

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT



M E M O R A N D U M

To: Larry Nelson, Ph.D., Chief
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1020 N Street, Room 234
Sacramento, CA 95814

From: Anna M. Fan, Ph.D., Chief *AMF*
Pesticide and Environmental Toxicology Section

Date: February 28, 1994

Subject: Mevinphos (phosdrin) Risk Characterization

Staff of the Pesticide and Environmental Toxicology Section have reviewed the draft Risk Characterization Document for Mevinphos. The following provides a summary of our comments. More detailed comments are provided in the attached memorandum.

We are in agreement with the Department of Pesticide Regulation (DPR) that the acute occupational exposure to mevinphos is unacceptable in some job activities such as mixer/loader/applicators using ground application and harvesters working in fruit trees. Also short-term occupational exposures within the range of the upper bound confidence limit are too high for all work categories associated with mevinphos application. Similarly, chronic occupational exposures do not provide an adequate MOS from adverse effects of mevinphos.

Inadequacy of health protection from exposure to mevinphos is not limited to the occupational environment. It extends to acute dietary exposure. This exposure was determined to be unacceptably excessive for non-nursing infants below the age of one.

The Risk Characterization Document clearly states that the excessive occupational risk from exposure to mevinphos cannot be mitigated. However, the document does not provide any recommendations as to the future use of this chemical.

Larry Nelson, Ph.D., Chief
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Because of the unacceptably high occupational and dietary exposures, and lack of potential mitigation measures for workers, we recommend that DPR seek options to prevent excessive exposure, including the consideration of cancellation in California. Related administrative procedures should be pursued in an expedited fashion. We would appreciate being informed about any actions taken by DPR in this regard. Also, it would be helpful if the final version of this and future Risk Characterization Documents contain a section on "Recommendations".

Other phosdrin-related issues, both of general and more specific character, are addressed in the attached report. They are of secondary importance in the light of the overall unacceptability of current occupational and some acute dietary exposures to this chemical.

We thank you for sending us the document for review. If you have any questions regarding our review or would like further discussions, please call me at 8/571-3066 or Michael DiBartolomeis, Ph.D., at 8/571-2665.



M E M O R A N D U M

To: Anna M. Fan, Ph.D., Chief
Pesticide and Environmental Toxicology Section

Via: Michael J. DiBartolomeis, Ph.D., Chief
Pesticide and Food Toxicology Unit *JMB for MJDIB*

From: Jolanta Bankowska, Ph.D.
Staff Toxicologist *JMB for JB*

Subject: Review of a draft risk characterization document
for mevinphos

The following are my comments on the mevinphos SB 950 risk characterization document prepared by the California Department of Pesticide Regulation (DPR). My concerns are addressed in detail in the attached review.

My recommendation is to consider the cancellation of registration of this chemical in California. The conclusions of the health risk assessment performed by DPR indicate that the margin of safety (MOS) for adverse health effects from occupational exposures is generally too narrow. These exposures cannot be mitigated. Also, the MOS for acute dietary exposure to mevinphos for non-nursing children less than one year old is unacceptable.



ATTACHMENT

REVIEW OF THE RISK CHARACTERIZATION DOCUMENT FOR MEVINPHOS

This report consists of three parts: background information, general and specific comments, and summary of recommendations.

BACKGROUND INFORMATION

Use

Mevinphos is used as a broad spectrum insecticide/acaricide on a variety of vegetables, fruits, and field crops. It serves mainly as a foliar insecticide to "clean up" crops just prior to harvest. Mevinphos can be applied by air or ground power equipment. In California it must be used through a closed mixing/loading system. Mevinphos is a restricted use pesticide because of its high acute toxicity to humans. Consequently, it can be used only by certified applicators or persons under their supervision.

Mevinphos is listed among the ten most risk prone pesticides ranked according to the following attributes: reported acute total illnesses in 1984-1990, low oral LD₅₀, and a low Reference Dose (RfD) (Pease et al. 1993).

Regulatory History

The United States Environmental Protection Agency (USEPA) established an RfD of 0.00025 mg/kg-day for mevinphos, based on a NOEL of 0.025 mg/kg-day for plasma and red blood cell (RBC) cholinesterase activity inhibition determined in a two-year dog study. The World Health Organization set an RfD of 0.0015 mg/kg-day.

Toxicology

The toxicological profile of mevinphos is primarily related to its action as a potent cholinesterase inhibitor. It causes headache, nausea, diarrhea, and tremors. Other adverse effects listed by DPR include mutagenic responses such as gene mutation, chromosomal aberration, and DNA damage. Mevinphos is not a developmental or reproductive toxicant. It does not cause delayed neuropathy or other adverse effects identifiable under SB 950. However, toxicity testing required under this program is not complete. Data gaps include chronic toxicity studies in rats and dogs (inadequate studies) and oncogenicity study in rats (no study submitted).

Worker Illnesses

According to the Department of Pesticide Regulation, Worker Health and Safety Branch (Appendix B), mevinphos was associated with numerous worker illnesses incurred in the course of job-related activities. "There were 578 cases of suspected illnesses associated with exposure to mevinphos in California during 1982 to 1989. Of these cases, 112 identified mevinphos as the primary pesticide and 466 involved exposure to mixture of mevinphos and other cholinesterase inhibitors. There were 68 cases involving one or more days of hospitalization and 201 cases involving one or more lost work days."

Risk Appraisal

MOS calculations were done for the following ten work tasks: mixer/loader and pilot in helicopters, mixer/loader, pilot, and flagger in fixed-wing aircraft, mixer/loader/applicator in an open cab and mixer/loader/applicator in a closed cab in ground applications, and field workers harvesting vegetables, fruits on trees, and grapes.

Based on the NOEL of 0.025 mg/kg for a human study, the estimates of the MOSs for mean acute occupational exposures were no higher than 50 for all of the listed work tasks with an exception of flagger in fixed-wing aircraft for whom the MOS value was 625. The lowest MOS of 2 was determined for tree fruit harvesters (apple harvesters). Also the MOS for the chronic occupational exposure to mevinphos could not be adequate (as low as 40, but ranges up to 500) for the same work task group. The MOSs for the chronic occupational exposures determined for other groups were higher than 100.

The MOS for potential acute dietary exposure to mevinphos ranged from 8 to 24. The population subgroup of non-nursing pregnant women greater than 13 years of age had the highest MOS. The lowest MOS of 8 was determined for non-nursing infants, less than 1 year of age.

Tolerances

Twenty-five of the USEPA tolerances for mevinphos on agricultural commodities do not provide an adequate MOS for acute dietary exposure to one or more population subgroups if commodities are consumed with residues at the tolerance level. The list of commodities with the lowest MOS includes but is not limited to apples, broccoli, cauliflower, citrus, grapes, melons, peaches, and plums.

COMMENTS

General Comments

Risk Appraisal and Conclusions

The Mevinphos Risk Characterization Document lacks a section on recommendations. The health risk analyses performed by DPR indicate that occupational exposures to mevinphos--both acute and short-term but in some cases also chronic--are too high for a number of the farm-job related activities (see above). These exposures cannot be mitigated because additional protective equipment or protective clothing does not seem possible at this time. Also, a number of tolerances for mevinphos on agricultural commodities are not health-protective for acute dietary exposure.

Because of the unacceptably high worker and dietary exposures, and lack of potential mitigation measures, we recommend that mevinphos be considered for cancellation in California.

Multiple Exposure to Cholinesterase Inhibitors

The issue of multiple exposures to cholinesterase inhibitors from both occupational and dietary sources should be addressed in this and other health risk assessment documents for this group of chemicals. OEHHA's concerns relate mainly to the seasonal and chronic occupational and dietary exposures to organophosphates. The health risk assessment documents for pesticides with cholinesterase inhibition activity should include scenarios that more closely approximate agricultural practices where farm workers can be exposed to a number of cholinesterase inhibitors during one season. Evaluating exposures and assessing health risk separately for chemicals causing the same effects during the same period of time is misleading. A farm worker may have an adequate MOS for cholinergic effects from the exposure to chemical A or chemical B, but the health risk from the total exposure from A and B may be excessive.

The same comments apply to dietary exposure assessments. Cholinergic effects and the related health risk from dietary exposure to the residues of a number of cholinesterase inhibitors should not be evaluated only for individual chemicals, but should also be estimated as a total.

OEHHA recommends that efforts be made to evaluate and assess health risk from combined occupational and dietary exposures to multiple cholinesterase inhibiting pesticides.

Assessment of Dietary Exposures

Assessment of dietary exposures is limited to raw agricultural commodities (RAC) hence is not complete unless it is assumed that "processing the RACs into various foods forms does not...increase the residue concentration". This DPR assumption needs to be substantiated.

Specific Comments

Choice of Noel Values for the Acute and Chronic Exposure Assessments

The criteria underlying the choices of NOELs for acute and chronic health risk assessments are different, although the values of these two NOELs are identical. The same NOEL value of 0.025 mg/kg-day was used for both acute and chronic health risk assessments for all exposure scenarios (occupational, dietary, and combined exposures). The NOEL chosen for the acute exposures was based on the lack of clinical signs and symptoms at 0.025 mg/kg in a 30-day human study. By the end of the study period, it appears that the inhibition of RBC cholinesterase was probably significant (19% decrease), i.e., that the subchronic and chronic NOEL for this effect is less than 0.025 mg/kg, although 0.025 mg/kg does appear to be a human NOEL for acute exposures. The NOEL for chronic health risk assessment was established in a rat chronic-feeding study and was based on the depression of brain cholinesterase activity.

The significance of this identical value should be further addressed in the risk characterization part of the document. For most chemicals the NOEL for chronic health risk assessments is lower than the NOEL for acute risk assessments.

Pinpoint pupils are one of the most characteristic signs of cholinesterase inhibition. These signs were observed in a three day study in rats at 0.005 mg/kg-day (LOEL). The NOEL value for this study would be 0.0005 mg/kg-day. The latter value is fifty times lower than the NOEL chosen for the acute risk assessment (0.025 mg/kg-day). The reasons for not choosing the lowest available value for risk assessment purposes should be provided.

Mutagenic Activity

Mevinphos was found to cause adverse effects in three major batteries of genotoxicity testing: gene mutation, chromosomal aberrations and DNA damage. The significance of these results should be addressed in the risk assessment document.

Worker Exposure

Estimates of occupational exposure to mevinphos assume a 75.9 kg body weight for workers (Appendix B). Since this value is different than the traditionally used 70-kg body weight, an explanation should be provided.

The use of mevinphos by air blast application equipment is not customary in California. Application of mevinphos by such equipment in the past was associated with illness of the workers. Product labels which do not prohibit the use of such equipment should be changed.

SUMMARY OF RECOMMENDATIONS

General

1. Because of the unacceptably high worker and dietary exposures, and lack of potential mitigation measures, we recommend that mevinphos be considered for cancellation in California.
2. Inform OEHHA about the time schedule for the above action.

Specific to the risk assessment document for mevinphos

1. Address the issue of multiple exposures for other cholinesterase inhibitors.
2. Complete assessments of dietary exposures by including processed food, if applicable.
3. Address the issue of identical values for NOELs used in the acute and chronic health risk assessments.
4. Substantiate choice of the higher than available value for the acute risk assessment.
5. Include a discussion of mutagenic activity of mevinphos in the body of the document.
6. Substantiate the assumptions behind the use of 75.9 kg body weight for workers exposure assessments.