



Mary-Ann Warmerdam
Director

Arnold Schwarzenegger
Governor

December 31, 2010

TO: Interested Parties

SUBJECT: RISK MANAGEMENT DIRECTIVE

This letter outlines the Department of Pesticide Regulation's (DPR's) risk management decision related to the development of use restrictions on pesticides containing the active ingredient chloropicrin as it relates to exposures to residents and bystanders. This risk management decision was made after consultation with the Office of Environmental Health Hazard Assessment, the Air Resources Board, and the California Air Pollution Control Officers Association, as required by Food and Agricultural Code section 14023(e). A subsequent risk management directive will be developed to address occupational exposures after completion of the comprehensive risk characterization document (RCD).

Chloropicrin has been used as an agricultural pre-plant soil fumigant for decades, either alone or in combination with other fumigants. DPR placed chloropicrin into reevaluation in 2001 on the basis of air monitoring data received from the Chloropicrin Manufacturers Task Force. The data indicated that air concentrations at some distances from treated greenhouses exceeded the National Institute of Occupational Safety and Health's reference exposure levels of 0.1 parts per million (ppm). In addition to its fumigant pesticidal properties, chloropicrin is also added (about 2 percent by weight) as a warning agent to odorless products that contain methyl bromide and methyl iodide. Chloropicrin is also added as a warning agent to structures just prior to the application of sulfuryl fluoride. Using the information from the reevaluation and other data, DPR completed an RCD for chloropicrin as a toxic air contaminant (TAC) in February 2010. Based on the RCD and the recommendation of the TAC Scientific Review Panel, DPR will designate chloropicrin as a TAC effective January 8, 2011.

In 2006, the U.S. Environmental Protection Agency (U.S. EPA) finalized its risk assessment of chloropicrin. Following that, U.S. EPA published its Reregistration Eligibility Decision (RED) for chloropicrin in July 2008. The RED specified certain required mitigation measures and identified data gaps that chloropicrin registrants must address to be eligible for reregistration. U.S. EPA is currently using a two-year, phased-in approach to ensure the required mitigation measures are incorporated in the labels beginning in 2011. DPR is collaborating with U.S. EPA on this endeavor.



Acute Effects: Methodology and Target Levels

After evaluating information available (including DPR's RCD), U.S. EPA's risk assessment and RED, chloropicrin pesticide use reports, and pesticide illness reports, U.S. EPA-approved labels, and California county permit conditions for counties with high uses of chloropicrin, DPR will develop mitigation measures for agricultural soil fumigation applications that will address the acute effects of chloropicrin for residents and bystanders. Although acute effects of eye irritation are to be expected, reversible, and necessary when used at the levels of a warning agent, protection of residents and bystanders against those effects could be attained.

DPR has determined that the appropriate regulatory target level to restrict acute exposure to chloropicrin is 73 parts per billion (ppb) or 0.073 ppm averaged over an eight-hour period. This level is based on the evaluation of human studies by Cain in 2004, literature review, U.S. EPA's risk assessment, and DPR's RCD. Based on the human study by Cain, acute effects of eye irritation will not be expected at 73 ppb. According to the same study, 20 percent of the individuals reported some eye discomfort at 100 ppb, and 40 percent of the individuals reported increasing discomfort at 150 ppb. Since the level of discomfort was reported subjectively by individual scoring instead of direct clinical observation, it is difficult to ascertain the dose levels at which the individuals experienced those effects. Additionally, a published study by Prentiss in 1973 noted that lacrimation or tearing was observed at 300 ppb, although no data supporting that statement was presented. Therefore, DPR will develop mitigation measures to restrict chloropicrin exposures to a regulatory target level of 73 ppb or 0.073 ppm averaged over an eight-hour period. This target level is also below the National Institute of Occupational Safety and Health's reference exposure level of 100 ppb. Additionally, since no nasal or throat irritation was reported at the 100 ppb up to the 150 ppb level in the study, protection of the eye irritation effect most likely protects against upper respiratory effects. DPR will use analytical modeling tools to develop mitigation measures using an eight-hour exposure. In order to minimize the likelihood of short-term peak concentrations, DPR will consider other information and tools when developing restrictions.

Since mild ocular effects were first experienced at the 100 ppb level in the study, eye irritation is deemed as a more sensitive endpoint than nasal effects. This is the conclusion reached in DPR's RCD. The RCD also notes an endpoint of increased nitric oxide in expired air at a reference concentration of 4.4 ppb. Increased nitric oxide in expired air is a precursor to the nasal effects of chloropicrin. Although this level is much lower than the regulatory target level, it was reached based on statistical calculations instead of considering both the toxicologically sensitive endpoint and statistical considerations.

According to the study, the acute effects of chloropicrin seen at the 100 ppb level are mild and reversible. Those effects are also consistent with the lowest level (level 1) of exposures identified by the acute exposure guidelines developed by the National Research Council for airborne

concentrations of substances. Because of the permeability of chloropicrin's vapors and the accessibility of ocular nerve endings, and eye effects resulting from those exposures, individuals may experience discomfort, irritation, or certain asymptomatic nonsensory effects, but they are also transient and reversible. These effects are consistent with the acute exposure guidelines level 1, although the small number of subjects inherently limits the human study and the group may not adequately represent the most sensitive individuals. However, not even these effects are expected to occur at the regulatory target level.

Seasonal and Chronic Effects

Since the chemical effects of chloropicrin make it very permeable to the mucous membranes, especially the ocular membranes, its ocular effects are much more of a concern in mitigation development than its nasal effects. According to DPR's RCD, submitted studies, reviewed literature, and other studies, eye irritation is the most sensitive endpoint for chloropicrin. This was also evident in the human exposure studies by Cain. Therefore, in developing mitigation measures, we believe that addressing the ocular effects during acute exposures will address the seasonal and chronic effects from inhalation exposures to chloropicrin.

Lifetime Exposure Effects

Carcinogenicity was discussed in DPR's RCD as one of the possible outcomes for lifetime exposures to chloropicrin. DPR scientists concluded this endpoint based on a weight-of-evidence approach using animal data that showed some tumor formation only in female mice and inconsistent in-vitro and in-vivo genotoxicity tests. From that determination, cancer potency factors were calculated from statistical tests based on a small set of animal data using multiple uncertainty factors to extrapolate to human exposures. Although instinctively conservative and health protective, the confidence in this approach is ambivalent. Additionally, U.S. EPA does not classify chloropicrin as a carcinogen, and a review of data presented by the National Toxicology Program also concludes that the results of the animal studies are inconclusive. After evaluating all available information on the carcinogenic potential of chloropicrin and the differing scientific opinions on this subject, the issue appears to be equivocal at this time.

Conclusion

Since DPR's comprehensive RCD, which includes occupational exposure scenarios, is undergoing internal review and has not been completed, DPR will determine which occupational exposures require risk mitigation through another risk management directive after completion of

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the comprehensive RCD. In the meantime, DPR will develop mitigation measures in consultation with the Air Resources Board, the air pollution districts, and the county agricultural commissioners, as required by Food and Agricultural Code section 14024(a) to protect public health concerns for residents and bystanders.

If you have any questions, please contact Dr. Marylou Verder-Carlos, DPR Assistant Director, at 916-445-3984 or mverdercarlos@cdpr.ca.gov.

Sincerely,



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cc: Dr. Marylou Verder-Carlos