dpr

Department of Pesticide Regulation

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MEMORANDUM

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TO: Gary Patterson, Ph.D.
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FROM: Lori O. Lim, Ph.D., DABT, Staff Toxicologist
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DATE: February 3, 2004

SUBJECT: RESPONSES TO COMMENTS SUBMITTED ON THE PROPOSED METHYL BROMIDE FIELD FUMIGATION REGULATION (DPR REGULATION NO. 03-004)

This memorandum addresses comments submitted by the Office of Environmental Health Hazard Assessment (OEHHA; November 10, 2003), environmental organizations[1] (collectively referred to as the Environmental Group; December 15, 2003), and the Alliance of Methyl Bromide Industry (AMBI; December 17, 2003) regarding the toxicology studies and the reference concentrations which formed the basis for the proposed regulation for acute and subchronic exposures (DPR Regulation No. 03-004). The OEHHA comments were submitted as part of the interagency consultation process. The Environmental Group and AMBI submissions were made during the public comment period for the proposed regulations. The Ventura County Agricultural Association also submitted a comment indicating that the subchronic reference concentrations should be increased. Response to this comment is included in those for the AMBI submission. In these submitted comments, similar issues were raised and DPR responses are summarized in this cover memorandum. The submitted comments, DPR response to each submission, and supporting documents are provided as Attachments[2] to this memorandum.

Summary of Comments and Responses

In these submissions, there were no new data or information, except for the concern about prostate cancer expressed by the Environmental Group. The issues raised are the same as those in previous comments submitted after the February 2003 workshop on the subchronic reference concentrations and interagency consultation with OEHHA. DPR has provided detailed responses

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[1] The organizations included: Environmental Defense Center (EDC), California Rural Legal Assistance, Inc. (CRLA), California Rural Legal Assistance Foundation (CRLAF), Central Coast Environmental Health Project (CCEHP), Center on Race, Poverty & the Environment (CRPE), Environmental Working Group, Environmental Center of San Luis Obispo (ECOSLO), and Pesticide Action Network (PAN).

[2] Some of the attachments are from electronic files submitted to the DPR. Because of differences in computer and software configuration, they may not appear the same as the original hard copy but there should be no alterations to the text.

to these comments (DPR, 2003 b and c[3]). A summary of the issues and DPR responses for the current comments are listed below.

1. Prostate cancer and Methyl Bromide Exposure

   The Environment Group expressed concerns on the association of methyl bromide exposure and prostate cancer based on the two studies on methyl bromide workers. DPR shares the concern and will address this issue when more data are available.

2. The Acute Reference Concentration

   a. OEHHA provided a detailed description of their interaction with the Scientific Review Panel (SRP) at the January 1999 SRP meeting regarding the acute Level I REL. DPR still has questions regarding the SRP recommendation and the basis for the REL.

   b. OEHHA stated that DPR and OEHHA had agreed that the acute REL should be 1 ppm for severe neurological effects observed in dogs from the Newton study. DPR considers this statement inaccurate. There is no such an agreement in DPR documents or in the cited OEHHA memorandum.

   c. OEHHA stated that there were three studies, which supported the acute REL at 1 ppm. The DPR response is that an analysis of two possible studies, using OEHHA current approaches, does not demonstrate such support.

   d. AMBI did not submit any comments regarding the acute reference concentration. OEHHA indicated that both the OEHHA 1 hour acute REL of 1 ppm and the DPR 24-hour reference concentration of 210 ppb may be applicable depending on the exposure scenario. The Environmental Group continued to support an acute reference concentration based on OEHHA acute REL of 1 ppm. The DPR response is that the DPR 210 ppb level is appropriate for the regulation of methyl bromide use. DPR questions the scientific basis for the REL regarding the study quality and assumptions used to derive that value.

3. The Schaefer (Schaefer, 2002) Subchronic Toxicity Studies in Dogs

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[3] All responses to comments and relevant documents are posted on DPR's web site: www.cdpr.ca.gov under ***Programs and Services***, then ***Methyl Bromide and Other Fumigants.*** Links to the risk assessment-related documents can be found on that page.

a. AMBI stated that the Schaefer study was conducted in coordination with DPR. DPR does not agree with such involvement. AMBI had requested and DPR only provided consultation on the proposed protocol.

b. The various opinions on the NOEL for this study centered on how the effects were interpreted and the strength of the evidence needed to establish the study NOEL. In this study, lack of proprioceptive placing response was observed in several dogs at 10 and 20 ppm, while tremors and twitching were reported for 1 dog at 5 ppm. Both OEHHA and the Environmental Group considered all these effects as treatment related and set 5 ppm as the lowest-observed-effect level (LOEL) and an estimated NOEL of 0.5 ppm. They also factored in concerns regarding the study design in this NOEL determination. AMBI supported a higher NOEL at 10 or 20 ppm because these effects did not show clear dose-response relationship, were transient, and were not corroborated with other findings. The effects at 5 ppm in a single dog were attributed to an illness. The DPR response is that the initial submission and additional information submitted support a NOEL at 5 ppm for this study[4]. DPR is in agreement with OEHHA and the Environmental Group that the effects at 10 and 20 ppm are treatment-related. However, DPR considers the effects at 5 ppm as too uncertain to form the basis for the NOEL of the study.

c. Both OEHHA and Environmental Group considered this study to be of poor quality with "severe" limitations and were concerned with the study design not following U.S. Environmental Protection Agency (U.S. EPA) FIFRA tesing guidelines. AMBI, on the other hand, described this study as well-designed and well-conducted special study. DPR response is that since the study was conducted to answer specific questions, it should be considered a supplemental study, not a guideline study. It has strengths and limitations but the data provided support for a NOEL of 5 ppm for neurotoxicity.

4. The Subchronic Reference Concentration

a. Both the OEHHA and the Environmental Group believed that the reference concentrations (1 and 2 ppb) should be based on the Newton study and noted that the National Research Council (NRC) considered these values appropriate to set regulations. The AMBI, in contrast, indicated that the Schaefer study should be the basis for the reference concentration, as recommended by several scientists. Furthermore, it was the type of study recommended by the NRC, which expressed

[4] The Toxicology Summary has been revised to include a 1-liner for this supplemental submission. The 1-liner paragraph is also included in the worksheet for this submission (see Attachment G).

reservations regarding the Newton study. The DPR response is that there are strengths and limitations to both the Newton and Schaefer studies. All studies in the methyl bromide database and comments from all reviewers should be considered in the overall weight of evidence. DPR has evaluated additional information on the Schaefer study and concluded that 5 ppm is the appropriate NOEL to characterize the risk for subchronic exposure to methyl bromide. The additional information has not been reviewed by OEHHA and the Environmental Group.

5. Additional Uncertainty Factor for Sensitive Population

   Both OEHHA and Environmental Group indicated that additional uncertainty factor should be considered. However, OEHHA had not advocated a specific uncertainty factor. The DPR response is that this issue has been adequately addressed based on currently available data. DPR will continue to evaluate data on this issue and will review OEHHA's selection of a specific uncertainty factor when available.

In summary, there remained divergent opinions on the interpretation of the toxicology data, strength of the evidence needed to establish the NOEL for the Schaefer study, interpretation of the NRC and external scientist reviews, the weight of evidence, and the adequacy of reference concentration to address potential increased sensitivity of infants and children from exposure to methyl bromide. For acute exposure, OEHHA indicated that both the OEHHA REL of 1 ppm and the DPR 24-hour reference concentration of 210 ppb may be applicable for some scenarios. The Environmental Group continued to support the OEHHA REL of 1 ppm, which would result in a reference concentration of 90 ppb as a 24-hour time-weighted average. AMBI did not comment on the acute reference concentration. For subchronic exposure, OEHHA and Environmental Group continued to support the 1 and 2 ppb levels. The AMBI indicated that the reference concentrations should be at least two fold higher (18 and 32 ppb) than the DPR levels (9 and 16 ppb).

Staff Recommendation

The submitted comments did not provide any additional scientific data or information to require revisions to the current DPR acute (210 ppb) or the subchronic (9 and 16 ppb, for children and adult exposures, respectively) reference concentrations used to develop the proposed methyl bromide regulations. These concentrations were derived after a comprehensive evaluation of the data and use of weigh of evidence approach to select the most appropriate NOEL to address the potential toxicity from acute and subchronic exposures to methyl bromide. Furthermore, DPR considered comments from OEHHA, industry, environmental groups, University of California, and the U.S. EPA. Therefore, the recommendation is to continue the use of 24-hour time-weighted average of 210 ppb as the acute reference concentration, and 9 ppb

(children) and 16 ppb (adults) as the subchronic reference concentrations to set the regulations for methyl bromide use in California.

cc. Chuck Andrews

Attachments:

A. Comments from the Office of Environmental Health Hazard Assessment (November 10, 2003)
B. DPR Responses to Comments from the Office of Environmental Health Hazard Assessment
C. Memorandum from G. Alexeeff to W. Vance (OEHHA, August 26, 1997)
D. Letter from K. Schuparra to K. Thuner and R.J. Smith (Cal/EPA, November 25, 2003)
E. Memorandum from J. Gee to G. Patterson (DPR, January 30, 2004)
F. Memorandum from J. Gee to G. Patterson (DPR, January 28, 2003)
G. DPR Worksheet on Additional Information on the Schaefer Study (November 25, 2003)
H. Comments from Environmental Organizations (December 15, 2003)
I. DPR Responses to Comments from Environmental Organizations
J. E-mail from A. Katten (CRLA) to P. Helliker (May 12, 2003)
K. Comments from the Alliance of Methyl Bromide Industry (December 17, 2003)
L. DPR Responses to Comments from the Alliance of Methyl Bromide Industry
M. Letter from W. Thomas to P. Helliker (March 19, 2003)
N. Response Letter from P. Gosselin to W. Thomas (April 24, 2003)
O. Letter from W. Thomas to P. Helliker and P. Gosselin (June 6, 2003)
P. Response Letter from T. Jones to W. Thomas (June 27, 2003)
Q. Response Letter from W. Thomas to T. Jones (August 1, 2003)

References used in the DPR Responses:

AMBI, 2003. Response to issues raised concerning the 6-week inhalation toxicity study of methyl bromide in dogs. Letter from W. Thomas to P. Gosselin and G. Patterson, March 11, 2003. Livinston & Mattesich Law Corporation, Sacramento, CA.

Breslin, W.J., C.L. Zablotny, G.J. Bradley, and L.G. Lomax, 1990. Methyl bromide inhalation teratology study in New Zealand white rabbits. The Toxicology Research Laboratory, Methyl Bromide Industry Panel. DPR Vol. 123-127#95930.

DPR, 2002. Methyl bromide risk characterization document, inhalation exposure Volume I, RCD 2002-2003 (February 14, 2002). Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

DPR, 2003a. Methyl bromide risk characterization document, inhalation exposure Addendum to Volume I (February 3, 2002). Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

DPR, 2003b. Response to comments from the Office of Environmental Health Hazard Assessment on proposed methyl bromide field fumigation regulations. Memorandum from L. Lim to G. Patterson, August 18, 2003. Department of Pesticide Regulations, California Environmental Protection Agency, Sacramento, CA.

DPR, 2003c. Response to comments from methyl bromide subchronic regulatory level workshop on February 26, 2003. Memorandum from L. Lim to G. Patterson dated May 1, 2003. Medical Toxicology Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA.

Newton, P.E., 1994. A four week inhalation toxicity study of methyl bromide in the dog. Study number 93-6068. Pharmaco LSR. DPR Vol. 123-164#132821.

Norris, J.C., C.D. Driscoll, and J.M. Hurley, 1993. Methyl bromide: ninety-day vapor inhalation neurotoxicity study in CD rats. Bushy Run Research Center. Methyl Bromide Industry Panel. DPR Vol. 123-159 #131619.

NRC, 2000. Methyl bromide risk characterization in California. Subcommittee on Methyl Bromide, National Research Council. National Academy Press, Washington, D.C.

OEHHA, 2003a. Comments on the risk characterization document for inhalation exposure to methyl bromide, addendum to Volume I, prepared by the Department of Pesticide Regulation. Memorandum from A. Fan to C. Andrews, March 11, 2003. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA.

OEHHA, 2003b. Comments and recommendations on the proposed methyl bromide field fumigation regulations. Memorandum from A. Fan to C. Andrews, June 30, 2003. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Sacramento, CA.

Schaefer, G.J., 2002. A 6-week inhalation toxicity study of methyl bromide in dogs. WIL Research Laboratories, Inc., study number WIL-440001. Alliance of the Methyl Bromide Industry. DPR Vol. 123-212#187459.

Watrous, R.M., 1942. Methyl bromide- local and mild systemic toxic effects. Industrial Medicine 11 (12):575-579.