

November 3, 2007



Re: FCA Risk Assessments and Toxicological Approaches

Mr. John Leahy, Senior Advisor  
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Office of Pesticide Programs  
Environmental Protection Agency  
1200 Pennsylvania Av NW  
Washington, DC 20460-0001

Dear Mr. Leahy,

We, the undersigned, are writing to provide comments on the following fumigant cluster assessment (FCA) dockets:

Telone: Docket # [EPA-HQ-OPP-2005-0124](#)

Metam sodium and potassium: Docket # [EPA-HQ-OPP-2005-0125](#)

Chloropicrin: Docket # [EPA-HQ-OPP-2007-0350](#)

Methyl bromide: Docket # [EPA-HQ-OPP-2005-0123](#)

Dazomet: Docket # [EPA-HQ-OPP-2005-0128](#)

This letter is focused on the risk assessments and toxicological approaches U.S. EPA is using to evaluate fumigant risks. Additional points on mitigations and worker protections are in separate letters, which we include here by reference: 1) the letter submitted to the same dockets from PANNA and other signatories with regard to mitigation measures, and 2) the letter submitted to the same dockets from CRLAF and other signatories with regard to worker protection issues. We also include by reference our original comment letter on the Phase 3 fumigant assessments, Docket ID # EPA-HQ-OPP-2005-0123-0113.

A close look at the fumigant risk assessments indicates that EPA has distorted the data in every way possible to make it appear that there is less risk than there actually is. In every fumigant risk assessment, EPA made most of the following decisions that lead to fewer protections for bystanders and workers. A few specific points only apply to a single fumigant.

- EPA only considered acute exposures, even though the Agency's own work indicates exceedance of subchronic and some chronic levels of concern.
- EPA continues to accept (and even require) inhalation toxicity tests that are unrepresentative of actual conditions humans will experience.
- Using questionable justifications, EPA selected less protective toxicological endpoints for the HECs when a more protective endpoint was available and more appropriate.
- EPA used unrepresentative year-round weather data to model exposure, when (at least in California) fumigations occur more frequently in certain times of the year more prone to inversions and calms.
- EPA failed to check its exposure model against field data.
- EPA created an exposure period of 24 hours, over which exposures are averaged. This approach does not account for short-term spikes in concentrations that are likely to be very harmful.

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- With no scientific justification and in the face of evidence demonstrating particular problems for children’s exposure, EPA did not incorporate any additional uncertainty factors to protect children or other vulnerable populations, basing its risk considerations on a healthy adult.
- Using questionable justifications, EPA extrapolated a 30-55 minute exposure test period (chloropicrin human study) to a 24-hour period.
- In an unprecedented move and in the face of evidence demonstrating wide variability among human study subjects, EPA removed the intraspecies uncertainty factor for chloropicrin.
- EPA used unrepresentative use data for 1,3-D to estimate cancer risks. The data used were from a time period and a location in California where 1,3-D had severe restrictions placed on its use.
- EPA has restricted its reporting of fumigant poisoning incidents to those incidents that involved only a single fumigant. Since most fumigants are increasingly being used as mixtures, this approach will vastly underreport fumigant poisonings and skew trends.
- In the face of much evidence to the contrary from worker poisoning reports, EPA assumes that dermal and ocular exposure to fumigants can be dismissed as unimportant because they are too “difficult” to measure.
- In the face of much evidence to the contrary from poisoning incidents that *continue to occur*, EPA assumes that no mistakes will be made in the application of fumigants—the most complex and difficult pesticide application processes currently in use—and that the weather will always cooperate.

In addition to adopting these systematic biases against protecting public health, EPA has obscured data, failed to summarize critical studies, and refused to respond to requests for additional information that would clarify the bases for Agency decision-making. “Because we said so” is not a valid scientific explanation for any decision, and the Agency needs to eliminate this mindset if it expects to be taken seriously for its science-based work.

The net effect of this unscientific generation, use and interpretation of data is to make it appear that fumigants can be used without “unreasonable adverse effects.” This is simply false. Unless EPA substantially changes its approach, entire communities and workers will continue to be acutely poisoned, cancer rates in areas of high fumigant use will remain elevated, chronic neurological injuries to workers will continue to be commonplace, and fetal deaths and birth defects will continue to occur from exposures to these highly toxic chemicals.

We are convinced that if EPA decides to allow continued use of fumigants without requiring what growers would characterize as “unworkable” buffer zones, these registrations will substantially violate FIFRA’s requirement of “no unreasonable adverse effects”.

We detail these concerns below. Sections 1–3 apply to all fumigants and sections 4-7 are focused on specific fumigants. Thank you for the opportunity to comment on this risk assessment.

Sincerely yours,



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# **1 Risk Assessment Methodology, General**

## ***1.1 Toxicology Assessment***

We are pleased that the Agency added some clarifications to the risk assessments, but still find them inadequate to fully assess what the registrants have done and what the agency has done. Many endpoints selected are still not adequately protective of public health. Please see our previous letter (Docket ID# EPA-HQ-OPP-2005-0123-0113) for suggestions that would improve the clarity and comprehensiveness of the Agency's risk assessments.

## ***1.2 Derivation of Human Equivalent Concentrations***

The HEC Arrays are useful and the descriptions of how they were obtained are clearer than before, although the references are still not present. Unfortunately, the five-days-per-week, six-hours-per-day exposure to a relatively constant concentration experienced by animals in laboratory studies and the 24-hours-per-day, 7-days-per-week uneven concentrations experienced by humans living next to a fumigated field in an area of high fumigation activity is just not comparable. Additional uncertainty factors are needed to better protect humans from more continuous exposure and spikes in concentration. The concentration spikes typically observed during fumigations may be toxicologically significant, but instead of evaluating the potential harm, the Agency has averaged the exposure over 24 hours to smooth out the risk profile. While this may make for cleaner calculations, it is unrealistic, and control measures based on these averages will not protect people from the harm that spikes in concentration can cause.

## ***1.3 Uncertainty Factors***

It seems that the Agency is moving in the direction of fewer and lower uncertainty factors, rather than a more protective approach. We note with concern that:

- No uncertainty factors are included for children or other sensitive populations, although there is evidence for enhanced susceptibility to toxic effects in children as well as in individuals with preexisting respiratory conditions for these fumigants.
- No uncertainty factors are included to account for human error.
- No uncertainty factors are included to account for exposures to multiple fumigants simultaneously, even though most applications are now mixtures of highly toxic chemicals.
- Uncertainty factors are not used consistently to compensate for data gaps.
- Some uncertainty factors were inappropriately eliminated, with no scientific justification.

This approach will not protect public health.

## ***1.4 Dermal Exposure Risk Assessment***

EPA's response to our concerns about dermal and ocular worker exposures is below:

“The high vapor pressure . . . [of fumigants] . . . makes it extremely difficult to reliably quantify dermal and ocular exposure. Additionally, however, the use of mitigation controls such as PPE and closed transfer systems minimizes the potential but does not completely eliminate it. The incidents cited are a result of equipment malfunction or improper use of PPE.” (from 1,3-D Response to Comments, EPA-HQ-OPP-2005-0124-0051)

Let's understand this . . . because it is “difficult,” EPA is not going to deal with this problem? Because exposure is caused by faulty equipment or improper use of PPE, EPA absolves itself from all responsibility? Does this mean that all applicators are assumed to have perfect equipment

and perfect use of PPE? The poisoning incident records tell a different story. The fumigant risk assessments are incomplete without assessment of dermal and ocular exposure

### **1.5 Developmental Toxicity**

We remain concerned that dosing in developmental studies occurs only on days 6-18 of gestation, which does not provide information on adverse effects that may occur in the human equivalent of the first trimester, the time period of greatest sensitivity for fetal development. In response to this concern, EPA noted that:

“ . . . given that the current prenatal developmental toxicity studies are designed to encompass gestation from the time of implantation, the Agency concludes that the first trimester of human pregnancy is adequately assessed in our current testing protocol.”

Implantation is an artificial marker of time. The fact remains that many critical fetal developmental processes are occurring before implantation that might be altered by exposure to a toxic agent. The current procedure for conducting this type of test provides an incomplete picture of developmental toxicity and should be modified to encompass any time after fertilization.

### **1.6 Aggregate Risks**

An aggregate exposure and risk assessment is still missing from the fumigant documents and should be part of a finalized risk assessment.

### **1.7 Cumulative Risk**

We again strongly urge U.S. EPA to broaden their definition of “cumulative risk” to include exposures to all chemicals, not just chemicals with common mechanisms of action. The fact that these pesticides are marketed to be used as mixtures means that people will be exposed to mixtures of chemicals. The effects of mixtures will not be the same as the effects of a single chemical, and the Agency needs to be taking these exposures into account when conducting risk assessments.

## **2 Bystander Exposure Assessment**

### **2.1 Air Model**

EPA has significantly enhanced the PERFUM model description and implications of its use, thus making this section one of the most clearly written in the fumigant documents. We appreciate this attention to detail and clarity.

#### **2.1.1 Recent Major Poisonings**

Several new poisoning events have highlighted the problems posed by calms and inversion conditions and the need for large buffer zones to protect people living and working near fumigations.

- On September 26<sup>th</sup>, 2007 in Yerington, NV, over 120 workers laboring in a field approximately 1/3 of a mile from the fumigation site were taken to a medical center for treatment for symptoms of acute poisoning from chloropicrin exposure.
- On October 23<sup>rd</sup>, 2007, dozens of households in a Salinas, CA neighborhood adjacent to a fumigation site were exposed in a drift incident involving methyl bromide and chloropicrin.

EPA must require buffer zones that are large enough to ensure that people are not driven from their homes and their workplaces because of fumigant drift.

### **2.1.2 Relative Frequency of Low Wind Conditions**

Because of the continued occurrence of poisoning incidents, we remain unconvinced that even 1,000-foot buffer zones will be protective against “unreasonable adverse effects,” much less the even smaller buffer zones the Agency appears to be favoring. As mentioned in our comment letter from Phase 3, we evaluated annual California weather data and found that low wind speeds occur frequently, during at least 10% of the hours annually, and up to 30% of the hours depending on the cutoff defining low wind speeds and the weather stations used for the estimates (see Docket ID # EPA-HQ-OPP-2005-0123-0113).

In the fumigant risk assessments, EPA notes the following:

“For this assessment, a process has been used where calm conditions (e.g., hours with calm wind conditions) are dropped from calculations and a time-weighted average result is calculated without those values. This approach is consistent with how ISCST3 has been historically used. For chemicals such as methyl bromide the impact on the calculated exposures due to handling calms in this manner is attenuated because 24 hour time-weighted averages are the basis for the results. However, for chemicals where risk estimates are based on shorter duration toxicity endpoints (e.g., 1 hour), this phenomena can significantly impact the results if the weather data used in the assessment include a high percentage of calm periods.” (page 29, MeBr Human Health Risk Assessment)

In simpler terms, the above statement says that the empirical treatment of calms may reduce the “spikiness” of predicted concentrations. 24-hour averages will not be badly affected. The frequency of occurrence of high, short-duration concentrations will be significantly less in the model than in the real world, if the weather has a high percentage of calm periods.

The above statement is consistent with the two serious, short duration incidents, one involving chloropicrin and one involving a mixture of methyl bromide and chloropicrin, that have occurred in the last several weeks, one near Yerington, NV<sup>1</sup> and one in Salinas, CA.<sup>2</sup> In both incidents, no violation of the label occurred. In both incidents, inversion conditions (inaccurately characterized as rare in the Nevada reporting), were listed as a key reason for the incident.

Because the PERFUM model averages a zero concentration in for hours where winds are calm, and because (at least in California) many of the fumigations take place during seasons where calm winds are more frequent than other times of the year, the model is not providing a representative concentration for the conditions most likely to result in mass poisonings. This is a serious failing of the model that suggests that either the model needs to be modified (perhaps the concentration from the previous hour could be substituted instead of a zero?), or larger buffer zones should be required.

While labels should certainly prohibit applications during inversion conditions, this prohibition will not be sufficient (nor do we think it would be enforced), since fumigant drift is problematic for several days at least after the application and it is difficult to predict with any certainty what the weather will be several days hence. Calms can even be difficult to predict the same day.

## **2.2 Other Exposure Modeling Considerations**

### **2.2.1 Model Calibration, Flux Estimates**

Accurate flux rates are essential inputs if accurate results are to be obtained from modeling. Yet the model does not account for changes in soil temperature, a major factor influencing the rate of off-gassing of fumigants from soils. The flux rates used in the model are based on studies that may not be representative of worst-case conditions, and in many cases are certainly not representative. We highlighted these problems in a presentation to U.S. EPA at the California hearing on May 31, 2007. Please see EPA-HQ-OPP-2005-0123-0393 in the methyl bromide docket for the presentation to EPA on this issue.

### **2.2.2 Use of Maximum vs. Whole Field Method**

The Agency continues to calculate “whole field” buffer zones and even developed mitigation measures for methyl iodide based on the “whole field” calculation, even though this approach might only, in theory, protect the theoretical person who spends the entire day moving from place to place around the field. This approach will not protect the stay-at-home mother and her small children or an elderly home-bound person or an entire school full of children in an area with a prevailing wind pattern that results in fumigant drift in their direction, and should be discarded. All buffer zones should be set based on the “maximum” calculation, recognizing even then that the model already misrepresents the peak exposures that may be the most problematic by averaging the concentrations over 24 hours.

### **2.2.3 Consideration of Exposure from Multiple Field Fumigations in the Same Geographic Area and Time Period**

If EPA decides to regulate based only on acute exposures by reducing application block size, the result will be more continuous exposure and a longer fumigation season. If this approach is to be part of the control strategy, we strongly recommend that the Agency reconsider the potential for problematic subchronic exposure in its risk assessment.

## **3 US EPA Must Seriously Consider Existing Viable Alternatives**

The introduction of substantial buffer zones would present an excellent opportunity for EPA to encourage non-fumigant alternatives for soil pest control. Contrary to the economic arguments being presented to EPA by growers, buffer zones do not need to be “no planting” zones. In fact, this is an opportunity for growers to test out existing non-fumigant alternatives and reduce their reliance on these toxic chemicals. Economic scenarios presented to EPA that include only a complete “loss” of crop in buffer zones are both unrealistic and unnecessary, when other viable alternatives are available.

## **4 Methyl Bromide Toxicology**

### **4.1 Subchronic and Chronic Toxicity**

We remain convinced that EPA's use of the Schafer dog study for development of the subchronic HEC for MeBr and the rat study for chronic HEC are inappropriate and unlikely to be protective of public health. Please see our previous letter (Docket ID# EPA-HQ-OPP-2005-0123-0113) for details.

### **4.2 Toxicology Data Gaps**

U.S. EPA did finally receive a developmental neurotoxicity test from the registrants. Unfortunately, no details are provided in the risk assessment. In the cover letter to the Human Health Risk Assessment, EPA used the existence of the DNT test to reduce the UF for acute bystander exposures from 300 to 30. Yet, in the revised Human Health Risk Assessment document, there is only a tangential reference to the study, where EPA attempts to justify not using the study as a critical endpoint (page 15):

Acute and developmental neurotoxicity studies in rats were available for consideration, however, the developmental toxicity study in rabbits was selected since it yields the lowest HEC (most health-protective) presumed to occur after an acute exposure. Although the DNT would yield a lower HEC for the effect of decreased motor activity, this effect was not considered to be related to a single MeBr exposure since it was observed on PND21 and not at earlier time points (*i.e.*, no compound-related effects changes in motor activity on PND 13, 17).

This rationale makes no sense. Although the animals were likely dosed for more than a day in the DNT study, (there is no detailed description of the study, so it is impossible to know), a single exposure at a critical time during gestation could still be the cause of the effect observed at PND21. Please explain how the Agency justifies this decision in light of the many examples that show developmental harm from a dose received during a critical period of development.

No additional information is provided about the DNT test—no dose range or description of the length of the study, number of animals, NOAEL, observed effects, or study summary. Was it a guideline study? If this DNT study followed EPA's guidelines, the experiment would have been conducted over the gestation period from GD6 to PND 10, yet the study was not mentioned in the assessment of the sub-chronic or chronic toxicity of the chemical.

EPA needs to make this study public and discuss its implications in the overall assessment of methyl bromide toxicity. If nothing else, the fact that DNT effects were observed indicates that additional safety factors are essential to protect the developing fetus. An action that results in a reduction in the level of protection by a factor of 10 needs to be accompanied by transparency in the presentation and evaluation of the data.

## **5 1,3-Dichloropropene Toxicology**

It is worth noting that the EU has decided to not allow reregistration of 1,3-D, requiring Member States to withdraw approvals for the pesticide effective March 2008 and allow no further use of existing stocks past March of 2009.

## **5.1 Acute and Short-Term Toxicity**

We are still concerned that the acute and short-term NOAELs selected by EPA are too high and that EPA is re-defining what “acute” means, without adequate peer review. The details about the dominant lethal assay for inhalation in rat are still missing from the report.

## **5.2 Carcinogenicity**

EPA is still underestimating the cancer risks from use of 1,3-dichloropropene, because the data from which exposure was estimated was collected when California’s township caps and other use restrictions for 1,3-D were in effect. Under these conditions, EPA’s exposure estimates are not accurate for other states where there are no such restrictions, nor will they be accurate if township caps are lifted in California and use continues to increase. In response to this concern, EPA indicates they “used the best available data.” However, additional information is available to modify the assessment to provide a more accurate picture of exposure. EPA failed to use this information. Thus, EPA’s conclusion that their assessment is representative of high-end exposure is not correct. The upper end cancer risks are likely to be higher than predicted by EPA, and the number of people exposed to levels above the unit risk are higher than estimated by EPA.

The appearance of increased rates of pancreatic cancer in human populations living in areas of high 1,3-D use for 20 years should not be dismissed by EPA.

# **6 Metam Sodium and Dazomet Toxicology**

## **6.1 Choice of NOAELs**

We remain concerned that EPA has consistently and systematically selected less-protective NOAELs for MITC and note again that the NOAEL for eye irritation is not a health protective endpoint. A reference level of 22 ppb for exposures of one hour or longer which incorporates a 10x uncertainty factor to protect children and other sensitive people was adopted by California DPR in 2002 when MITC was declared a Toxic Air Contaminant in California. At that time, the TAC Scientific Advisory Panel pointed out that since the human dosing study used to establish this involved only exposure to the eyes, it could only be used to very roughly estimate a no-effects level for respiratory effects.

The revised MITC Human Health Risk Assessment fails to discuss the uncertainty in extrapolating from eye irritation testing results in healthy adults to expected effects in children and other populations. The discussion begins by stating that the HSRB concluded that air concentrations of methyl isothiocyanate sufficient to produce eye irritation would lead to a conservative point of departure for inhalation risk, based on observation that eye irritation LOAELs are often lower than respiratory irritation LOAELs. Later in the document, it is acknowledged (pg 8) that due to limitations of the inhalation toxicology database the degree to which eye irritation predicts more serious outcomes is unclear but can be considered an appropriate biomarker and surrogate for potential respiratory effects. Still later (Pg 20) a full quote reveals that the HSRB urged caution in using this eye irritation data as a surrogate for respiratory irritation data.

## **6.2 Uncertainty in Acute Toxicity**

PERFUM modeling runs to calculate buffer zones were performed using both 1x and 10x uncertainty factors with the NOAEL for the eye irritation study. This implies that the Agency is considering setting buffer zones which only protect to the NOAEL for the human eye irritation

study. This approach will not be health protective because the study was conducted using healthy adults with no history of eye or respiratory problems. A more sensitive endpoint can be expected in children and other sensitive populations such as asthmatics. In addition, an uncertainty factor is appropriate when extrapolating from eye irritation to respiratory effects.

### **6.3 Averaging Times for MITC PERFUM Modeling**

The PERFUM modeling in the revised MITC Risk Assessment update is based on 8-hour averaging time in contrast to 4 hour averaging time used in previous metam assessments. The Agency states that they have made this change because the NOAEL for the eye irritation study was for up to 8 hours and also to be consistent with the 8-hour averaging time used by California DPR. However, as elaborated on pg 9 of the Human Health Risk Assessment, the NOAEL is relevant for exposures from 1 hour to 8 hours. It would therefore be more appropriate and health protective for the Agency to reduce the averaging time to one hour in modeling since effects above the NOAEL can occur after as little as one hour of exposure.

### **6.4 Failure to Consider Cumulative Exposure to Metam Degradation Products**

We still feel the Agency is giving insufficient attention to the presence of the mixture of toxic compounds that results from a metam application, including MITC, MIC, hydrogen sulfide and carbon disulfide. These multiple breakdown products cause the same toxicological endpoints of eye and respiratory irritation and should be considered whether or not the breakdown products have similar mechanisms of toxicity. The revised RED points out on Pg 17 that the pharmacokinetic study of MITC is incomplete but it is known that MITC is converted into carbon disulfide, carbon oxide sulfide and carbon dioxide in the body, with highest uptake in thyroid, lungs, liver and kidney and primary excretion through urine, some through lungs. The fact that carbon disulfide is both a metabolite of MITC and a breakdown product of metam sodium could have toxicological implications and should be addressed in the risk assessment.

### **6.5 MITC and Dazomet Data Gaps**

We remain concerned about the extensive data gaps on MITC toxicology. EPA's response is to indicate they will ask the industry to provide more data *after* the RED process. This is puzzling indeed. The re-registration period is the time for the Agency to request data from registrants. And for public and worker health protection, it is too late to ask for data after the RED is completed. In the meantime, larger uncertainty factors should be used to develop mitigations until the data gaps can be filled.

### **6.6 Updated Incident Summary Does Not Accurately Characterize Metam Sodium or Other Fumigant Illness Reports**

The April 15, 2007 update of Review of Fumigant Group Incident Reports (EPA-HQ-OPP-2005-0125-0074) is confusing and misleading. It appears that EPA is only counting poisoning incidents involving a single fumigant; on page 3 of the review, EPA notes "Cases involving exposure to multiple products . . . are excluded." Since fumigants are increasingly being used as mixtures, this criterion should be discarded to obtain a more accurate picture of fumigant poisonings.

The review also concludes that there is not much exposure of children to metam sodium because there aren't many pediatric metam sodium poisonings in the Poison Control Centers database.

This is not a valid conclusion because poison control data includes few drift incident cases compared to California incident data. Many middle class parents know contact Poison Control if their child ingests a poison but not during a pesticide drift incident. Many immigrants who are not fluent in English have never heard of poison control centers. In contrast, the discussion of California fumigant poisoning data does not mention age of poisoning victims. However, a published account of the Arvin 2002 incident (O'Malley 2005) referenced in the Summary of Fumigant Group Incident Reports EPA-HQ-OPP-2005-012500075 reports that 83 of the residents exposed in this incident were under 20 years of age. A high percentage of the residents affected by MITC in Earlimart in 1999 and by chloropicrin in Lamont in 2003 were also children.

The conclusion in the revised MITC RED (Pg. 31) and fumigant incident report update of April 15, 2007 that effects of MITC drift are usually minor to moderate is simply wrong and is contradicted by published peer review studies. According to a peer-reviewed analysis of the July 2002 Arvin MITC drift incident (O'Malley 2005), directly following the incident, a woman with pre-existing pulmonary disease was hospitalized for a week with respiratory distress and symptoms potentially representing asthma or lower respiratory irritation were reported by 33 victims representing 18.5% of the area residents reporting symptoms directly after the incident. In addition, 20% of the residents exposed during the Earlimart MITC drift incident in November of 1999 reported lower respiratory symptoms (O'Malley 2004).

On page 32, the RED concludes that there was a downward trend in occupational incidents for metam sodium, chloropicrin and methyl bromide "over time" from 2002 -2004 in contrasted with 101 Telone incidents in 2004. Three years is not a long enough period to establish a trend. More to the point, any possible trend has not been maintained. In August of 2005, drift from a 75-acre metam sodium application in Kern County, California affected at least 42 workers in an adjacent vineyard. One of these workers went on to develop a serious form of pneumonia (CDPR 2005 PISP). In August of 2007, drift from a chloropicrin fumigation in Nevada affected over 120 workers over 1/3 mile from the application. Twelve of these workers were treated at the hospital.

In addition, in 2005 there were 303 definite or probable non-occupational illnesses reported in California associated with chloropicrin exposure from drift into a single neighborhood. Half were systemic and half affecting only the eyes and/or skin (2005 PISP). Just this past week (October 2007) a neighborhood in Salinas on California's central coast was affected by drift from an application of 63% methyl bromide and 37% chloropicrin.

# 7 Chloropicrin Toxicology

## 7.1 Removal of the intraspecies uncertainty factor is inappropriate

U.S. EPA inappropriately removed the intraspecies uncertainty factor in the revised risk assessment with the following rationale.

The Phase 5 chloropicrin risk assessment has one key update which is the reduction of the 10X intraspecies factor to 1X for the acute inhalation assessment. This reduction is based on the following:

- First, the human eye irritation study involved young adult subjects (average 23 years) that are considered to be the most sensitive subpopulation to sensory irritants (e.g., can detect chloropicrin at lower concentrations). Transient eye irritation is the most sensitive endpoint determined for the sensitive subpopulation used in the human study. Therefore, the human study suggests that protecting for transient eye irritation would also protect against adverse irritation of the eyes, nose, and the upper respiratory tract.
- Second, the incident reports for chloropicrin do not suggest that individuals with asthma are more sensitive to chloropicrin. In addition, these incident reports suggest that children are as responsive to chloropicrin as adults.
- Lastly, chloropicrin at low concentrations may serve to act as a “warning” to the exposure of other fumigants that may not otherwise be detected. Therefore, regulating chloropicrin below a level that can be detected by any population subgroup increases the risk of exposure to chloropicrin and those fumigants that are used in combination with chloropicrin.

There is no scientific justification for this action, and much scientific justification for adding additional uncertainty factors to fully protect public health. U.S. EPA is putting the public at great risk with this decision. We examine the flaws in EPA’s position below.

### 7.1.1 Variability Among Healthy Human Test Subjects is High

In Appendix A, Table 1A, p. 78 of the revised Human Health Risk Assessment (relevant part reproduced below) for chloropicrin, HED’s analysis indicates that eye irritation thresholds varied by a factor of 42 between the 10<sup>th</sup> percentile (most sensitive) and 90<sup>th</sup> percentile (most sensitive) subjects for eye irritation determined from the Phase I study. While not reported, the variation in sensitivity of the most sensitive one percent of subjects compared to the least sensitive one percent must have been greater still, and this in a group of only 62 *healthy, adult* subjects. Variability among the general human population will be higher.

| Effect         | Threshold conc. 10 <sup>th</sup> percentile (most sensitive subjects) | Threshold conc. 90 <sup>th</sup> percentile (least sensitive subjects) | Threshold conc. median (average subject) | Factor by which 10 <sup>th</sup> percentile differs from 90 <sup>th</sup> percentile |
|----------------|---|--|--|--|
| Eye irritation | 37 ppb  | 1,565 ppb  | 242 ppb                                  | 42   |
| Odor           | 216 ppb   | 764 ppb  | 406 ppb                                  | 1.9  |

Interestingly, the Agency selected 73 ppb as the Level of Concern, based on eye irritation from the Phase III study. This value corresponds approximately to the *median* ocular detection level of 75 ppb (Phase II study, N = 42). Thirty-eight percent of subjects initially and consistently identified eye irritation caused by chloropicrin at 50 ppb, the lowest dose tested.

| Appendix A/Table 1A: Chloropicrin Toxicity Profile                |  |  |
|---|--|--|
| Guideline No./Study Type  | MRID No. (year)/Classification/Exposure Conditions   | Results  |
| Special Human Study: Odor Threshold, Nose, Eye, Throat Irritation | 46443801 (2004)<br>Acceptable/Non-Guideline<br>3 Phases<br><b>Phase 1:</b> 62 subjects (356, 533, 800, and 1200 ppb) for 1-2 seconds from a vapor delivery device<br><b>Phase 2:</b> 62 subjects (0, 50, 75, 100, 150 ppb) for 30 minutes in a walk-in chamber<br><b>Phase 3:</b> 32 subjects (100, 150 ppb) for 60 mins/day for 4 consecutive days in a walk-in chamber | <b>Phase I:</b><br>Registrant Analysis:<br>median odor threshold: 700 ppb; (M=590 ppb and F=810 ppb)<br>median eye irritation: 900 ppb; (M=790 ppb and F=1010 ppb)<br>No localization of the throat; >1200ppb<br>HED Analysis:<br>Odor: 10 <sup>th</sup> percentile 216 ppb; median 406 ppb; 90 <sup>th</sup> 764 ppb<br>Eye: 10 <sup>th</sup> percentile 37 ppb; median 242 ppb; 90 <sup>th</sup> 1565 ppb<br><br><b>Phase 2:</b> 38% of subjects (8M/8F) detected chloropicrin initially at 50 ppb and consistently up to 150 ppb. Severity of eye irritation not examined. NOAEL not determined. Nose and throat irritation not as sensitive as in eyes.<br><br><b>Phase 3:</b> NOAEL not established. However, BMCL <sub>10</sub> of 73 ppb, based on eye irritation scores of 1.5 during the maximal response period of 30-55 minutes. Nasal nitric oxide increased and changes in air flow both at 100 ppb and 150 ppb. Nose and throat irritation less sensitive endpoints. |

In the Data Evaluation Report (DER) on the human study, EPA summarizes the 3-phase human study as follows:

In summary, the concentrations and durations explored in each of the three Phases of this study failed to identify a level at which none of the subjects responded to either irritation or odor of chloropicrin. Likewise, the concentrations and durations were not sufficient to produce a response in all of the subjects during any phase of the study. Therefore, this study does not provide a concentration or duration where none of the healthy individuals were responsive or all healthy individuals detected chloropicrin. This study provides information as to the variability of the responses of healthy individuals to a ‘sniff’ scenario versus the variability of responses over time and concentration and with repeated exposure to chloropicrin.

And

“ . . . variability of the subject’s responses to chloropicrin was large.”

There are no data indicating that removal of the intraspecies uncertainty factor will be protective. In fact, all data point to the need to maintain the intraspecies uncertainty factor.

### **7.1.2 Members of the Human Subjects Review Board Question the Capacity of the Study to Determine a Dose That Adequately Protects Bystanders**

The U.S. EPA Human Subjects Review Board (HSRB) reviewed the chloropicrin study and pointed out a number of scientific weaknesses that indicate flaws in the study that could contribute to lessened protection for bystanders.<sup>3</sup> The most problematic were:

1. In Phase III, no lower doses were tested—in spite of the low-dose responses in Phase II—and no NOAEL could be determined. Additionally, there was no correspondence between the doses used in Phase II and Phase III.
2. The concentrations and durations explored in each of the three Phases of this study failed to identify a level at which none of the subjects responded to either irritation or odor of chloropicrin.
3. Lack of confidence intervals for the data.
4. The study did not include the most-sensitive individuals who are part of the potential bystander population. Only subjects who reported, *inter alia*, 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. An examination of the nose, throat, and eyes was performed for each participant with any irritation, abnormalities, or abnormal redness scored on 0-3, with a score greater than 1 grounds for exclusion of the study. The examination also included measurement of nasal resistance (Rhino; MultiSpiro or HR-Rhinomanometry) and pulmonary function (MultiSPIRO SX-SILVER). Cells were also taken from the surface of the inferior turbinate of one nasal cavity via a Rhinoprobe scraping.

With these problems identified by the HSRB, especially the fact that only healthy adults with no pre-existing respiratory irritation were part of the study, EPA's conclusion that the intraspecies uncertainty factor is unnecessary is further called into question.

### **7.1.3 Rationalization that Children Don't Need Additional Protection Is False**

One of EPA's justifications for removing the intraspecies uncertainty factor is that "incident reports suggest that children are as responsive to chloropicrin as adults." This is not true.

The analysis in the chloropicrin incident reports (pp. 4-5)<sup>4</sup> states instead that:

"II. Poison Control Center Data - 1993 through 2001

Results for the years 1993 through 2001 are presented below for occupational and non-occupational reports involving adults and older children. *There were insufficient numbers for children under age six to warrant a detailed analysis.* Cases involving exposures to multiple products or unrelated outcome are excluded."

This statement indicates that there are not enough data to determine if children are more sensitive than adults. In the absence of data, and with the knowledge that developing lungs are typically especially sensitive to respiratory insults, EPA needs to extend additional protections to children, not rationalize away the need for them.

## **7.2 Buffer zones Are Definitively Inadequate**

Recent poisoning incidents indicate that chloropicrin can poison people quite far from the treated field, at much greater distances than the 24-hour, “whole-field” buffer zones calculated using an MOE of 1 and an HC determined from a 1-hour exposure study and an exposure model that does not account for calms. There will continue to be mass poisonings unless these errors in the methodology are corrected.

### **7.2.1 An MOE of One Is Not Sufficiently Protective**

See section 7.1 above.

### **7.2.2 A One-Hour Test Exposure Period Does Not Accurately Model Effects for Exposures over a 24-Hour Period**

The Agency has no scientific basis to justify using a 1-hour acute HC to determine buffer zones that are stated to be protective for a 24-hour period.

The HC of 73 ppb on which the buffer zone calculations were based was determined from a human study in which subjects were exposed for 30–55 minutes. EPA concludes that:<sup>5</sup>

The Agency has selected the human sensory irritation study and BMCL10 of 73 ppb for deriving a PoD for assessing 1-hour acute risk to chloropicrin.

It is interesting to note that some study participants walked out of the chamber after 15 minutes in the Phase II and III tests. No explanations were given. Also worthy of note is that the California Office of Environmental Health Hazard Assessment (OEHHA) has set a 1-hour Reference Exposure Level (REL) of 4.3 ppb, a factor of 17 less than the Agency’s choice.

What is the Agency’s scientific basis for using a 1-hour REL for a 24-hour time period?

### **7.2.3 Poisoning Incidents Demonstrate that Buffer Zones Calculated Using PERFUM Will Be Inadequate**

A number of acute chloropicrin poisonings have occurred in locations very far removed from the fumigation site. A sampling of distances at which effects were noted are given below:

- Reference 4, p. 9: More than one mile away, 5-8% of the 190 adults interviewed reported possible symptoms.
- Reference 4, p. 9: Residents that lived about one-quarter mile from the land reported irritant symptoms that evening. . . . A retrospective air dispersion model estimated exposures of 0.20 ppm with peak concentrations estimated above 1 ppm. As a result of this incident, the County Agricultural Commissioner prohibited applications within one-quarter mile of occupied structures and mandatory use of a heavy-duty tarp or water seal for applications within one-half mile of such structures.
- Reference 2: Poisonings of >120 workers in a field ~1/3 mile from the fumigated field.

## Endnotes

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<sup>1</sup> Daily Californian Article on the October 23rd drift incident in Salinas, CA:

<http://www.thecalifornian.com/apps/pbcs.dll/article?AID=/20071025/NEWS01/710250310/1002>

<sup>2</sup> Reno Gazette-Journal Article on the September 26th drift incident near Yerington, NV:

<http://news.rgj.com/apps/pbcs.dll/article?AID=2007709280333>

<sup>3</sup> 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.

<sup>4</sup> August 24, 2004 Memo from J. Blondell and M. Hawkins to Charles Smith, *Review of Chloropicrin Incident Reports*, DP Barcode D306838, Chemical#081501, U.S. EPA.

<sup>5</sup> June 7, 2006 Memo from E. Reaves to T. Levine, *Human Studies Review Board: Weight of Evidence Discussion for Trichloronitromethane (Chloropicrin)*, DP Barcode D314364, TXR No.: 0054218, U.S. EPA.