



Mary-Ann Warmerdam
Director

Arnold Schwarzenegger
Governor

July 7, 2005

TO: INTERESTED PARTIES

SUBJECT: LIST AND RANKING OF ACTIVE INGREDIENTS PRIORITIZED FOR RISK ASSESSMENT INITIATION, AND RESPONSES TO PUBLIC COMMENTS ON THE LIST AND RANKING

On March 8, 2005, the Department of Pesticide Regulation (DPR) published a "Request for Comments on Active Ingredients Prioritized for Risk Assessment Initiation." The comment period closed on April 22, 2005. This comment period was extended to May 6 to accommodate anyone who had difficulty responding electronically. Two sets of comments were received:

- Dupont Crop Protection provided comments regarding methomyl and esfenvalerate. Toxcel, LLC, on behalf of CYTEC Industries, provided comments on phosphine and phosphine-producing compounds.
- Comments were also provided (May 19) after the close of the comment period by McDermott, Will, and Emery representing the Propanil Task Force II.

Comments and the Department's responses follow the list and rankings.

List and Rankings:

Based on the comments and responses, active ingredients prioritized for risk assessment initiation and their ranking will remain unchanged, are considered final, and are as follows.

1. Sodium tetrathiocarbonate
2. Paradichlorobenzene
3. Methomyl
4. Phosphine and phosphine generating compounds
5. Acrolein
6. Esfenvalerate
7. Linuron
8. Propanil
9. Boric acid

Comments and Responses:

The comments or a summary of the comments and responses to them are as follows.



Dupont Crop Protection

Methomyl

Comment: “Similar to organophosphates, carbamates are currently undergoing cumulative risk assessment at U.S. EPA. Since the results of this assessment may result in regulatory decisions that may have an impact on future use patterns for carbamates, including methomyl, we recommend that methomyl either be removed from the list and reconsidered at a later time, or moved down in priority on the current list. This will align with DPR’s stated intention to concentrate on active ingredients that will avoid duplication of effort with U.S. EPA and to focus on active ingredients that may be receiving less attention from U.S. EPA.”

Response: During the prioritization process, the members of Risk Assessment Prioritization Work Group (RAPWG) were aware of the U.S. EPA work on the assessment of the carbamates, but were in agreement that methomyl should still be prioritized for risk assessment initiation. The progress of U.S. EPA on the risk assessment of the carbamates in general, and methomyl specifically, will be considered at the time of the next annual prioritization of active ingredients for risk assessment initiation and at the time DPR prepares to initiate the risk assessment on methomyl.

Comment: “Paragraph 2, first two sentences; suggest rewording: “Methomyl has a reported half-life of 14 days in soil **under anaerobic conditions and an average half-life of 8.5 days in aerobic soil**. It is highly soluble in water and does not bind tightly to soil, suggesting the potential to **reach** groundwater. **However, it is not likely to persist under many conditions.**”

Response: The first two changes have been incorporated in the documentation. The sentence in the original documentation to which the third suggested change refers is unclear and not critical; therefore, that sentence has been deleted.

Comment: “Paragraph 3: The rat LD₅₀ for methomyl technical, as reported in the RED, is **30-34 mg/kg**, higher than the upper value reported in the range listed (10 to 24 mg/kg).”

Response: That sentence has been changed to reflect both the rat LD₅₀s referenced in the U.S.EPA RED and the LD₅₀s for other animal species.

Comment: “Paragraph 4, second sentence; suggest rewording: “**No clinical signs of toxicity were present at 24 hours post-exposure, as might be expected for a carbamate.**” This wording change is suggested since the signs likely disappeared much sooner but the time-course was evaluated separately in a different study.”

Response: The wording was changed as suggested.

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Comment: "Paragraph 5, first sentence: Change 5 mg/kg to **9.4 mg/kg/day**."

Response: The NOEL in the referenced study was presented in the original study report as 100 ppm. The parenthetical 5 mg/kg value was a calculation based on default food consumption values for the rat. At this point, the critical value is 100 ppm, rather than 5 or 9.4 mg/kg. The 100 ppm value has been retained in the documentation, but the parenthetical 5 mg/kg has been deleted.

Comment: "Paragraph 6, last sentence; suggest rewording: "**Hematologic effects observed in chronic studies with methomyl were consistent across the species evaluated. There was no evidence of oncogenicity with methomyl.**" This wording change/splitting of the sentence is suggested since evaluation of oncogenicity is unrelated to hematology findings."

Response: The original sentence was unclear, therefore, the change was made as suggested.

Comment: "It appears that the chronic rat feeding study results are reported twice (same NOEL and effects). We believe this is just one study."

Response: Two different chronic studies were reviewed by DPR. Both studies had the same NOEL.

Esfenvalerate

Comment: "Paragraph 4, first sentence: "dermal exposure has been associated with skin irritation" should more appropriately read "...**has been associated with skin stimulation (paresthesia)**" since both technical and formulated materials are Toxicity Category IV for skin irritation."

Response: "Skin irritation" has been changed to "paresthesia."

Comment: "Paragraph 4, third sentence: The LD₅₀ is listed as 458 mg/kg. That sentence should read, "The rat oral LD₅₀ for esfenvalerate is **87.2 mg/kg**." The LD₅₀ of 458 mg/kg is actually for a formulation containing esfenvalerate, not for the technical material."

Response: Change made as suggested.

Comment: "Paragraph 6: We believe the citation of "a subchronic neurotoxicity study in rats has a NOEL for 12.5 mg/kg for nerve damage" is not accurate and should be revised. There was a subchronic rat study with fenvalerate in which the NOEL was 12.5 mg/kg/day and clinical signs were observed at the next higher dose (100 mg/kg/day). However, nerve morphology changes were only observed at the highest dose tested (200 mg/kg/day). Two recent 90-day rat

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neurotoxicity studies (by two different registrants, including DuPont) have been conducted on esfenvalerate and followed OPPTS guidelines (in which the high doses did not exceed the MTD). There were no findings of abnormal neuropathology at the highest doses tested (23 mg/kg/day in one study and 35 mg/kg/day in the other). Therefore, if reference is left in, it should be amended to read “Minor axonal degeneration has been observed with fenvalerate only at near lethal doses. No neuropathology has been observed in recent subchronic rat studies with esfenvalerate at doses up to and including 35 mg/kg/day.”

Response: The sentence in question has been changed to read “A subchronic neurotoxicity study in rats exposed to fenvalerate had a NOEL of 12.5 mg/kg for clinical signs of neurotoxicity.”

Comment: “The last paragraph states the justification for including esfenvalerate in the prioritization for risk assessment is its use in a wide variety of situations including residential/consumer products. If this is the reason for inclusion, then in the risk assessment document, risk and incidents involving residential and consumer uses should clearly be separated from agricultural uses and evaluated separately.

As noted above, esfenvalerate has the ability to produce skin stimulation (paresthesia). Therefore, in assessing risk, potential effects from local dermal contact should be evaluated separately from systemic effects. In addition, when risk from local dermal contact is assessed, consideration should be given to whether the contact is to concentrated vs. diluted product since chance for stimulation is greater with undiluted material but the number of people handling is less.”

Response: Both of these comments will be considered during the conduct of the risk assessment.

Toxcel LLC/CYTEC Industries

The comments submitted by Toxcell LLC, on behalf of CYTEC Industries, were in the form of an Adobe PDF document and are not reproduced in its entirety, since the comments relate essentially to a single issue.

Comment: “CYTEC Industries Inc. (“CYTEC”) is providing the following comments on CDPR’s proposal to list “Phosphine and Phosphine Generating Compounds” fourth on the list of active ingredients prioritized for risk assessment initiation. Although we agree that phosphine gas is highly acutely toxic, particularly by the inhalation route, it is important to note that the potential for exposure to applicators, workers, or bystanders is very low when phosphine is used according to label directions”

“All phosphine labels were revised in 2004 and now meet the risk mitigation measures stipulated in the Memorandum of Understanding (MOA) between US EPA and the Phosphine Producers

Association (PPA), of which CYTEC is a member. The MOA was developed following publication of the RED for aluminum and magnesium phosphide, and users and regulators (including California) were included in discussions concerning protective label language. The revised labels greatly reduce potential risk of exposure because they include the requirement to develop a fumigation management plan for each fumigation. The guidance for developing fumigation management plans is included as Attachment 1.”

“In conclusion, CYTEC respectfully requests the complete removal of phosphine from consideration for prioritized risk assessment initiation. All phosphine labels were revised last year to incorporate risk mitigation measures designed to protect bystanders and prevent offsite movement of phosphine gas from fumigation facilities. The primary basis for listing phosphine and phosphine generating products (potential off-site and bystander exposure) is no longer an issue.”

Response:

DPR intends to assess the risk of all the fumigants. In the case of phosphine and phosphine-producing compounds, as is the case for all DPR risk assessments, all available relevant scientific information will be considered during the conduct of the risk assessment. This information would include the U.S. EPA RED and any new phosphine exposure studies. This situation is somewhat unique in that a number of active ingredients result in the release of phosphine gas. DPR will consider all such active ingredients as well as the various use situations in California. If some potential air exposures are low, perhaps due to newly instituted mitigation measures, then the resulting risk should also be low. However, for the reasons cited in the initial documentation, DPR feels that these risks should be assessed.

[McDermott, Will, and Emery/Propanil Task Force II](#)

While the comments of McDermott et al were received after the close of the comment period, they deal with a similar issue to that of Toxcell et al and do not change the conclusions of the Department. Therefore, these comments are also addressed in this notice.

Comment: McDermott et al state the U.S.EPA is in the process of determining labeling changes for propanil and these determinations should be reached by December 2005. In addition, DPR has already issued regulations regarding use restrictions for propanil to control drift (resulting in phytotoxicity) and these changes would also reduce potential offsite human exposure and resulting risk. The comments also included a published article; Richards SM, McClure GY, Lavy TL, Mattice JD, Keller RJ, and Gandy J (2001), **Propanil (3,4-Dichloropropionanilide) particulate concentrations within and near the residences of families living adjacent to aerially sprayed rice fields**, Arch Environ Contam Toxicol, 41 (1): 112-116. The measurements presented in this article were used to support the commenters’ position that the

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offsite human risk would be low. The comments also included a published article; McClure GY, Helm RM, Stine K, Burks AW, Jones SM, and Gandy J (2001, Evaluation of immune parameters in propanil-exposed farm families, Arch Environ Contam Toxicol, 41(1): 104-11. The article was used to indicate, "individuals living near rice fields are not at increased risk of altered immune function due to propanil exposure." The comments conclude, "We believe that there is no need for an additional risk assessment to address bystander risk."

Response: As was stated in the response to the comments arguing against the prioritization of phosphine for risk assessment initiation, all available relevant scientific information will be considered during the conduct of the risk assessment on propanil. This information would include the U.S. EPA RED, any new propanil exposure studies, and relevant scientific data in the scientific literature, including the two papers submitted by McDermott et al. If potential air exposures are low, perhaps due in part to recently instituted use restrictions, then the resulting risks should also be low; however, that determination is the purpose of the Department's risk assessment process. DPR feels that these risks should be assessed in detail.

If you have any questions, please contact Dr. Jay Schreider, DPR Medical Toxicology Branch, at (916) 445-4241, or by email at <jschreider@cdpr.ca.gov>.

Sincerely,

A handwritten signature in black ink that reads "Tobi Jones". The signature is written in a cursive, flowing style.

Tobi L. Jones, Ph.D., Assistant Director
Division of Registration and Health Evaluation
(916) 445-3984

cc: Dr. Jay Schreider