



ENVIRONMENTAL HEALTH SCIENCES
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April 1, 2010

Mary-Ann Warmerdam
Director
Department of Pesticide Regulation
1001 I Street
Sacramento, CA 95812

Dear Director Warmerdam:

Attached to this letter are the findings from the Scientific Review Panel (SRP) in its review of the risk assessment for the fumigant, chloropicrin and our recommendation it be declared a Toxic Air Contaminant. The findings contain the history of the review process and I won't repeat the dates. The purpose of this letter is to transmit the findings of the SRP on chloropicrin for your consideration. I should emphasize that the interaction between the SRP and DPR was excellent and we enjoyed the discussion and agreed upon the conclusions.

The Panel was concerned to learn that over and above current exposure, the use of chloropicrin in California is likely to increase substantially should methyl iodide be introduced as an agricultural chemical, given that chloropicrin is present in relatively high concentration in many proposed methyl iodide formulations.

The SRP recognizes that occupational risk is not covered in this toxics evaluation as it is outside the SRP's charge. The SRP appreciates that DPR will be addressing occupational risk in a separate evaluation.

The SRP recognizes that chloropicrin is a compound that is genotoxic and the evidence of carcinogenicity suggests the compound is a potent carcinogen. While not wanting to enter the world of policy there is a concern for the carcinogenic properties of chloropicrin.

The SRP is interested in addressing other compounds perhaps as a group that are non-genotoxic, non-carcinogenic warning agents. We need to be sensitive to their potential toxicity.

Again, we appreciate the professional interaction with DPR staff and look forward to working with you in the future.

Sincerely

A handwritten signature in black ink, appearing to read "John R. Froines".

John R. Froines, Ph.D.
Chair

**Findings of the Scientific Review Panel on
"Evaluation of Chloropicrin as a Toxic Air Contaminant" as adopted at the Panel's
February 24, 2010 Public Meeting**

The Scientific Review Panel on Toxic Air Contaminants (Panel) met Thursday December 10, 2009 to review the document "Evaluation of Chloropicrin as a Toxic Air Contaminant," prepared by the Department of Pesticide Regulation (DPR) of the California Environmental Protection Agency. This included the following: Part A, "Environmental Fate Review and Exposure Assessment" prepared by the Worker Health and Safety Branch (dated November 3, 2009 and reflecting revisions to an original draft dated November 14, 2008 and a later June 2009 interim draft); Part B, "Human Health Assessment" prepared by the Medical Toxicology Branch (dated November 9, 2009 and reflecting revisions to an original draft dated December 2, 2008 and an interim draft in June 2009); and Part C, "Comments on the June 2009 Draft Report and Responses" (November 2009; including responses to comments by the Chloropicrin Manufacturers Task Force). In addition, the Panel reviewed the salient content in memoranda prepared by the Office of Health Hazard Assessment (OEHHA) dated November 14, 2009 and March 23, 2009. In addition to hearing presentations from DPR and OEHHA staff, the Panel also heard oral reports by two of its members who were lead reviewers for chloropicrin (Drs. Katherine Hammond and Paul Blanc) and took comments from other Panel members. This is documented in the December 10, 2009 meeting transcript (see <http://www.arb.ca.gov/srp/srpmeetings.htm>).

The materials as noted above convincingly demonstrate that:

- (1) Chloropicrin (trichloronitromethane) is a widely used fumigant pesticide and warning agent.
- (2) Its physical and chemical properties are such that its environmental fate includes substantial release into the airborne environment.
- (3) Such airborne release regularly occurs through its routine use.
- (4) The patterns of use over time indicate more intense use as a primary active ingredient (as opposed to a warning agent), thus increasing levels of exposure.
- (5) Bystander over-exposures have been well documented.
- (6) Chloropicrin is a severe irritant.
- (7) Clinical experience with human overexposures demonstrates unequivocally that respiratory tract injury over a range of severities can occur from chloropicrin exposure, including data arising from its historical use as a chemical warfare agent.
- (8) Controlled human exposure data are also available that are pertinent to chloropicrin irritant effects.

Findings of the Scientific Review Panel on Chloropicrin
February 24, 2010

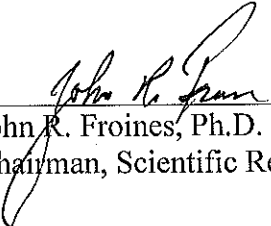
- (9) Animal experimental data, some of it in relation to chemical warfare applications, are consistent with the irritant effects noted in humans.
- (10) The weight of the available evidence also supports classifying chloropicrin as a genotoxic cancer-causing substance warranting cancer risk estimations.
- (11) For acute one hour exposure, nasal air nitric oxide in humans is a scientifically appropriate endpoint based on controlled human exposures. In addition, ocular irritation in humans based on controlled human exposures is supportive of these acute one-hour exposure effects.
- (12) For 8- and 24-hour acute exposure, a constellation of effects in exposed rabbits served as scientifically appropriate endpoints.
- (13) For seasonal exposure, rhinitis in a rat model provided an acceptable basis for modeling risk to humans.
- (14) For chronic inhalation, bronchiectasis in experimentally exposed mice is an appropriate endpoint for benchmark modeling and, given its severity, use of a benchmark response (BMR) level of 2.5% rather than a 5% level.
- (15) The cancer potency factor for chloropicrin was reasonably derived and is consistent with substantive risk of cancer arising over a range of exposures to chloropicrin. Chloropicrin, a genotoxic carcinogen, should be modeled on the basis of a linear no-threshold dose-response curve.
- (16) The calculated cancer risk from lifetime exposure to chloropicrin yielded maximum likelihood estimates as high as 3.2×10^{-2} and none lower than 2.0×10^{-3} . These are very high risks.
- (17) Experimental animal studies provide sufficient data to derive scientifically acceptable modeling of human equivalent concentrations (HEC) and reference concentrations (RfC) for various endpoints in acute, seasonal and chronic exposure scenarios and, for lifetime exposure, cancer risk.
- (18) The estimated bystander exposures to chloropicrin following soil fumigation, structural fumigation and enclosed space fumigation are at levels that cause great concern about the associated health risks. California regulations state that if the air concentrations of a pesticide are not ten-fold below the RfC that is considered protective of human health, the pesticide meets the criteria to be listed as a toxic air contaminant (i.e., exposures should be less than 10% of the RfC). As an example of the very high levels of exposure, all children bystander exposure scenarios to chloropicrin and nearly all those for adults following soil fumigation exceeded 2000%. A margin of exposure approach leads to the same conclusions for all exposure scenarios.

**Findings of the Scientific Review Panel on Chloropicrin
February 24, 2010**

The Panel finds that chloropicrin should be classified as a Toxic Air Contaminant.

Moreover, the Panel is also concerned having learned that over and above current exposure, the use of chloropicrin in California may increase substantially should methyl iodide be introduced as an agricultural chemical, if chloropicrin is present in relatively high concentrations in many proposed methyl iodide formulations.

I certify that the above is a true and correct copy of the findings adopted by the Scientific Review Panel on February 24, 2010.



John R. Froines, Ph.D.
Chairman, Scientific Review Panel