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MEMORANDUM

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DATE: December 17, 2012

SUBJECT: COMMENTS ON THE DRAFT EXPOSURE ASSESSMENT DOCUMENT FOR CHLOROPICRIN

The Office of Environmental Health Hazard Assessment (OEHHA) has reviewed the draft exposure assessment document (EAD) for chloropicrin, prepared by the Department of Pesticide Regulation (DPR), dated December 27, 2011. Our comments are provided n the attachment. Exposure estimates reported in this document were used to estimate risks to human health in the Risk Characterization Document, previously reviewed by OEHHA. OEHHA reviews risk assessments prepared by DPR under the authority of Food and Agriculture Code section 11454.1.

In general, OEHHA agrees with the exposure assessment methodology and conclusions of the draft EAD. Several specific comments and recommendations are contained in the attachment.

Thank you for providing this draft document for our review. If you have any questions regarding OEHHA's comments, please contact Dr. Charles Salocks at (916) 323-2605 or Dr. Anna Fan at (510) 622-3200.

Attachment

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Attachment

Comments on the 2011 Draft Exposure Assessment Document for Chloropicrin

Office of Environmental Health Hazard Assessment

December 2012

General Comments

In general, the Office of Environmental Health Hazard Assessment (OEHHA) agrees with the exposure assessment methodology and the conclusions in the draft chloropicrin Exposure Assessment Document (EAD).

The draft "Estimation of Exposure of Persons in California to Pesticide Products that Contain Chloropicrin" summarizes exposures related to the uses of chloropicrin in California. Exposure estimates are made for bystanders, persons who handle chloropicrin during fumigation, persons who breach tarps, and individuals involved with structural fumigation when chloropicrin is used as a warning agent. Comments on each major section of the document are provided below. Editorial suggestions are provided after the technical comments.

1. Abstract

In some instances, the percentage of chloropicrin as the Active Ingredient (AI) in the various studies used to estimate exposure is unclear. For example, on page 8 (lines 42-43), formulations that have chloropicrin as an AI are defined as "...products containing chloropicrin concentrations above 2%." For the purpose of obtaining "*screening level* estimates of exposure" (page 8, line 6), it would be reasonable to assume a default chloropicrin concentration of 100%. This assumption would be consistent with the summary of chloropicrin-containing products registered for use in California (Table 2, page 13), which indicates that eight products have chloropicrin as the sole AI and they range in concentration from 94 to 100%. For screening purposes, it appears that a more transparent and health protective approach would be to estimate exposure for products that contain 100% chloropicrin, knowing that use of products with a lower percentage AI would result in proportionally lower exposures.

OEHHA suggests that summarizing the exposure estimates presented in the top half of page 9 in a table rather than writing them out as text would improve readability and greatly facilitate comparison of these results.

The statement that exposures resulting from use of a methyl bromide formulation that contains 10.5% chloropicrin are "anticipated to be greater" than exposures resulting from use of formulations that contain 2% chloropicrin as a warning agent (page 9, lines 5-6) appears to be more nuanced than it needs to be. Given the five-fold concentration difference, the exposure resulting from use of 10.5% chloropicrin would surely be greater than the exposure resulting from use of 2% chloropicrin.

2. Introduction

At the end of the introduction, the mode of action is discussed. OEHHA concurs that the mode of toxic action is not well characterized. OEHHA recognizes that Sparks et al., 2000 conclude that the reaction with sulfhydryl groups of hemoglobin (Hb) and decreased oxygen transport are potential pathways for toxicity. However, OEHHA recommends that the report also point out that acute pulmonary and ocular irritation do not occur via this mode of action (page 11, lines 1-5).

The report adequately covers the physiochemical properties, formulations, and pesticide use and sales. However, OEHHA recommends that, if possible, the information on number of registered products containing chloropicrin be updated. Are the data for chloropicrin use in California available for 2009-2011, and can this information be incorporated into the report?

3. Reported Illnesses

The EAD summary of reported illnesses associated with chloropicrin is clear and concise. The EAD summarizes the reported illnesses associated with chloropicrin when used alone and in combination with another fumigant as a warning agent. As reported, in the Kern County (2003) incident, nearby residents complained of eye and throat irritation after soil fumigation even though an 18 meter buffer zone had been established. In the 2005 Monterey incident, residents 2-3 miles away complained of odor and eye irritation following a tarped bed application.

OEHHA was not able to replicate all the percentage of illness types described in the text at the bottom of pages 18 and19. The discrepancies are relatively small but should be re-checked by the authors.

The systemic effects reported in Table 4 and footnote (b) (eye, respiratory, and systemic effects) associated with chloropicrin exposure and illness cases suggest that chloropicrin exposure may cause additional chronic effects (e.g., degeneration of the nasal epithelium) that are similar to those seen with other Toxic Air Contaminants (TACs) such as acrolein, acetaldehyde, and formaldehyde. The text at the bottom of page 9 indicates that systemic effects were reported in 32% of the cases where chloropicrin was used alone and in 44% of the cases where chloropicrin was used in combination with other fumigants.

OEHHA suggests that consideration be given to potential adverse effects in sensitive sub-populations that may be exposed to chloropicrin. Studies have shown that children and asthmatics are more sensitive to the irritating effects of chemicals that can adversely affect respiratory health. In addition, eye irritation can be increased in those wearing glasses or contact lenses or those with pre-existing eye conditions. OEHHA believes that an additional uncertainty factor is warranted to establish short-term risk-based exposure standards for chloropicrin.

Bystander exposure is also a concern for continuous (seasonal) exposure. The EAD cites a study where fourteen people experienced symptoms upon entering a structure after the application was concluded (page 18, lines 16-24). In another report (Teslaa et al., 1986), a family developed serious symptoms 3 to 4 weeks post fumigation (page 21, lines 4-13). In the latter study, the residual chloropicrin level was 30-48 parts per billion (ppb) [202-323 micrograms per cubic meter ($\mu g/m^3$)] six weeks after the application. In addition, Table 7 notes that the reported concentrations of chloropicrin in ambient air may underestimate actual short-term exposures (page 42, line 25). The EAD also points out that the public may be exposed in locations that are far from the sites of application (page 25, line 41).

OEHHA further recognizes that there are data gaps in the characterization of bystander exposure that need to be addressed. The effects of simultaneous exposure to chloropicrin and its photodegradation byproduct phosgene have not been characterized. Furthermore, the EAD notes that no phosgene monitoring has been conducted in conjunction with any chloropicrin application (page 105, line 32).

4. Label Precautions and California Requirements

It appears that the criteria for use of air-purifying respirators (APRs) were established without taking into consideration the results of the Cain (2004) study. The criteria are described on page 23, lines 28-31: "Handlers can resume work activities without air-purifying respirators, if two consecutive breathing zone samples taken at the handling site at least 15 minutes apart show levels of chloropicrin have decreased to less than 0.15 ppm (150 ppb), provided that handlers do not experience sensory irritation." However, the Cain (2004) study established that the threshold for acute (one-hour) sensory (ocular) irritation in humans is lower than 150 ppb. Benchmark dose analysis of the data indicated a $BMCL_{10}$ for ocular irritation of 26 ppb. [See Chloropicrin Risk Characterization Document (DPR 2011), page 49.] At concentrations of 100 and 150 ppb, eye irritation was clearly detectable in humans subjects after exposure durations of just 19 and 10 minutes, respectively (DPR 2011; page 21). These data demonstrate that persons exposed to 100-150 ppb *will* experience eye irritation after relatively short exposure durations. For this reason, it appears that the relevance of the 150 ppb analytical criterion for respirator use needs to be re-evaluated and perhaps lowered to no more than 100 ppb. Furthermore, since APRs are assumed to confer 90% protection, it would be reasonable to restrict APR use to situations where the airborne concentration of chloropicrin is ≤ 1,000 ppb [1 part per million (ppm)]. Working in environments where the concentration is greater than 1 ppm should not be permitted, even when APRs are available.

5. Exposure Scenarios

The exposure scenarios presented in the EAD include occupational handlers exposed during chloropicrin applications (before aeration or tarp removal), occupational handlers conducting aeration activities (tarp punching, splitting and removal), reentry scenarios, airborne exposures of bystanders, and ambient air exposures. OEHHA concurs that the highest realistic exposures, based on available data, should be used for quantitative risk assessment purposes. OEHHA agrees with the parameter values used to estimate bystander exposure, including an 8-hour workday for occupational bystanders and a residential 24-hour/day scenario. This section provides a thorough review of the data on occupational handler scenarios and reentry scenarios.

The EAD states that exposures to the public are possible in areas that are far from application sites. OEHHA recommends that the California Air Resources Board continue to conduct air monitoring in counties with high use to improve the data available.

The field fumigation scenarios were based on typical application rates to calculate ambient air concentrations. OEHHA is concerned that the data used for these calculations may not adequately reflect the increased use of chloropicrin in California (see Table 3 and Figure 2). OEHHA recommends using more recent data from the Pesticide Use Report to update Appendix III and to address the possibility that maximum application rates have increased. In addition, it would be important to determine if greater statewide use might lead to higher cumulative (multiple source) exposures, particularly in those counties where use of the fumigant is high. As statewide chloropicrin use increases and use of methyl bromide declines, cumulative exposure to chloropicrin might be particularly critical for residential bystanders. DPR may want to consider a sensitivity analysis that assumes higher cumulative exposures.

6. Pharmacokinetics

One metabolic pathway briefly mentioned in the EAD is the formation of thiophosgene intermediates. This is a pathway of concern as these types of adducts may lead to chronic health effects. OEHHA notes that studies using the intraperitoneal route of exposure for determining the pharmacokinetics of chloropicrin are of questionable relevance for extrapolating to the inhalation route of exposure (page 29, lines 18-29). However, OEHHA recognizes that DPR must use the data available to them.

7. Environmental Fate

Persistence in Soil Environment

The potential for chloropicrin persistence in soil and groundwater is a concern and should be further evaluated as this can represent a potential exposure long after soil fumigation and may lead to long-term bystander exposure via infiltration into residential indoor air. The increased use of chloropicrin in California has potential to exacerbate this situation. On page 34, lines 21-26, Guo et al., 2003b noted that levels as high as 500 milligrams per kilogram (mg/kg) persisted in the soil 7 years after a manufacturing facility had ceased operations, and groundwater beneath the facility had chloropicrin concentrations ranging from 10-150 milligrams per liter (mg/l). Other studies were reviewed examining the half-lives of chloropicrin in different soil types and conditions. This section would benefit from a conclusion paragraph that summarizes the major findings on half-lives and soil types and conditions.

In a soil metabolism study, Olson and Lawrence (1990) added 250 ppm of radiolabeled chloropicrin to sandy loam under aerobic conditions. The EAD notes that "The estimated half-life "...was approximately 5 days; about 70% of the applied radiolabel was recovered by the 90^{th} day of the study as CO_2, while most of the rest was volatilized chloropicrin" (page 31 lines 32-35). This suggests that the parent compound degrades quickly ($t_{½}$ = 5 days) but that ultimate degradation to CO_2 requires considerably longer time. Did the authors of this study analyze for the presence of any specific degradation by-products? This may be significant since reductive dechlorination by-products of chloropicrin appear to be mutagenic (Chloropicrin Risk Characterization Document, page 56). A more detailed explanation of these results would probably be helpful.

Persistence in Water Environment

While exposure to light may decrease persistence of chloropicrin in some water environments by photodegradation, ground water is not typically exposed to light prior to consumption and therefore would not be degraded by this mechanism. OEHHA recommends this distinction be made on page 35. OEHHA also recommends that the studies on hydrolysis and photohydrolysis (pages 35-37) be summarized through the use of a table, or some over-arching conclusions about the results of these studies be listed at the end of the section. The section on oxidation-reduction reactions adequately summarizes the limited existing data on this subject. The section on chloropicrin disinfection byproducts in drinking water states that chloropicrin is present in drinking water only at low concentrations (< 10 µg/L). Use of the word "low" may be misinterpreted to mean insignificant or of no concern. OEHHA recommends that the report simply state that "the concentrations were measured at <10 µg/L," rather than characterizing or describing them as "low". On page 38, lines 4-7, the EAD reviews a study by Wells et al. (2001) that found boiling tap water samples decreased chloropicrin concentrations to below the LOD. However, it should be noted in the report that very few people boil their tap water prior to use.

OEHHA concurs with the analysis and conclusion regarding bioconcentration in "Aquatic Organisms" section (page 38): the potential for chloropicrin to bioconcentrate in aquatic organisms is low.

Persistence in Air Environment

<u>Photolysis</u>

While chloropicrin is reactive with a short half-life in the presence of sunlight, tarping of fields during soil fumigation will probably limit the amount of sunlight reaching the soil. While OEHHA recognizes that field data on phosgene generation are not available, we also recommend a cautious approach in relying on laboratory experiments (e.g., Helas and Wilson, 1992; Carter et al., 1997) examining the rates of photodegradation in flasks or chambers, using incident light levels comparable to ground level measurements, to estimate production of phosgene as a photodegradation product (page 39, line 31-32). The estimated half-lives do not take into consideration tarping of the soil which will limit sunlight penetration and not be comparable to estimations based on full ambient sunlight (page 39-40, line 38, 1-3).

There is a concern for phosgene exposure in ambient air after soil fumigation with chloropicrin. In one laboratory study, phosgene was formed at almost a 1:1 ratio with the amount of chloropicrin added, which ranged from 500-2000 ppb (page 40 line 41-44). Chloropicrin and phosgene are both acute eye and respiratory irritants but their chemical and physical properties are different. As a result, they may have adverse impacts in different regions of the airways and/or lungs. Therefore, the effect of concurrent exposure to these compounds could be more severe than exposure to either chemical alone. OEHHA believes that the issue of phosgene production and concurrent exposure to chloropicrin and phosgene should be evaluated further.

8. Environmental Concentrations

Air

OEHHA recommends citing the actual TAC document with a reference at the beginning of this section (page 42, line 2).

Ambient Air

The EAD states that the concentrations shown in Table 7 (page 42, line 25) may underestimate actual ambient air concentrations for short-term exposures. The use of chloropicrin has increased since 2001, when the most recent studies cited in this table were conducted. Has ambient air monitoring been performed in counties where chloropicrin use is high since 2001?

Application Site Air – Soil Fumigation

OEHHA agrees with the statement that it is unlikely that the measurements from one particular study will capture the highest possible air concentrations for an application method (page 44, line 6-7).

OEHHA also concurs that direct flux estimation is an appropriate method for estimating chloropicrin flux in conjunction with an air dispersion model to estimate off-site concentrations associated with soil fumigation. The report provides a very clear explanation of the ISCST3 model (page 44, lines 20-45).

Off-Site Concentrations

The review of the ARB studies of off-site concentrations (pages 46-48) was clear and informative, and addressed known data limitations. The data from these studies are reported in Tables 8 and 9. OEHHA agrees with the use of both laboratory and field spikes to check on both the analytical procedure and the environmental conditions. The percent recoveries were provided and the results appropriately adjusted.

Field Volatility (flux)

OEHHA agrees with the methodology used in the field volatility studies, which included lab and field spikes, recovery rates, replications and validation for quality assurance, as well as calculation of coefficients of variation (CVs). OEHHA recommends that an explanation be added (page 51 lines 22-27) to further explain how and why flux values for different application methods vary between night and day (Table 10).

OEHHA concurs with the rationale for the selection of the highest concentration (230 $\mu g/m^3$) associated with bedded tarp applications for seasonal and bystander exposures (page 54, lines 17-26).

Application Site Air – Structural Fumigation

OEHHA recommends adding an additional column to include the corrected concentrations after field spike recoveries in Table 13 (35 $\mu g/m^3$, 54 $\mu g/m^3$, and 27 $\mu g/m^3$) (pages 56, line 23; page 57, line 11; page 57, line 23).

In the discussion of the study conducted by Barnekow and Byrne (2006), OEHHA recommends citing Table 15 ("Concentrations Used to Estimate Exposure of Bystanders to Chloropicrin from Structural Fumigation") on page 58 (lines 31 and 40), and page 59 (line 8).

Water

Considering the large increase in use of chloropicrin in California (as shown in Table 3 and Figure 2) and the statement that no ground water sampling has been performed since 1996, OEHHA recommends that further testing of well water samples in California be performed.

9. Exposure Assessment

Bystander Exposure

OEHHA concurs with the use of the 24 hour/day time period as the worst case assumption for residential bystander exposure (page 61). OEHHA also agrees with the use of the highest realistic exposures to bystanders in the exposure assessment.

Soil Fumigation

OEHHA concurs with the values used for the estimated exposure of bystanders to chloropicrin from soil fumigation (Table 16).

Were the data on applications of chloropicrin in Ventura County (Figure 6) used in calculating the seasonal, annual, and lifetime estimates reported in Table 16, or is this graph only being shown to represent the seasonal nature of chloropicrin's use in the county?

Structural Fumigation

While Table 17 partially replicates data that were already presented in Table 15, OEHHA recommends retaining Table 17 because it assists the reader in understanding the discussion in the "Structural Fumigation" section (page 63).

Residential Reentry

OEHHA concurs with the calculations for residential reentry exposure based on indoor air concentrations.

Ambient Air

OEHHA recommends referencing earlier sections in the report that discuss the ambient air monitoring in this section (page 65) for ease of cross-referencing information and understanding the details of the cited studies.

Occupational Exposure: Soil Fumigation

OEHHA recommends that earlier sections of the report that reviewed the studies discussed here should be cited here (page 66 line 3-4) for ease of cross-referencing information and understanding the details of the cited studies.

With limited data, OEHHA concurs that data from short-term studies are the best available for estimating mean daily exposures. However, most of the calculations are based solely on two key studies (Beard et al., 1996; Rotondaro, 2004). This suggests a significant data gap; there is a need for additional studies to be done in this area.

The following 1-hour exposure estimates for occupational handlers were taken from Tables 36 and 37 (pages 86 and 87) and Tables 21 and 23 (pages 70 and 72). They describe two exposure scenarios involving two chloropicrin formulations and two different application methods.

Concentration	Scenario (Application Method)	Handler Population	Exposure (ppb)	Ratio
100%	surface drip irrigation, tarped	tarp punchers	7.79	11.46
10.5%	surface drip irrigation, tarped	tarp punchers	0.68	
100%	broadcast shank, tarped	tarp removers	2310	7.52
10.5%	broadcast shank, tarped	tarp removers	307	

Intuitively, it seems logical to presume that – for any given exposure scenario – the airborne exposure concentration will be proportional to the concentration of chloropicrin in the formulation. However, this does not appear to be the case: for both exposure scenarios, the ratio of the exposure concentrations (11.46 and 7.52) is not equivalent to the ratio of the chloropicrin concentrations in the two formulas (9.52). While the discrepancies are not large, an explanation for the lack of direct proportionality should be provided.

Occupational Exposure: Structural Fumigation

OEHHA recommends that earlier sections of the report reviewing the studies mentioned here should be cited in this section (page 66 line 3-4) for ease of cross-referencing information and understanding the details of the cited studies.

10. Exposure Appraisal

Overall, OEHHA recognizes that there are very little data available for the exposure estimates. In general, OEHHA believes that DPR used the best data available for estimating exposures. However, OEHHA does recommend, wherever possible, updating the use data in the report. In addition, OEHHA recommends that DPR in conjunction with ARB consider further air monitoring studies. The uncertainties and assumptions reviewed in this section, including application rates, likelihood of multiple applications and likelihood of adjacent applications should be taken into account when addressing overall exposure and consequent health risk.

OEHHA is also concerned about chloropicrin's degradation to phosgene and the potential for concurrent exposure to both chemicals. There is a lack of toxicity information on concurrent exposure to chloropicrin and phosgene. Both chemicals cause acute eye and pulmonary toxicity. This represents a serious data gap. OEHHA recommends concurrent monitoring of both chloropicrin and phosgene in all future field studies.

OEHHA is concerned with the systemic effects associated with chloropicrin exposure that may cause additional chronic effects (e.g., degeneration of the nasal epithelium). In addition, OEHHA suggests that consideration be given to potential adverse effects in sensitive sub-populations that may be exposed to chloropicrin. Therefore, OEHHA believes that an additional uncertainty factor is warranted to establish short-term risk-based exposure standards for chloropicrin.

Additional Editorial Comments

1. Summarizing Conclusions

The studies summarized throughout the report are well-reviewed. OEHHA recommends providing conclusions at the end of each section after a group of studies are reviewed, which would be helpful for the reader. The document contains a large amount of data that are reported for a wide variety of parameters. Conclusions at the end of these sections would be helpful in justifying the values that were selected for use in the exposure assessment section.

2. Table 4

Table 4 summarizes the types of illnesses and cases reported in California from 1992-2008. If available, updated information for 2009 to the present should be added.

3. Table 8

Table 8 contains a wealth of information and is accompanied by excellent summaries of the studies in the text. However, it is very difficult to match the studies with the table because the references are footnoted. It would be much easier to compare the summaries of the studies with the values summarized in the table if an additional column were created, and the citations were listed next to each description in the row rather than footnoted. Additional details and notes can remain as footnotes.

4. Use of the Adjective "Low"

OEHHA recommends that the term "relatively low concentrations" mentioned in the introduction be better defined with respect to both its use as a warning agent (page 9) and its ability to cause eye irritation (page 10). Perhaps a specific range of concentrations would be less vague.

The introduction states that chloropicrin has the potential to cause adverse health effects at low doses (page 10). OEHHA suggests that the term "low" not be used here. OEHHA suggests that a range of doses be provided at which adverse health effects were observed. Does the Cain (2004) study provide a scientifically valid basis for assessing whether a given exposure concentration is indeed "low" or is in fact sufficient to cause eye and airway irritation in humans?