

August 28, 2013

Secretary Matthew Rodriguez
California Environmental Protection Agency
1001 I Street, PO Box 2815
Sacramento, CA 95812-2815

Director Brian Leahy
California Department of Pesticide Regulation
1001 I Street, PO Box 4015
Sacramento, CA 95812-4015

Dear Secretary Rodriguez and Director Leahy:

As health professionals and scientists, we are writing to urge the Department of Pesticide Regulation to preserve scientific integrity in the evaluation of the toxicity of the soil fumigant chloropicrin and adopt control measures to protect farmworkers and other rural residents from acute respiratory effects and cancer.

The soil fumigant chloropicrin is heavily used in fields along the central and south central California coast before planting strawberries and other crops. In 2011, over 7.2 million pounds of the fumigant were used in California on 70,000 acres.¹ As a highly volatile chemical applied at rates ranging from 100 to 350 pounds an acre, chloropicrin is hard to contain, even with use of tarps and water seals. In the past 10 years, over 700 people have been made ill in 22 separate chloropicrin drift incidents.

The actual number of chloropicrin-related illnesses is likely many times higher because of low rates of pesticide illness reporting, particularly among agricultural workers who can be exposed both working in the fields and living nearby.² Chloropicrin can cause severe respiratory harms, with some individuals developed asthma symptoms³ — an indication of substantial exposure in these communities. The chemical has been used in warfare and has traits similar to tear gas. It is included in the Defense Treaty Inspection Program of the US Department of Defense.

When chloropicrin was evaluated as a Toxic Air Contaminant, the toxicologists from DPR who wrote the Human Health Risk Assessment,⁴ the scientists from the Office of Environmental Health Hazard Assessment (OEHHA),⁵ and the Scientific Review Panel⁶ who peer reviewed it

¹ DPR Pesticide Use Report Summary 2011.

² Reeves MR, Katten A, Guzman M, 2002. Fields of Poison 2002. Pesticide Action Network.
<http://www.panna.org/issues/publication/fields-poison-2002-english>.

³ DPR CalPIQ Pesticide Illness Query database

⁴ DPR, Evaluation of Chloropicrin as a Toxic Air Contaminant(TAC), Part B Human Health Assessment, February 2010 http://www.cdpr.ca.gov/docs/emon/pubs/tac/part_b_0210.pdf

⁵ OEHHA Memorandum to DPR. Findings on the Health Effects of Chloropicrin. November 4, 2009.
http://www.cdpr.ca.gov/docs/emon/pubs/tac/chloropicrin_findings.pdf

all concluded that chloropicrin is a potent carcinogen with a low threshold for acute eye and respiratory irritation. A comprehensive chloropicrin risk assessment completed by DPR toxicologists last year reaffirmed DPR scientists' conclusion that chloropicrin is a carcinogen and severe irritant.⁷

We are concerned that DPR managers have since issued a risk management directive setting a regulatory target level of 73 ppb averaged over eight hours that we conclude will not adequately protect against irritant effects.

Further, DPR managers contradicted the carcinogenicity conclusion reached by the scientists, stating that "the conclusion of the Toxic Air Contaminant assessment was not adequately supported and that the evidence on the carcinogenicity of chloropicrin was equivocal."⁸ DPR managers also issued a memorandum reconsidering the carcinogenicity of chloropicrin⁹ in an attempt to justify this decision.

Our primary concerns include:

- 1) The acute regulatory target level of 73 ppb will not be sufficiently protective.
- 2) Evidence of carcinogenicity is clear, not equivocal
- 3) The risk management decision does not reflect best available science.
- 4) DPR must collaborate with OEHHA to ensure that the risk mitigation directive developed for chloropicrin protects farm workers from respiratory effects and cancer.
- 5) California has reduced health impacts in the past by adopting more health protective policies than the federal government and should not shy away from leadership in this area.

Below, we provide a more detailed review of these concerns.

1) The Acute Regulatory Target Level of 73 ppb Will Not Be Sufficiently Protective

We are concerned that DPR managers have set a regulatory target level of 73 ppb averaged over eight hours. The 73ppb level is 25 times higher than the 2.7 ppb 8-hour Reference Exposure Level (REL) to prevent acute illness in children established by DPR scientists in both the Chloropicrin TAC Report and Risk Characterization. This level also ignores the 4.4 ppb one hour REL also established in the TAC Report and Risk Characterization.

⁶ Scientific Review Panel 2010. Findings of the Scientific Review Panel on the Evaluation of Chloropicrin as a toxic Air Contaminant as adopted in the Panel's February 24, 2010 meeting.

http://www.cdpr.ca.gov/docs/emon/pubs/tac/tacpdfs/chloropicrin/letter_0410.pdf

⁷ DPR Chloropicrin Risk Characterization 2012 http://www.cdpr.ca.gov/docs/risk/rcd/chloropicrinrisk_2012.pdf

⁸ DPR Chloropicrin Risk Management Directive December 31, 2010.

<http://www.cdpr.ca.gov/docs/emon/pubs/chloropicrin/directive.pdf>

⁹ DPR Memorandum, The Risk Management Directive: Reconsideration of the Carcinogenicity of Chloropicrin April 23, 2013 Appendix 3 pg 23 of link

http://www.cdpr.ca.gov/docs/whs/pdf/dpr_chloropicrin_mitigation_proposal_and_app_1-3.pdf

Consideration of the human study on which the regulatory target level is based indicates that reducing exposures to this concentration will not adequately protect against irritant effects in the exposed population. In setting the Reference Concentration (RfC), DPR has eliminated all uncertainty factors (UFs). The fact that a human study was done supports the elimination of the interspecies UF, but there is no justification for the elimination of the intraspecies UF (typically a factor of 10). In fact, the variability in eye irritation thresholds among the subjects in the human study were found to vary by *greater than* a factor of 10 between study participants—see Table 1 below.¹⁰ Note that the final “acceptable” acute concentration of 73 ppb is twice the concentration that the 10th percentile subject responded to and the variability between the most and least sensitive subject was a factor of 42, far greater than the intraspecies factor of 10 typically used in risk assessment. In the Phase III study, no low dose was even tested, resulting in a study that produced only a LOAEL, not a NOAEL.

Table 1: Chloropicrin Concentrations At Which Adverse Effects Were Observed

Effect	Threshold conc. 10 th percentile (most sensitive subjects)	Threshold conc. 90 th percentile (least sensitive subjects)	Factor by which 10 th percentile differs from 90 th percentile
Eye irritation	37 ppb	1,565 ppb	42
Odor	216 ppb	764 ppb	1.9

Indeed, in their review of the chloropicrin human study, members of the Human Subjects Review Board recommended that not only should the intraspecies UF be retained, but that an additional UF be used.¹¹ This conclusion was based on the fact that only young healthy adults were included as study subjects. Only subjects who reported no smoking within a year, no use of recreational drugs within a year, no recent illness, and no history of chronic illness qualified to go on to screening in the laboratory. In addition, to be approved for inclusion in the study, subjects were required to have pulmonary function at or above 83% of predicted forced expiratory volume at 1 sec (FEV1) or forced vital capacity (FVC) for testing by American Thoracic Society criteria. These criteria clearly exclude people with asthma or other respiratory illness, children whose lungs are still developing, and the elderly and other vulnerable populations.

There are two additional factors that DPR’s regulatory target level of 73 ppb averaged over eight hours does not account for. First, no subject in the human study was ever exposed to chloropicrin for more than 60 minutes at a time. Second, during a fumigation, the concentration of chloropicrin varies over time, with concentration peaks that are substantially above the 73 ppb level. DPR’s decision to eliminate the intraspecies UF for an exposure period averaged over eight hours and based on a study in which humans were exposed at most for 60 minutes will not be protective of the health of even healthy individuals, and could pose very serious risks for vulnerable populations.

¹⁰ US EPA, 2009. Human Health Risk Assessment for Chloropicrin. Appendix A, Table 1A, Appendix A, p. 78. Docket # EPA-HQ-OPP-2007-0350-0398.

¹¹ From the July 25, 2006 Minutes of the United States Environmental Protection Agency (EPA) Human Studies Review Board (HSRB), June 27-30, 2006 Public Meeting, Docket Number: EPA-HQ-ORD-2006-0384

2) Evidence of Carcinogenicity Is Clear, Not Equivocal

DPR management's memorandum outlining reconsideration of chloropicrin's carcinogenicity attempts to justify their characterization of evidence of carcinogenicity as equivocal but this characterization is not supported by the body of evidence from animal and in vitro studies.

Management's memo claims that the probability for carcinogenicity in the comprehensive chloropicrin risk characterization (completed in 2012) was stated with "caveats and uncertainties". However, in the executive summary in the 2012 risk assessment,¹² the toxicologists are clear in their assertion that chloropicrin is carcinogenic: *"Although the increases in the tumors in neither study were dramatic and all the in vivo genotoxicity studies were negative, DPR made a health protective assumption that chloropicrin was carcinogenic with a genotoxic mode of action based on its electrophilic structure and the positive in vitro genotoxicity tests."* The detailed discussion of carcinogenicity later in the risk assessment unequivocally concludes that "based on the weight of evidence it was determined that the tumor data could not be dismissed". OEHHA reiterated this point in its response to DPR's Risk Management Directive,¹³ noting: *"OEHHA respectfully disagrees with DPR's conclusion that evidence on the carcinogenicity of chloropicrin should be viewed as equivocal. Chloropicrin has been observed to induce gene mutations and chromosomal damage. The DPR chloropicrin TAC document, the OEHHA chloropicrin findings and the SRP chloropicrin findings all state that chloropicrin is a genotoxic carcinogen and can be assigned a cancer potency factor of 2.2 (mg/kg-day)⁻¹. This information should be considered in the development of an RMD for chloropicrin."*

The TAC evaluation concluded that in the 78-week chloropicrin inhalation exposure study, female mice showed statistically elevated incidence of lung adenomas and carcinomas at the highest dose tested by trend analysis using the Poly-3 trend test, which better accounts for survival in the different dose groups. The assessment also pointed out that the 37% incidence of adenomas at the highest dose was clearly outside the historical control range of 0-27% reported by the supplier and that that tumor incidence might have been higher if the study duration were the standard 104 weeks rather than 78 weeks, if dose levels were higher, and if body weights and caloric intakes were not reduced.

DPR recently had a Department statistician review the relevance of using this particular type of statistical test.¹⁴ This critique concludes that use of the Fischer test alone without the Poly-3 test might have been more appropriate. However, DPR neglected to mention that the statistician also stated that *"the results from this particular study, regardless of the manner in which the data are statistically analyzed, provide some (albeit borderline) evidence that high dose female mice develop increased numbers of lung tumors."*

¹² DPR Chloropicrin Risk Characterization 2012 http://www.cdpr.ca.gov/docs/risk/red/chloropicrinrisk_2012.pdf

¹³ OEHHA, 2010. Memo from Anna Fan to Marylou Verder-Carlos *re* Chloropicrin—OEHHA comments on DPR's Draft Risk Management Directive (RMD). December 29, 2010.

¹⁴ Jessop, H. 2013. CDPR Memorandum: Relevance of the Bieler-Williams poly-3 trend test in the analysis of carcinogenicity of chloropicrin. April 3, 2013.

Chloropicrin tested positive in a total of 13 *in vitro* mutagenicity tests, including three tests for DNA damage, eight reverse mutation assays with Salmonella strain TA100, and two tests for clastogenicity, characterized by a DPR toxicologist as “overwhelming positive results.”¹⁵ Instead of summarizing the weight of the evidence, the DPR risk management directive focuses on the two *in-vivo* tests in which chloropicrin tested negative. We note that OEHHA characterized the *in vivo* studies as quite limited, inconclusive and suffering from experimental deficiencies.¹⁶

The combination of the animal studies and the *in vitro* studies indicate that there is no question that there is evidence of carcinogenicity. If DPR is to protect public health, the Department should take a proactive approach to reduce exposure, not justify a decision to take no action on the basis of an analysis that contradicts the conclusion of DPR and OEHHA toxicologists and the SRP reviewers.

3) The Risk Management Decision Does Not Reflect Best Available Science

The best available science is often inconvenient for the regulated community; however, any move to change the science to fit the desired conclusion violates the scientific integrity of the process. Independent scientific assessment of a chemical’s toxicology is a cornerstone of scientific integrity and transparent policies to protect the public and workers from harmful chemical exposures.

Under the Toxic Air Contaminant Act, state scientists review toxicological data and set reference levels intended to minimize health risks. Management then has both the responsibility to make rules that are health protective and the authority to determine that it is not possible to mitigate immediately to reference levels because of technical or economic limitations. The Air Resources Board has done this in the past by gradually phasing in mitigations for Toxic Air Contaminants such as perchloroethylene and diesel exhaust. Though it is at times appropriate for management to implement phased-in mitigations to meet reference levels, it is not appropriate to revise these levels without solid scientific backing. With chloropicrin, by reconsidering the evidence of carcinogenicity and contradicting the consensus conclusion of the scientists, DPR management has exceeded their authority and inappropriately manipulated the risk assessment process.

4) DPR must collaborate with OEHHA to ensure that the chloropicrin risk management directive protects farm workers

Agricultural workers are more heavily exposed to chloropicrin than any other sector of the state’s population because they are exposed as fumigant handlers and as bystanders working and living near fumigated fields. State law mandates both that the development of regulations relating to pesticides and worker health and safety shall be the joint and mutual responsibility of DPR and OEHHA (FAC 12980 and that regulations that relate to health effects shall be based upon the recommendations of OEHHA (FAC 12981). Any chloropicrin mitigation rules based on a risk

¹⁵ DPR Memorandum 2012 From Carolyn Lewis to Gary Patterson. Response to OEHHA’s Comments on the Chloropicrin Risk Characterization Document.

¹⁶ OEHHA Memorandum to DPR. Comments on the Draft Risk Characterization Document for Chloropicrin. October 15, 2012. http://www.cdpr.ca.gov/docs/risk/rcd/oehha_comments.pdf

management directive that contradicts OEHHA's recommendations on regulatory target levels for mitigating risk of respiratory effects and cancer will violate these legal requirements.

5) California Should Take a Leadership Role in Protecting Public Health

DPR and OEHHA have toxicologists on staff and the Scientific Review Panel (SRP) as scientific peer reviewers specifically to allow California to conduct an *independent* evaluation of pesticide toxicology. It is perplexing then that DPR management justifies their argument that carcinogenicity is equivocal based on the conclusions of the U.S. EPA and the Italian Ministry of Health. California has a strong history of leading the nation and the world with forward-thinking, health protective policies that are years ahead of the conclusions of agencies elsewhere. In the words of the current California Attorney General, California "*has served as a laboratory of innovation for other states and the federal government.*"¹⁷ DPR and Cal/EPA should not ignore the strong science of DPR's and OEHHA's staff toxicologists whose role is explicitly to conduct independent evaluation of pesticide toxicology. Our state should be proud of past examples of recognizing health hazards of pesticides including methyl bromide, chromated copper arsenate and methyl iodide before the federal government and should not shy away from continued leadership in this area.

Conclusion

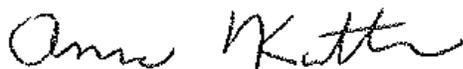
In the interest of preserving DPR's scientific integrity, we urge you to let the conclusions by DPR and OEHHA toxicologists and the Scientific Review Panel be your primary guide in making risk management decisions for chloropicrin.

We firmly support the strongest health protections possible; however, if the reference levels set in the risk assessment to protect against irritant effects and cancer require stronger protections than DPR management deems are currently feasible due to technical or economic limitations, management has the authority to determine that it is not possible to mitigate immediately to these levels and can create a clear, enforceable phase-in schedule to strengthen mitigations to appropriately protective levels over time. There is precedent within Cal/EPA for such an approach. As mentioned above, the Air Resources Board has gradually phased in mitigations for toxic air contaminants including formaldehyde and perchloroethylene. One option available to DPR management is to create a scheduled phase-in of mitigation measures over the next three years. This would both minimize impacts on agriculture and preserve scientific integrity by acknowledging chloropicrin's high acute toxicity and carcinogenicity and making an enforceable commitment to achieve necessary protections in the near term.

In conclusion, given the public health risks of chloropicrin, including carcinogenicity and the low threshold for acute irritant properties, we urge DPR to immediately put in place tighter restrictions on use of chloropicrin. At the same time, Cal/EPA and DPR should increase their investment in helping farmers transition to safer alternatives to fumigants.

¹⁷ Letter from California DOJ to Senator Barbara Boxer regarding Concerns with Preemption Language in Chemical Safety Improvement Act, S 1009. June 11, 2013. <http://prop65news.com/Portals/0/Nelson-Boxer%20%20Final%20%286-11-13%29.pdf>

Sincerely,



Anne Katten, MPH
Pesticide and Work Safety Specialist
California Rural Legal Assistance
Foundation



Susan Kegley, PhD
Principal and CEO
Pesticide Research Institute and
Consulting Scientist
Pesticide Action Network North America

Caroline Cox, MS
Research Director
Center for Environmental Health

Robert Gould, MD
President
San Francisco Bay Area Chapter
Physicians for Social Responsibility

Emily Marquez, PhD
Staff Scientist
Pesticide Action Network North America

Miriam Rotkin-Ellman, MPH
Staff Scientist
Natural Resources Defense Council

Jennifer Sass, PhD
Senior Scientist
Natural Resources Defense Council

Harry Wang, MD
President
Sacramento Chapter
Physicians for Social Responsibility

Dorothy Wigmore, MS
Occupational Health Specialist
Worksafe