M E M O R A N D U M

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SUBJECT: COMMENTS ON THE FINAL DRAFT RISK CHARACTERIZATION DOCUMENT FOR THE ACTIVE INGREDIENT PROPARGITE PREPARED BY THE DEPARTMENT OF PESTICIDE REGULATION

Thank you for the opportunity to review the draft risk characterization document (RCD) for propargite prepared by the Department of Pesticide Regulation (DPR). The Office of Environmental Health Hazard Assessment (OEHHA) reviews risk assessments prepared by DPR under the general authority of the Health and Safety Code, 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.

Propargite is an organosulfur miticide/acaricide used for the control of mites on a variety of bearing and non-bearing agricultural crops, as well as non-food agricultural sites. Bearing crops include grapes, citrus, nectarines, peanuts, almonds, and mint; non-bearing crops include cherries, grapefruit and navel oranges; non-food agricultural sites include roses and evergreen conifers. There are no registered residential uses for propargite. Nearly one million pounds of propargite was applied in California in 2002.

We note that the registrant voluntarily canceled a number of uses of propargite in 1996 due to unacceptable dietary cancer risks. Indeed, propargite is listed by Proposition 65 as a carcinogen and as a reproductive toxicant. U.S. EPA considers propargite a B2 (probable human) carcinogen based on the appearance of rare jejunal tumors in both sexes of rats following chronic oral exposure.

DPR initiated this risk assessment to address potential adverse health effects for the general public as a result of the remaining registered uses of propargite. This version of the RCD evaluates dietary and drinking water exposures to the general public. An addendum is planned that will address aggregate exposures to propargite from occupational, diet, water and ambient air sources.

Overall, we find the RCD for propargite to be appropriate, comprehensive and well written. Accordingly, our comments focus on a relatively few areas of concern:

1. OEHHA is concerned that because the chronic "no observed adverse effect level" (NOAEL) of 3.8 mg/kg-day used in the RCD is higher than the acute NOAEL of 2 mg/kg, protection against acute developmental effects is not sufficient. A NOAEL of 2 mg/kg from a rabbit developmental study based on anorexia in dams and delayed ossification of the skull in offspring at the next higher dose of 6 mg/kg was used in the RCD for evaluating acute exposures to propargite (Serota et al., 1983). We note that the NOAEL selected for evaluating chronic exposures was 3.8 mg/kg-day from a rat study and was based on reductions in body weights and food consumption at the next higher dose of 19.2 mg/kg-day (Trutter, 1991). Clearly, the chronic NOAEL is insufficient to protect against the acute or subchronic effects observed in the rabbit studies. Accordingly, OEHHA suggests the adoption of 2 mg/kg-day (or 1 mg/kg-day from the dermal study in rabbits; see comment #2, below) from the developmental study in rabbits for the evaluation of chronic exposures to propargite.

2. Systemic effects in adult animals may also not be sufficiently protected against if a chronic NOAEL of 3.8 mg/kg-day is adopted. A systemic NOAEL of 1 mg/kg-day was observed in a 21-day dermal study in rabbits (Bailey, 1987). This NOAEL was based on reduced body weights, changes in clinical chemistry and hematological values, and increased relative liver and kidney weights observed at the next higher dose of 10 mg/kg-day. It is mentioned in the RCD that "the veterinary pathologist for the study suggested that the hematological and clinical chemistry changes may be due to dermal irritation" (with a LOAEL of 0.1 mg/kg-day). OEHHA finds this insufficient justification for discounting the systemic NOAEL of 1 mg/kg-day and, similar to the case in comment #1 above, we believe that there may be insufficient protection against systemic effects (reduced body weights, increased relative liver and kidney weights and changes in clinical chemistry and hematological values) in the evaluation of chronic exposures to propargite presented in the RCD. Accordingly, we suggest adding additional discussion supporting the conclusion that the observed systemic effects are secondary to dermal irritation. If appropriate justification is not possible, then OEHHA recommends adopting 1 mg/k-day for evaluating chronic exposures to propargite.

3. Subchronic/seasonal exposures to propargite were not evaluated in the RCD. The rationale provided was that "No seasonal exposure to propargite is anticipated since dietary and drinking water exposure to propargite did not vary significantly with season." We assume this to mean that because exposure to propargite does not appreciably vary over the course of a year, it is not necessary to evaluate seasonal exposures. OEHHA disagrees since seasonal exposures are estimated differently than acute and chronic exposures (e.g., different assumptions regarding chemical concentrations in food and environmental media, and seasonal qualitative and quantitative changes in food consumption), it is important that subchronic exposure is characterized and evaluated. Accordingly, OEHHA recommends adding this evaluation to the RCD.

4. Acute Margins of Exposure (MOEs) for combined dietary and drinking water exposures range from 290 for children aged 1 to 6 years old to 1,200 for non-nursing pregnant females >13 years old. Although greater than 100, the level typically associated with a potential health concern, they are relatively low, particularly considering that four levels of refinement to the dietary exposure analysis were required to arrive at acceptable MOEs. Accordingly, monitoring for propargite residues (since the bulk of the aggregate exposure is dietary) in California crops should be intensified and closely followed.

5. There is a significant difference between the values used by U.S. EPA and DPR for surface water concentrations in evaluating carcinogenic risk. U.S. EPA used a value of 8.7 ppb in their calculations while DPR applied a value of 0.089 ppb. The value used by U.S. EPA resulted in the calculation of an unacceptable carcinogenicity drinking water risk ($> 1 \times 10^{-6}$ risk). The differences in water concentrations result from the use of a different dataset by DPR than the one used by U.S. EPA. We note that in the most recent version of the Reregistration Eligibility Decision (RED) for propargite, U.S. EPA (2001) states (page 16) that because their earlier modeling was very conservative and because of labeling changes regarding propargite applications near surface water agreed to by the registrant their remaining concerns regarding carcinogenic risk are largely mitigated. Nevertheless, on page 19 of the RED, U.S. EPA continues to express some concern about carcinogenic risk from propargite in surface water. It is yet to be shown that the measures specified by the labeling change will actually reduce surface water concentrations to levels below that pose an unacceptable cancer risk. The registrant has agreed to conduct a drinking water study to verify the adequacy of the labeling changes. OEHHA recommends that DPR participate in this study and verifies that the results do indeed confirm that actual residues of propargite fall below levels of concern for carcinogenic effects. If the mitigation measures prove ineffective, OEHHA

recommends that DPR develop additional mitigation measures to further protect surface waters from propargite contamination

6. Tolerance assessment for propargite yielded acute dietary MOEs significantly less than 100 (<10 for some population subgroups) for oranges, grapes, grapefruit, and nectarines. Residues on these commodities near the legal tolerance level are therefore of potential health concern. OEHHA urges DPR to advise U.S. EPA of this potential public health issue and request that propargite tolerances on oranges, grapes, grapefruit, and nectarines be reevaluated.

Again, thank you for the opportunity to review this document and we hope that you find our comments useful. We look forward to our review of the addendums to this document that evaluate occupational exposure and aggregate exposures that include residues in ambient air as a source of exposure to propargite. Should you have any questions regarding OEHHA's review of this RCD, please contact Dr. David Rice at (916) 324-1277 (primary reviewer), Mr. Robert Schlag at (916) 323-2624, or me at (510) 622-3165.

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