **Office of Environmental Health Hazard Assessment**
2. **Air Resources Board**
3. **Dow AgroSciences**

Office of Environmental Health Hazard Assessment

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MEMORANDUM

Terry Tamminen
Agency Secretary

Arnold Schwarzenegger
Governor

TO: Gary T. Patterson, Ph.D., Chief
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FROM: Anna M. Fan, Ph.D., Chief
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DATE: May 4, 2004

SUBJECT: COMMENTS ON THE DEPARTMENT OF PESTICIDES REGULATION'S SULFURYL FLUORIDE RISK CHARACTERIZATION AND EXPOSURE ASSESSMENT DOCUMENTS

Thank you for the opportunity to review the Risk Characterization and Exposure Assessment documents prepared by the Department of Pesticide Regulation (DPR) for the active ingredient, sulfuryl fluoride. The Office of Environmental Health Hazard Assessment (OEHHA) reviews risk assessments prepared by DPR under the general authority of the Health and Safety Code (HSC), Section 59004, and also under the Food and Agricultural Code (FAC), Section 13129, in which OEHHA has the authority to provide advice, consultation, and recommendations to DPR concerning the risks to human health associated with exposure to pesticide active ingredients.

In addition, pursuant to Food and Agricultural Code sections 14022 and 14023, OEHHA provides consultation to DPR on the evaluation of the health effects of candidate toxic air contaminants 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, which will be developed after DPR considers OEHHA's comments.

Currently, only one product is registered in California that contains sulfuryl fluoride as the active ingredient. This product, Vicane, is used for structural and non-food commodity fumigation. It controls a variety of pests such as dry wood termites, powder post beetles, old house borers, bedbugs, clothes moths, rodents, and cockroaches in dwellings, buildings, construction materials, furnishings, and vehicles. Vicane contains chloropicrin as a warning agent. In California, sulfuryl fluoride is a candidate for consideration as a toxic air contaminant under AB 1807, the Toxic Air Contaminant Act. Sulfuryl fluoride is not listed under Proposition 65, the Safe Drinking Water Act because it is not considered a developmental/reproductive toxicant or carcinogen.

The documents that were submitted to us provide an excellent overview of the available studies and scientific literature relevant to the toxicology of sulfuryl fluoride. Sulfuryl fluoride is a toxic gas that acts as a central nervous system depressant. Symptoms of poisoning include depression, slowed gait, slurred speech, nausea, vomiting, stomach pain, drunkenness, itching, numbness, twitching, and seizures. Inhalation may be fatal due to respiratory failure. Inhalation of high concentrations may cause respiratory tract irritation. Individuals with a history of chronic respiratory disease are at increased risk from exposure to sulfuryl fluoride. Skin contact with sulfuryl fluoride normally poses no hazard, but contact with liquid sulfuryl fluoride can cause pain and frostbite due to rapid vaporization.

In animal studies, neurotoxicity was observed in rats, mice, rabbits and dogs as a result of acute, subchronic, and chronic exposures. The primary target for sulfuryl fluoride toxicity in all species studied (rats, mice, rabbits, and dogs) was brain. The most common lesion found both in subchronic and chronic studies was vacuoles in the cerebrum.

For the most part, we agree with the presentation and discussion of the toxicology and risk assessment issues in these documents. However, we have several concerns and a number of observations and recommendations that we believe can improve the documents in achieving our mutual goals of protecting public health interests. While the current versions of the documents are comprehensive, they would benefit from clarifying and expanding specific issues that we have identified. We acknowledge and especially appreciate broad and thorough discussions of exposure related issues in the Exposure Assessment Document. The key recommendation of this review is that the quantitative risk assessment be revised by applying an additional ten-fold uncertainty factor, as suggested by U.S. EPA to account for toxicological data gaps and the potential additional sensitivity of infants and children to sulfuryl fluoride exposures.

A summary of our comments on the Risk Characterization and Exposure Assessment documents for sulfuryl fluoride is presented below. For more details please refer to the attachment.

1. OEHHA recommends revision of the quantitative risk assessment of sulfuryl fluoride by applying an additional ten-fold uncertainty factor to account for current lack of developmental neurotoxicity study and potential increased sensitivity of infants and children to sulfuryl fluoride exposures.

2. We recommend a decrease in the reentry levels (air concentration) of sulfuryl fluoride.

3. We suggest that the label for Vicane be included in the documentation of risk characterization and exposure assessment documents.

4. We support the choices of critical studies and toxicological endpoints used in the DPR RCD for sulfuryl fluoride. We suggest that DPR provide further justification for not assessing health risks from lifetime exposures to sulfuryl fluoride.

5. Discussion of sulfuryl fluoride data gaps and related uncertainties in the risk characterization part of the RCD would enhance the quality of the risk assessment documents.

6. Available information or data on possible interaction of sulfuryl fluoride and chloropicrin, a warning agent that is required in Vicane, would be useful. We suggest that information be included regarding the range of chloropicrin concentrations in Vicane.

7. Justification of choice of default breathing rate for rabbits used in risk assessment, which is different than U.S. EPA's default rate, should be provided.

8. Brief discussion of potentially sensitive subpopulations (young, elderly, and those with medical conditions, particularly asthma) would improve the document.

9. We suggest that DPR consider evaluating chronic and subchronic exposures to bystanders, since it is plausible that a family could live adjacent to more than one home being fumigated over the course of a year.

Thank you for providing the document for our review. If you have any questions about our comments, please contact Dr. Jolanta Bankowska (RCD reviewer), (510) 622-3162, Dr. David Rice (916) 324-1277 (exposure assessment reviewer), Robert Schlag (916) 323-2624, or Dr. Anna Fan at (510) 622-3165.

ATTACHMENT

COMMENTS ON THE DEPARTMENT OF PESTICIDES REGULATION'S SULFURYL FLUORIDE RISK CHARACTERIZATION AND EXPOSURE ASSESSMENT DRAFT DOCUMENTS

RISK CHARACTERIZATION DOCUMENT

BACKGROUND INFORMATION

Only one product is currently registered in California that contains sulfuryl fluoride as the active ingredient. This product, Vicane, is used for structural and non-food commodity fumigation. It controls a variety of pests such as dry wood termites, powder post beetles, old house borers, bedbugs, clothes moths, rodents, and cockroaches in dwellings, buildings, construction materials, furnishings, and vehicles. Vicane contains chloropicrin as a warning agent. According to information derived from the DPR website, the total statewide use of sulfuryl fluoride was 3,045,084 pounds, a vast majority of which was used in structural pest control applications. In 2002, one definite/probable and eight possible acute sulfuryl fluoride-related illnesses were reported. Additionally, 9 of 27 (33%) of reported fumigant illnesses were attributed to sulfuryl fluoride. Sulfuryl fluoride is a candidate for consideration as a toxic air contaminant under AB 1807, the Toxic Air Contaminant Act. Sulfuryl fluoride is not listed under Proposition 65, the Safe Drinking Water Act because it is not considered a developmental/reproductive toxicant or carcinogen.

Our comments provided below focus on issues that in our evaluation require further discussions and/or explanations.

COMMENTS

Uncertainties

Uncertainties involved in risk assessments in general and some uncertainties specific for sulfuryl fluoride are mentioned in various appropriate different parts of the documents. We suggest that a brief summary of all uncertainties relevant to sulfuryl fluoride risk assessment be included under the "Risk Characterization" section of the document. This section could also address but not be limited to: the current status of sulfuryl fluoride risk assessment, possible future requirements of new data that would allow further refinements of the risks and possible underestimations of the current sulfuryl fluoride risk assessment because of the lack of developmental neurotoxicity study, unknown mechanism of action, lack of data on metabolite/s and their contribution to sulfuryl fluoride toxicity, lack of the methods to measure the impact of

cumulative toxicity of sulfuryl fluoride and other chemicals that degrade or metabolize to fluoride ion.

Absence of Important Study Data

Throughout the RCD a number of potentially useful studies that have not been conducted or are unavailable were identified. We suggest that these studies specific to sulfuryl fluoride be summarized in one section. We refer not only to the data that are required under SB 950, but also to the data that would facilitate and improve health risk assessment. Such data for sulfuryl fluoride include but may not be limited to; developmental neurotoxicity study, pharmacokinetic studies, metabolic studies that would help to determine the role of fluoride ion in overall toxic effects of fluoride sulfate, and ecological effects of sulfuryl fluoride or fluoride ion. Absence of particular studies that relate to specific uncertainties in health risk assessment and a brief discussion of this issue in the risk characterization part of the RCD would be useful.

Sensitive Subpopulations

No potentially sensitive subpopulations are discussed in the RCD other than a mention of infants and children, who are not considered in this document to be more sensitive than the general population. OEHHA disagrees and believes infants and children should be regarded as potential sensitive subpopulation due to the neurotoxic effects of sulfuryl fluoride. In the light of the results of the RCD that show the brain is a primary target for sulfuryl fluoride toxicity we are concerned that younger populations may be especially sensitive to sulfuryl fluoride exposures. The developing organism with rapid cell proliferation, migration, and differentiation is uniquely sensitive to any kind of disruptions. In the brain these processes are unidirectional and occur at very specific times for different structures. Prenatal events include closure of the neural tube, proliferation of neurons, and migration of cortical neurons. During infancy and early childhood, proliferation and migration continue along with synaptogenesis, myelination, and development of the blood-brain barrier. Structural maturation of neural pathways, including an increase in the diameter and myelination of axons, continues through adolescence. During adolescence the rate of synaptic pruning peaks. Sulfuryl fluoride exposures can have profound effects on all of these neurologic developmental processes (OEHHA, 2001). OEHHA also recommends a brief discussion of other potentially sensitive subpopulations (elderly and others with medical conditions, such as asthma) be added to the document even though there are no mandated requirements or methods available to assess this probable higher sensitivity

Risk Appraisal

In general, human health risks associated with the current use of sulfuryl fluoride in structural and non-food commodity fumigation was determined in the RCD as being too high. As a general rule, a margin of exposure greater than 100 is considered protective of human health when it is calculated from a NOEL derived from an animal study. The MOEs were less than 100 for the following exposure scenarios:

1. Structural fumigation

   a. Workers at submaximal application rate: introducing fumigant (chronic), total fumigator activities (subchronic and chronic), fumigator and tent crew tasks (all durations), ground seam opening (subchronic and chronic), roof seam opening (1-2 weeks, subchronic and chronic) ground snake removal (chronic), tarpaulin folding (chronic), and general detarping (all durations).

   b. Workers at maximal application rate: introducing fumigant (all durations), total fumigator activities (all durations), fumigator and tent crew tasks (all durations), and all tent crew activities for all durations.

   c. Residents following clearance: < one year old (acute), <one year old to eight years old (one to two weeks).

   d. Bystanders during maximal rate application phase: three to five years old (acute).

   e. Bystanders during aeration: < one and three to eleven years old (acute, TRAP method, submaximal rate), all age groups (acute, both methods, maximal application rates).

2. Non-food commodity fumigation: handlers (one to two weeks, chronic).

Because of the high probability that infants and children are more sensitive to neurotoxic effects of this fumigant than adults, health risks resulting from current use of sulfuryl fluoride may be even higher (i.e., MOEs may be lower than those determined by DPR), especially for younger subpopulations. At present, this has not been demonstrated because of the absence of required developmental neurotoxicity study, and also because in currently available developmental toxicity studies in rats and rabbits (see pg. 36), no histological examination of the brain was not performed. These examinations might have shown the presence of vacuoles that were observed in studies of adult rats, rabbits, and dogs exposed to sulfuryl fluoride.

Although the currently available (or lack of) data do not trigger the Food Quality Protection Act criterion for applying a ten-fold uncertainty factor in risk assessment (due to the absence of studies for potential increased sensitivity by infants and children to the pre- and post-natal toxicity) the ten-fold uncertainty factor was used by U.S. EPA in sulfuryl fluoride risk assessment to account for database uncertainty (lack of developmental neurotoxicity study). We agree with that decision and strongly urge that DPR apply an additional ten-fold uncertainty factor in calculating risks from current exposures to sulfuryl fluoride.

Lifetime risk of sulfuryl fluoride exposure

Lifetime exposure assessment is a part of different exposures of sulfuryl fluoride determined in the Exposure Assessment document. However, lifetime risk from this exposure is not evaluated. The reason given in the RCD for this is that: "...sulfuryl fluoride has not been shown to be oncogenic in either humans or experimental animals" (see pg. 55 of the RCD). This explanation does not seem to be adequate, since other toxic effects of sulfuryl fluoride, e.g. neurotoxicity, should justify such evaluation. We suggest either performing risk assessment from lifetime exposures to sulfuryl fluoride or providing further convincing justifications for not performing it.

Comparison between DPR and US EPA Risk Assessment of sulfuryl fluoride

As mentioned above, the major difference between the U.S. EPA and DPR health risk assessment of sulfuryl fluoride is that U.S. EPA includes a ten-fold database uncertainty factor to account for the lack of developmental neurotoxicity study, while DPR does not in this document. The U.S. EPA health risk assessment of sulfuryl fluoride was based on dietary and inhalation exposures of "Profume," another sulfuryl fluoride product being considered for food uses registration. DPR documents under review refer to non-food uses of Vicane and only inhalation exposures.

Both DPR and U.S. EPA selected the same studies and the same NOELs (expressed in ppm) to address repeated exposures of less than one year. The NOELs expressed in mg/kg/day were different due to different default breathing rates used for rabbits by the two agencies. DPR used 0.54 m^3/kg/day and U.S. EPA used 0.38 m^3/kg/day. No explanation was provided within the DPR documents supporting the use of the breathing rate of 0.54 m^3/kg/day as a more appropriate factor for the risk assessment. Such an explanation would be useful.

For chronic inhalation exposure, both agencies used different studies, different NOELs and different toxicological endpoints. OEHHA supports DPR's approach, even though the resulting risk estimates may imply that EPA was more conservative in its assessment. Overall, comparing risk assessment approaches used by the two agencies enhances the quality of the risk and exposure assessment documents.

Reentry Clearance Level

The reentry air level for Vicane, according to the California and U.S. EPA product label, is 5 ppm. In the past, this level raised health concerns that it is insufficiently health protective (U.S. EPA, 1993). At that time U.S. EPA suggested the reentry (clearance) air concentration of 2 ppm for adults and 1 ppm for children. Subsequently, Dow Elanco provided data to support the 5 ppm reentry air level (see pg. 3 of the DPR Exposure Document).

Results of the sulfuryl fluoride risk assessment showed an unacceptably high risk (low MOE estimates) for most of the exposure scenarios for adults and for children. In light of these results, OEHHA recommends that the Dow Elanco data supporting higher reentry level of sulfuryl fluoride for Vicane be reevaluated and that a lower air concentration of sulfuryl fluoride as the reentry levels be reconsidered. Additionally, page three, paragraph one of the Exposure Document states; "*In subsequent reports to be discussed in more detail later in this assessment, Dow Elanco provided data to support the 5 ppm reentry air level....*" It would be much more useful and transparent if these important data were summarized and discussed in detail in a single place in the document, rather than in different sections. It also would help if the bibliography could be provided when the Dow Elanco data are initially referenced.

Selection of critical studies and endpoints for risk assessment in RCD

We support the choices of critical studies and toxicological endpoints used in the DPR RCD for sulfuryl fluoride.

Conclusion

Thorough evaluation of health risks from current non-food uses of sulfuryl fluoride shows that the risks are too high (non-protective of human health) for the majority of exposure scenarios. In OEHHA's opinion these risks may be underestimated by about ten-fold. We are concerned that DPR is considering the expanded use of sulfuryl fluoride in the near future that could result in even more situations where unacceptable health risks could occur.

References:

U.S. EPA 1993. Reregistration eligibility decision, sulfuryl fluoride, list A, Case 0176. Washington DC: Office of Pesticide Programs, Special Review and Reregistration Division, Environmental Protection Agency.

OEHHA, 2001. Prioritization of Toxic Air Contaminants - Children's Environmental Health Protection Act - Final Report).

EXPOSURE ASSESSMENT DOCUMENT

In general, we find the exposure assessments reasonable and scientifically defensible, with an exception is noted below. Exposure assessments were conducted for three general classes of potential receptors: workers (occupational exposure), residents (in fumigated homes) and bystanders (general public). Exposure durations of short-term (7 days or less), intermediate-term (7 days - one year), annual (one year), and lifetime (75 years) were evaluated for all receptor types. We assume that exposure of bystanders is considered ambient exposure and, therefore, relevant to the TAC statutes.

Occupational exposures:

Task-specific exposure estimates were based on actual worker activities that were monitored during residential fumigations conducted in California in 1993 and 1994. Analytical results were appropriately corrected for recovery using the most conservative estimate of recovery available (66.1%). Exposure estimates were normalized (increased) to simulate applications of the material at the maximum allowable concentration (160 oz/1000 cf). Scenarios were evaluated with and without personal protective devices. Workers handling post-fumigation commodities were also evaluated; exposures were assessed based on the maximum sulfuryl fluoride levels allowed under the label (5 ppm as an 8 hour TWA).

Residential exposures:

Residential exposure estimates were based from sampling of several California homes fumigated with sulfuryl fluoride. Analytical results were appropriately corrected for recovery using the most conservative estimate of recovery available (66.1%). Estimates were not adjusted for maximum application rates since it was assumed that residues left after ventilation were not based on the application rate. This is a reasonable assumption since the structure must be aerated to less than 5 ppm to be cleared regardless of the application concentration.

Based on the collected data, air concentrations for hypothetical fumigations were modeled to predict average and upper-bound exposure estimates. Modeling was necessary to predict air concentrations of sulfuryl fluoride for the various exposure scenarios since the actual sampling lasted only for 48 hours. Modeled results (for the first 48 hours) compared favorably with actual measured values. Assumptions of inhalation rates and proportion of hours spent indoors and outdoors for various age groups were standard and appropriate.

Bystanders:

Ambient air monitoring data collected during two different types of structural sulfuryl fluoride applications were used for estimating exposure of bystanders. Samples were corrected for an experimentally verified 83% recovery. Exposure estimates were normalized (increased) to simulate applications of the material at the maximum allowable concentration (160 oz/1000 cf).

We suggest that DPR consider evaluating chronic and subchronic exposures to bystanders, since it is plausible that a family could live adjacent to more than one home being fumigated over the course of a year.

Exposure of bystanders to sulfuryl fluoride in ambient air as a result of commodity fumigation was also evaluated. No monitoring studies were available, so the 5 ppm maximum level allowed by the label was used to estimate exposures.

Two human occupational exposure studies (Anger *et al.*, 1986; Calvert *et al.*, 1998 - described in section III.H.2. Occupational Exposure) report reduced performance on cognitive, pattern memory, and olfactory tests. These studies are not directly applicable to quantitative risk assessment because of the lack of quantitative exposure assessment. However, they are applicable to human hazard identification, and should be discussed in this section.

OEHHA has developed a chronic (REL) for fluorides of 13 $\mu g\ F/m^3$ based on a benchmark dose evaluation of human occupational skeletal fluorosis data. Since fluoride is substantially metabolically available from absorbed sulfuryl fluoride, this section would be improved by a short description of the OEHHA chronic fluoride REL. We would be happy to provide you that additional information, which can also be found at:
http://www.oehha.ca.gov/air/chronic_rels/pdf/2apna_fluoride_final.pdf)

The U.S. EPA and DPR Reference Concentrations (RfC) are listed in Table 29 on a mg/kg-day basis. Unfortunately, US EPA actually publishes its RfCs on a mg/m^3 basis. Also, OEHHA lists its Reference Exposure Levels (RELs) on a mg or $\mu g/m^3$ basis. It would be less confusing if DPR would include a listing for its sulfuryl fluoride RfC on a mg/m^3 basis.

References:

Anger, W. K., Moody, L., Burg, J., Brightwell, W.S., Taylor, B.J., Russo, J.M., Dickerson, N., Setzer, J.V., Johnson, Bl., and Hicks, K. 1986. Neurobehavioral evaluation of soil and structural fumigators using methyl bromide and sulfuryl fluoride. *Neurotoxicology* 7(3): 137-56.

Calvert, G.M., Mueller, C.A., Fajen, J.M., Chrislip, D.W., Russo, J., Briggle, T., Fleming, L.E. Suruda, A.J., and Steenland, K. 1998. Health effects associated with sulfuryl fluoride and methyl bromide exposure among structural fumigation workers. *Am. J. Public Health* 88(12):1774-80.

Department of Pesticide Regulation

Paul Gosselin
Acting Director

M E M O R A N D U M

Arnold Schwarzenegger
Governor

TO: Gary Patterson, Ph.D.
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Medical Toxicology Branch

VIA: Keith Pfeifer, Ph.D., DABT [*original signed by Keith Pfeifer*]
Senior Toxicologist
Medical Toxicology Branch

FROM: Lori O. Lim, Ph.D., DABT [*original signed by Lori Lim*]
Staff Toxicologist
(916) 324-3515

DATE: July 30, 2004

SUBJECT: RESPONSE TO COMMENTS FROM OFFICE OF ENVIRONMENTAL HEALTH AND HAZARD ASSESSMENT ON DRAFT SULFURYL FLUORIDE RISK CHARACTERIZATION DOCUMENT

This memorandum addresses comments from the Office of Environmental Health Hazard Assessment (OEHHA) on the Department's draft Risk Characterization Document (RCD) for the active ingredient sulfuryl fluoride in Vikane® (March 16, 2004). With respect to the toxicology and risk characterization, OEHHA supported the selected critical endpoints and No-Observed-Effect Levels (NOELs) but recommended the use of an additional ten-fold uncertainty factor to account for toxicological data gaps and the potential additional sensitivity of infants and children to sulfuryl fluoride exposures. Responses to the specific comments are:

Comment 1: OEHHA recommended applying an additional ten-fold uncertainty factor to account for lack of a developmental neurotoxicity study and potential increased sensitivity of infants and children to sulfuryl fluoride exposures.

Response: DPR has a concern regarding potential developmental neurotoxicity in humans exposed to sulfuryl fluoride, which caused vacuoles in the adult brain after repeated exposures and in multiple species. The consequence of this vacuolation lesion in the adult is unclear. In majority of the studies, the presence of brain vacuoles occurred without clinical signs. Since the U.S. EPA waived the data requirement for a developmental neurotoxicity (Dellarco and Baetcke, 2004), DPR will address the developmental neurotoxicity concern by including an additional ten-fold factor in the reference concentration calculation and margins of exposure considerations in the revised RCD. While DPR prefers to have experimental data to address this concern, this approach expedites the completion of the risk assessment for this compound. The use of this 10-fold default factor results in uncertainty of the risk estimate, which may be an over- or under-estimation of the actual risk.

DPR disagrees that there is a potential for increased sensitivity of infants and children to sulfuryl fluoride in terms of developmental (excluding developmental neurotoxicity) and reproductive effects. The developmental and reproductive toxicity studies showed decreased fetal or pup body weight in some studies with NOELs higher than those for maternal effects. U.S. EPA also concluded that a FQPA factor for infants and children sensitivity was not necessary.

Comment 2: OEHHA recommended a decrease in reentry levels

Response: (see Worker Health and Safety Branch response).

Comment 3: OEHHA recommended including the label for Vikane in the RCD.

Response: DPR disagrees with the need to include the label in the document. Since label information is readily available on the Internet, it is unnecessary to include a copy in the document. Essentially information for the risk assessment is already presented in various sections of the document.

Comment 4: OEHHA supported the choices of critical studies and toxicological endpoints used in the DPR RCD for sulfuryl fluoride. OEHHA suggested further justification for not assessing risks for lifetime exposures to sulfuryl fluoride.

Response: DPR does not consider it appropriate to calculate the risks for lifetime exposures when there is no evidence of oncogenicity. As shown in the draft RCD, lifetime exposures are much lower than those for chronic exposures. The use of the same chronic NOEL, which is already based on lifetime exposure of experimental animals, will result in margins of exposures for lifetime exposures much higher than those for chronic exposures. The implication is that there is less risk with lifetime exposure than chronic exposure.

Comment 5: OEHHA suggested additional discussion on data gaps and related uncertainties in the risk characterization.

Response: DPR will add discussion.

Comment 6: OEHHA suggested discussion on possible interaction of sulfuryl fluoride and chloropicrin, and information regarding the range of chloropicrin concentration in Vikane.

Response: DPR will add information about chloropicrin.

Comment 7: OEHHA commented on the difference in rabbit breathing rates used by DPR and U.S. EPA and the need for justification.

Response: The rabbit inhalation rate (BR) used by the U.S. EPA was apparently based on allometric equation of inhalation rate in m^3/day=0.46 Body weight$^{0.8307}$ and body weight of 3 kg from a 1988 U.S. EPA Document (U.S. EPA, 1988). That value is no longer valid; the Agency currently uses mean inhalation rates of 0.55 m^3/kg/day and 0.52 m^3/kg/day, respectively, for males and female rabbits (U.S. EPA, 1994). These values are similar to the DPR default value of 0.54 m^3/kg/day.

Comment 8: OEHHA suggested brief discussion the effect of sulfuryl fluoride on potentially sensitive subpopulations (young, elderly, and those with medical conditions, particularly asthma).

Response: DPR will add a brief statement on the potential effects of sulfuryl fluoride to these subpopulations in the Risk Appraisal section. As indicated by OEHHA, there are no methods available to assess their potential higher sensitivity.

Comment 9: OEHHA suggested evaluation of chronic and subchronic exposures to bystanders since it is plausible that a family could live adjacent to more than one home being fumigated over the course of the a year.

Response: (see Worker Health and Safety Branch response on probability of this scenario).

Additional Comments from Attachment- The following comments were under **Exposure Assessment Document** subtitle *Bystanders* in the OEHHA memorandum. DPR assumes that they were misplaced and is responding with revision to the proper sections of the RCD.

Page 7, 3rd Paragraph: Anger et al (1986) and Calvert et al (1998) are "applicable to human hazard identification, and should be discussed in this section."

Response: Results from the Anger and Calvert studies will be added the discussion on neurotoxicity as an endpoint of concern under **IV.A.1.a. Hazard Identification- Neurotoxicity**.

Page 7, 4th Paragraph: "...this section would be improved by a short description of the OEHHA chronic fluoride REL."

Response: OEHHA REL for fluoride will be added to **II.B.2. Regulatory Limits and Standards**.

Page 7, 5th Paragraph: "It would be less confusing if DPR would include a listing for its sulfuryl fluoride RfC on a mg/m^3 basis.

Response: Reference concentrations expressed as mg/m^3 will be added to Table 16.

cc. Joyce Gee
Jay Schreider

References:

Anger, W.K., L. Moody, J.Burg, W.S. Brightwell, B.J. Taylor, J.M. Russo, N. Dickerson, J.V. Setzer, B.L. Johnson, and K. Hicks, 1986. Neurobehavioral evaluation of soil and structural fumigators using methyl bromide and sulfuryl fluoride. Neurotoxicology 7(3):137-156.

Calvert, G.M., C.A. Mueller, J.M. Fajen, D.W. Chrislip, J. Russo, T. Briggle, L.E. Fleming, A.J. Suruda, and K. Steenland, 1998. Health effects associated with sulfuryl fluoride and methyl bromide exposure among structural fumigation workers. American J. Public Health 88:1774-1780.

Dellarco, V.L. and K. Baetcke, 2004. Waiver justification of inhalation rat developmental neurotoxicity study with sulfuryl fluoride. Memorandum from Dellarco and Baetcke to Lois Rossi. April 22, 2004. Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C.

U.S. EPA, 1988. Recommendations for and documentation of biological values for use in risk assessment. PB88-179874. U.S. Environmental Protection Agency, Cincinnati, OH. Published by the U.S. Department of Commerce National Technical Information Service.

U.S. EPA, 1994. Methods for derivation of inhalation reference concentrations and application of inhalation dosimetry. EPA/600/B-90/065F, October, 1994. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC.

Department of Pesticide Regulation

Paul Gosselin
Acting Director

M E M O R A N D U M

Arnold Schwarzenegger
Governor

TO: Joseph P. Frank, D.Sc.
Senior Toxicologist
Worker Health and Safety Branch

FROM: Donna DiPaolo, Ph.D. *(original signed by D. DiPaolo)*
Associate Toxicologist
916-445-4262

DATE: July 27, 2004

SUBJECT: RESPONSE TO COMMENTS FROM OFFICE OF ENVIRONMENTAL HEALTH AND HAZARD ASSESSMENT ON DRAFT SULFURYL FLUORIDE RISK CHARACTERIZATION DOCUMENT

This memorandum addresses comments directed to the exposure assessment sections of the Sulfuryl Fluoride Risk Characterization Document (RCD; March 16, 2004) provided by the Office of Environmental Health and Hazard Assessment. The comments have been considered and the Worker Health and Safety Branch response is provided below. The RCD main text and Appendix C (Exposure Assessment) has been revised when applicable.

Comment 2:
OEHHA recommends a decrease in the reentry levels of sulfuryl fluoride from 5 ppm to 1 or 2 ppm based on a risk concern raised in the U.S. EPA Reregistration Eligibility Decision (1993) and the present RCD. In addition, OEHHA suggests that the registrant's data in support of the 5 ppm reentry level be discussed in more detail on Page 3 of Appendix C (exposure assessment).

Response 2:
WHS will address any need for reduction in the reentry level of sulfuryl fluoride during the mitigation process. The citation and description of the registrant data in support of the 5 ppm reentry level has been revised accordingly.

Comment 9:
OEHHA suggested evaluation of chronic and subchronic exposures to bystanders since it is plausible that a family could live adjacent to more than one home being fumigated within a year.

Response 9:
WHS respectfully submits that it is unlikely an individual would live adjacent to more than one structural fumigation per year. Appendix C of the RCD presents estimates for short-term, annual and lifetime bystander exposures. Short-term and annual exposures assumed a bystander is exposed to an upper-bound level of sulfuryl fluoride. It is not likely that an individual would be exposed to the upper-bound level of sulfuryl fluoride more than once during the same year. Lifetime bystander exposures were estimated assuming an individual may be exposed to a mean level of sulfuryl fluoride once a year for 57 years over a lifetime which is likely an overestimate.