Appendix P. Fumigant Screening Levels

Office of Environmental Health Hazard Assessment

MEMORANDUM

TO: Jay Schreider, Ph.D., Chief Toxicologist
Medical Toxicology Branch

FROM: Anna M. Fan, Ph.D., Chief
Pesticide and Environmental Toxicology Section

DATE: November 24, 1999

SUBJECT: Comments on the Screening Levels for Fumigants Used in Lompoc Prepared by Department of Pesticide Regulation

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We have reviewed the October 15, 1999 memorandum, which includes screening levels for fumigants proposed by the Department of Pesticide Regulation (DPR). In this memorandum, it is emphasized that the screening levels are not health standards, but rather the first tier in an analysis to provide a context in which to view measured air levels of the fumigants to be monitored in Lompoc, California. We appreciate the opportunity to work with DPR and other members of the Technical Advisory Group (TAG) in developing these screening levels. Our comments are provided below.

1. The tiered approach proposed in the screening level memorandum is confusing. We propose that one value for each of the potential exposure scenarios, acute (24-hour), subchronic, and chronic, be used. The numbers we propose are provided in Table 1. While we agree that chronic exposures are probably not relevant to the fumigant applications in Lompoc, we are including the chronic screening levels in the table to be complete. We recommend that any air monitoring values above the screening level should undergo further evaluation, and measures be taken to mitigate unacceptable exposures. We further recommend that any values that fall below the screening level would generally not undergo further evaluation, but they should not automatically be considered "safe" levels. DPR, in consultation with the TAG, may choose to evaluate further any environmental levels that are below these screening levels.

2. The acute screening levels proposed by DPR for the most part do not have an exposure time associated with them. We recommend that the exposure time (e.g., 1, 4, 8, 24 hours) be included for each screening level.

Table 1. Screening Levels Proposed by the Office of Environmental Health Hazard Assessment

Chemical	Exposure Scenario	Proposed Screening Level ($\mu g/m^3$)	Comparison to DPR Screening Levels
Methyl bromide	Acute (24-hour)	82 (21 ppb)	10-fold lower
	Subchronic	270	same
	Chronic	3.9	same
Methylisothiocyanate	Acute (24-hour)	6.6 (2.2 ppb)	10-fold lower
	Subchronic	3 (1 ppb)	~1.5-fold lower
	Chronic	To be determined	---
Telone	Acute (24-hour)	140	same
	Subchronic	91	same
	Chronic	0.07	same
Chloropicrin	Acute (24-hour)	10	~3-fold lower
	Subchronic	(1*)	---
	Chronic	1	same

* Proposed same as chronic value; no separate literature review conducted

3.   We recommend that the screening levels document include a detailed discussion of the default parameters and calculations used to derive the screening levels. This would enable the reviewers to duplicate and verify the calculations.

SPECIFIC COMMENTS

A.   Methyl Bromide

1.   We recommend that an uncertainty of 1,000 instead of 100, be used to calculate the acute screening level. Given that children may be more sensitive than adults to methyl bromide neurotoxicity, and that the rat and rabbit developmental toxicity studies and the dog neurotoxicity study are inadequate for assessing children's neurotoxicity risk from methyl bromide, we believe that the uncertainty factor of 100 is insufficient. An additional factor of ten is warranted for protecting children's health. The 24-hour acute screening level would then become 21 ppb, or 82 $\mu g/m^3$ (see Table 1).

2. In the first paragraph, fourth line, "rat inhalation developmental" should read "rabbit inhalation developmental study." The rabbit no-observed-adverse-effect-level (NOAEL) of 40 ppm from Breslin et al. (1990) is used in DPR's draft risk characterization document (RCD) for methyl bromide.

3. It is not clear from the text whether the acute NOAEL of 40 ppm is based on maternal or developmental toxicity. In addition, no reason was given why this NOAEL "is inappropriate for deriving a human equivalent NOEL for children."

B. Methylisothiocyanate

1. We propose a 24-hour acute screening level of 6.6 μg/m^3 (2.2 ppb) for methylisothiocyanate (MITC). Our review of the human study upon which the DPR proposed value of 66 μg/m^3 is based indicated several problems with the study, including using only healthy adult subjects, eye only exposure instead of inhalation, and some problems with the selection of controls. While we do not consider the Nesterova (1969) study using cats, rats and mice to be satisfactory for risk assessment, we do not want to discount the lower NOAELs measured in animals for eye and respiratory irritation. In addition, respiratory symptoms were reported in humans exposed to MITC levels below the proposed DPR acute screening level during the 1991 metam spill at the Cantara Loop near Dunsmuir, California. Therefore, we propose that an additional uncertainty factor of ten be applied to the proposed screening level of 66 μg/m^3 to account for sensitive individuals, such as persons with asthma. Therefore, We propose an acute screening level of 6.6 μg/m^3 (see Table 1).

2. In deriving the subchronic screening level for MITC, we would not make any adjustments for differences in breathing rates between rats and humans because the conventional uncertainty factor of ten used for interspecies extrapolation would account for this and other differences between rats and humans. We propose a subchronic screening level of 1 ppb (3 μg/m^3) compared to 1.5 ppb (5 μg/m^3) proposed in the screening levels memorandum.

3. We recommend that a chronic screening level for MITC be calculated. In the absence of a chronic inhalation study, the subchronic study could be used for this purpose.

C.   Telone (1,3-Dichloropropene)

It appears that the appropriate studies and NOAELs and/or lowest-observed-adverse-effect-levels (LOAELs) have been selected from which to derive the various screening levels. We agree with the screening levels proposed by DPR.

D.   Chloropicrin

1.   For derivation of an acute screening level for the fumigant chloropicrin, it was assumed that the OEHHA one-hour reference exposure level (REL) of 29 $\mu g/m^3$ (based on respiratory irritation in a ten-minute mouse exposure) is also appropriate as a 24-hour REL. However, based on the available scientific evidence, it is not clear that the irritant effects of chloropicrin are maximal in one hour. A time correction appears appropriate, based on an assumed time to maximum sensitivity. We propose a Haber's Law correction, according to the recommendations in the OEHHA acute REL guidelines.

2.   The time base for maximal sensitivity to irritant effects of chloropicrin with a 24-hour exposure is unknown. Using a Haber's Law exponent of two, as per the OEHHA guidelines for time extrapolations over one hour, the 24-hour REL would be 10 ug/m3, using the assumption of maximal sensitivity within eight hours, and 6 $\mu g/m^3$ if sensitivity is assumed to keep increasing for 24 hours. We recommend the eight-hour assumption, for a 24-hour REL of 10 $\mu g/m^3$, which seems to be more consistent with precedent and expectations from biological mechanisms.

3.   We agree with the proposed screening level for chronic exposures to chloropicrin, which is the OEHHA chronic REL of 1 ug/m3 based on systemic effects in a chronic rat study.

Again, thank you for the opportunity to review the proposed screening levels for fumigants. Please feel free to contact me at (510) 622-3200 or Dr. Joy Wisniewski (916) 327-7324 if you have any questions regarding our comments.

cc: See next page

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MEMORANDUM

TO: Lisa Ross, Ph.D.
               Environmental Monitoring and Pest Management Branch

FROM: Jay Schreider, Ph.D.
               Medical Toxicology Branch

DATE: November 29, 1999

SUBJECT: SCREENING LEVELS FOR FUMIGANTS IN PHASE TWO

This memorandum contains screening levels for the four fumigants to be monitored in Phase Two of the Lompoc Project. The fumigants are methyl bromide (MeBr), 1,3-dichloropropene (Telone), methyl isothiocyanate (MITC), and chloropicrin. Potential screening levels, their derivations, and a possible framework for their application were presented in my October 15, 1999 memorandum to you. Many helpful comments were received from the members of the Technical Advisory Group, especially from the Office of Environmental Health Hazard Assessment (OEHHA, memorandum from Anna M. Fan to Jay Schreider, November 24, 1999). The screening levels, the explanation of their derivation, and the framework in which they fit have been modified in response to these comments. To the extent possible, Department risk assessments (either finalized or in final draft), in the form of Risk Characterization Documents (RCDs), are used as the basis for the screening levels.

It is important to keep in mind that the screening levels are not health standards and should not be viewed as such. The screening levels represent the first tier in an evaluation and provide a context in which to view measured levels of the fumigants that are monitored in Phase Two. The screening levels should be viewed in the following context. A measured air level that is below the screening level for a given fumigant would not be considered to represent a significant health concern and would not generally undergo further evaluation, but also should not automatically be considered "safe." DPR, in consultation with the TAG, may choose to evaluate further any environmental levels that are below the screening levels. By the same token, a measured level that is above the screening level would not necessarily indicate a significant health concern, but would indicate the need for a further and more refined evaluation. Significant exceedances of the screening levels could be of health concern and would indicate the need to explore the imposition of mitigation measures. This framework was also suggested by OEHHA in their memorandum.

Since chronic exposure is not being monitored in Phase Two, screening levels are only presented for acute and subchronic exposure or toxicity. Acute toxicity can be defined as the toxicity manifested within a relatively short time interval, generally not longer than one day, from a single exposure. In this document, unless specifically noted, acute screening levels are for 24 hours. Subchronic toxicity can be defined as the toxicity manifested within a more extended interval, but not one that constitutes a significant portion of the lifespan of the species in

question. In subchronic toxicity testing using mammalian test species, the period of exposure is generally 30 to 90 days.

One quantitative descriptor of the results of a toxicity study is the No Observed Effect Level (NOEL). The NOEL can be defined as the highest dose level of a chemical (in this case, a pesticide) that causes no observable adverse or toxic effect in the animal test species in the study. A related term, the Lowest Observed Effect Level (LOEL), can be defined as the lowest dose of a chemical that still causes an observable adverse or toxic effect. In some cases, a study will demonstrate adverse effects at all dose levels, and a NOEL will not be readily apparent. In these situations, an Estimated No Effect Level (ENEL) can be generated by applying an uncertainty factor (generally 10-fold or less) to the LOEL. The units of the NOEL, LOEL, and ENEL will depend on the route and method of exposure in the animal study. In the current application, all studies are by the inhalation route, with the pesticides delivered in the air. Therefore, these dose levels are expressed in terms of air concentrations, such as parts per million (ppm), parts per billion (ppb), or micrograms per cubic meter (ug/m^3).

The toxicology database for a pesticide contains a series of toxicity studies. The particular study and corresponding NOEL that is selected as the basis for the risk calculations or screening level derivations can be described as the "critical" study or NOEL. These studies are performed on a variety of experimental animals, including rats, rabbits, and dogs. In the case of inhalation studies, due to logistical reasons, the period of exposure is for less than a full 24-hour period, and the resulting NOEL is usually normalized to a 24-hour period. Likewise, subchronic inhalation studies are often conducted for 5 days per week, and the results are normalized to a 7-day week. In addition, since the experimental animals have different respiration rates than humans, different amounts of toxicant will be inhaled over the same time period. Therefore, the air concentrations from the animal studies are generally adjusted to account for the differential respiration rates in order to derive a "human equivalent" concentration. It should be noted that this adjustment does not factor in potential differences in toxicologic sensitivity. This potential differential toxicologic sensitivity is taken into account in the application of uncertainty factors. The human equivalent concentration is calculated, taking the above factors into account, according to the following equation.

$$\textit{ppm or ug/m}^3 \textit{ (human)} = \textit{ppm or ug/m}^3 \textit{ (animal)} \times \frac{\textit{animal respiration rate}}{\textit{human respiration rate}} \times \frac{\textit{hours exposed}}{\textit{24 hours}} \times \frac{\textit{days exposed per week}}{\textit{7 days}}$$

The term for "days exposed per week/7 days" is used in the calculation only for subchronic inhalation studies. Unless otherwise noted, the default respiration rates used are: 0.20 m^3/kg/day for adult humans, 0.76 m^3/kg/day for children, 0.96 m^3/kg/day for rats, 0.54 m^3/kg/day for rabbits, and 0.39 m^3/kg/day for dogs.

Telone

An RCD for Telone was completed as an interim document in 1994 and finalized in 1997 (Department of Pesticide Regulation, Risk Assessment of 1,3-Dichloropropene, January 10, 1997). In the RCD, the critical acute ENEL of 77.5 ppm was estimated from a 775 ppm LOEL

(salivation, lacrimation, and lethargy at the LOEL) in a 4-hour rat inhalation study. Adjusting for purity and a 24-hour exposure time resulted in an ENEL of 13 ppm. Correcting for differences in breathing rates, the equivalent human child ENEL is 16 ppm (72 mg/m^3). The RCD used a critical subchronic NOEL of 10 ppm (for changes in the nasal epithelium at the LOEL of 30 ppm) from two rat subchronic inhalation studies in which rats were exposed 6 hours per day, 5 days per week. Adjusting for purity and a 24-hour, 7 day per week exposure time resulted in a NOEL of 1.6 ppm. Correcting for differences in breathing rates, the equivalent subchronic human child NOEL is 2.0 ppm (9.1 mg/m^3; 9,100 ug/m^3).

After the completion of the RCD, a rat dominant lethal toxicity study was submitted to the Department (Department of Pesticide Regulation, Summary of Toxicology Data, 1,3-Dichloropropene (Telone II), September 23, 1999). While this study is designed to assess genotoxicity and did not demonstrate any dominant lethal effects, the large number of animals exposed yielded other toxicity information that was not available when the RCD was drafted. In this study, rats were exposed by inhalation 6 hours per day 7 days per week for 10 weeks. A NOEL of 10 ppm (45.3 mg/m^3) was demonstrated for body weight loss (as opposed to the more frequently seen decreased body weight gain) of rats within 7 days (the first body weight measurement) of exposure to 60 ppm (272 mg/m^3). The use of this endpoint is supported by several studies in rats, mice, and rabbits that consistently reported the same effect during the first week of Telone inhalation exposure. The earliest body weight measurement was day 3 of exposure. In some cases, concomitant reduction in food consumption was reported. Unfortunately, no information on any possible mechanism for this effect was available, since this endpoint was not the focus of any of the studies. Nevertheless, the consistency of occurrence within the first week of inhalation exposure in multiple species, showing a clear dose-response relationship, signifies an acute endpoint that should be considered. The overall database supports the use of the NOEL of 10 ppm (45.3 mg/m^3) from the dominant lethality study. This is lower than the ENEL of 77.5 ppm used in the RCD. The Department is currently evaluating the impact of this study on estimations of acute inhalation risk. For the purposes of generating screening values, it seems appropriate to use the more conservative value of 10 ppm. Adjusting for purity and a 24-hour exposure time results in a NOEL of 2.4 ppm. Correcting for differences in breathing rates, the equivalent acute human child NOEL is 3.0 ppm (14 mg/m^3; 14,000 ug/m^3).

Applying the conventional uncertainty factor of 100 for results based on animal studies to the acute NOEL of 3.0 ppm based on body weight loss results in **a 24-hour acute screening level of 30 ppb (140 ug/m^3)**. For reference, the corresponding acute screening levels for 8 and 16 hours can be calculated to be 90 and 45 ppb, respectively. Applying the uncertainty factor of 100 to the subchronic NOEL of 2.0 ppm results in a **subchronic screening level of 20 ppb (91 ug/m^3)**. OEHHA concurred with these screening levels.

Chloropicrin

A risk assessment of chloropicrin has been initiated at DPR, but has not been completed. However, as part of the air Toxics Hot Spots Program, OEHHA has generated acute and chronic Reference Exposure Levels (RELs) for chloropicrin (OEHHA, Determination of Acute

Reference Exposure Levels for Airborne Toxicants, March, 1999; Proposed OEHHA Chronic Inhalation REL Summaries-Second Set of 40 Chemicals, September 27, 1999). The RELs have undergone scientific peer review by the Toxic Air Contaminant Scientific Review Panel (SRP). An acute REL of 4.4 ppb (29 ug/m³) was derived for a 1-hour human exposure. This value was based on decreased respiratory rates in an acute mouse inhalation study in a 10-minute exposure. A 24-hour value of 0.18 ppb (1.2 ug/m³) could be derived from this 1-hour value (by dividing by 24); however, the resulting overall extrapolation from a 10 minute exposure to a 24-hour exposure is somewhat questionable, especially since the resulting 24-hour REL would be less than the chronic REL. In the memo of November 24, 1999, OEHHA points out that "considering the available scientific evidence, it is not clear that the irritant effects of chloropicrin are maximal in one hour. A time correction appears appropriate based on an assumed time to maximum sensitivity. We propose Haber's Law correction, according to the recommendations in the OEHHA acute REL guidelines. The time base for maximal sensitivity to irritant effects of chloropicrin with a 24-hour exposure is unknown. Using a Haber's law exponent of two, as per the OEHHA guidelines for time extrapolations over one hour, the 24-hour REL would be 10 ug/m³, using the assumption of maximal sensitivity within eight hours, and 6 ug/m³ if sensitivity is assumed to keep increasing for 24 hours. We recommend the eight hour assumption, for a 24-hour REL of 10 ug/m³, which seems to be more consistent with precedent and expectations from biological mechanisms." The **24-hour REL of 10 ug/m³** (2 ppb) is used for acute exposure. It should be noted that this REL would also apply to time periods between 8 and 24 hours. Since the REL already incorporates the appropriate uncertainty factors, it will be used unmodified as the screening level.

A chronic REL of 1 ug/m³ (0.2 ppb) was derived for chronic human inhalation exposure. This value was derived from a chronic rat inhalation study showing increased mortality, nasal rhinitis, and increased absolute and relative lung and liver weights at higher dose levels. A subchronic REL was not derived as part of the Hot Spots program; therefore, **the chronic REL of 1 ug/m³ (0.2 ppb)** is used as a surrogate (conservative) for subchronic exposure. Since the REL already incorporates the appropriate uncertainty factors, it will be used unmodified as the screening level.

Methyl Bromide

An RCD for methyl bromide has been completed and is used as the source for the values for methyl bromide (Department of Pesticide Regulation, Methyl Bromide Risk Characterization Document for Inhalation Exposure, October 15,1999). This RCD is currently undergoing detailed external scientific peer review by the National Academy of Sciences. This review is expected to be competed by June 2000. Given the function of peer review, it is possible that the review could result in changes to some of the values, which could result in changes to the screening levels presented in this document. It should be noted that for the methyl bromide RCD, a child breathing rate of 0.46 m³/kg/day and an adult breathing rate of 0.26 m³/kg/day were used.

The RCD uses an acute NOEL of 40 ppm (156 mg/m³) for developmental effects from a rabbit inhalation developmental toxicity study as the critical NOEL for acute exposure. In this study,

exposure occurred for 6 hours per day. While exposure occurred for the period of organogenesis, an adverse effect observed in the fetus is considered an acute effect under the current assumption that only a single exposure at a critical time is necessary for the induction of developmental effects. This value of 40 ppm is equivalent to a human NOEL of 21 ppm (82 mg/m^3), after adjusting for differences in breathing rate and exposure period. Since the NOEL from this study is based on effects in the fetus from exposure of an adult, it may not be appropriate for deriving a human equivalent NOEL for children. However, a human child equivalent NOEL of 25 ppm (97 mg/m^3) was derived from a dog neurotoxicity study (exposure 7 hours per day, NOEL of 55 ppm), so children would be protected by the use of the NOEL of 21 ppm (82 mg/m^3; 82,000 ug/m^3).

In another inhalation rabbit developmental toxicity study, maternal neurotoxicity became evident after exposures of 7 hours per day for 1 week at a LOEL of 70 ppm (272 mg/m^3). The NOEL was 20 ppm (78 mg/m^3). The equivalent child NOEL is 7 ppm (27 mg/m^3; 27,000 ug/m^3) and can be used for subchronic exposures of shorter duration (1 week).

Applying the conventional uncertainty factor of 100 for results based on animal studies (10-fold uncertainty factors for both interspecies and intraspecies variability) to the acute NOEL of 21 ppm results in an acute screening level of 210 ppb (820 ug/m^3). In their comments, however, OEHHA recommended "that an uncertainty factor of 1,000 instead of 100, be used to calculate the screening level. Given that children may be more sensitive than adults to methyl bromide neurotoxicity, and that the rat and rabbit developmental toxicity studies and the dog neurotoxicity study are inadequate for assessing children's neurotoxicity risk from methyl bromide, we believe that the uncertainty factor is insufficient. An additional factor of ten is warranted for protecting children's health." For the purposes of generating a screening level for this project, OEHHA's recommendation will be followed and a 24-hour **acute screening level of 21 ppb (82 ug/m^3)** will be used. However, this does not indicate a change in DPR's approach in the RCD, which will be addressed in the peer review. For reference, the corresponding acute screening levels for 8 and 16 hours can be calculated to be 63 and 32 ppb, respectively.

Applying the 100-fold factor to the subchronic NOEL of 7 ppm (27 mg/m^3) results in a short duration subchronic screening level of 70 ppb (270 ug/m^3). If, for consistency, an additional uncertainty factor of 10 were applied to the subchronic screening level, a screening level of 7 ppb (27 ug/m^3) would result. For the purposes of generating a subchronic screening level for this project, the additional factor of 10 will be applied and a **subchronic screening level of 7 ppb (27 ug/m^3)** will be used. However, this does not indicate a change in DPR's approach in the RCD, which will be addressed in the peer review.

The RCD also considered studies that showed that methyl bromide caused biochemical changes in the brain that may be associated with neurotoxicity. However, an extensive review, in the RCD, of the published articles on this subject showed inconsistencies in the findings; thus they were not considered appropriate for use in the determination of regulatory levels. The results of one of these studies were used by the Agency for Toxic Substances and Disease Registry of the Public Health Service to derive a minimum risk level (50 ppb) as a screening tool for regulatory agencies to determine the need for regulation. As such, the study review did not critically

analyze the results. This minimum risk level has not been adopted as an action level by any regulatory agency. The peer review will consider the relevance of these findings.

MITC

A draft RCD for MITC has been completed and is used as the source for the values for MITC (Department of Pesticide Regulation, Evaluation of Methyl Isothiocyanate as a Toxic Air Contaminant, Part C, Health Assessment, October 28, 1999). This RCD is currently undergoing detailed external scientific peer review by the SRP. This review is expected to be competed in the next several months. Given the function of peer review, it is possible that the review could result in changes to some of the values, which could result in changes to the screening levels presented in this document

In an evaluation of the health risks associated with the 1991 spill of metam sodium in the upper Sacramento River, OEHHA developed an acute 1-hour inhalation REL of 0.5 ppb (Alexeff et. al., Dose-Response Assessment of Airborne Methyl Isothiocyanate (MITC) Following a Metam Sodium Spill, Risk Analysis, Vol. 14, No. 2, 1994) based on ocular irritation in the cat (M.F. Nesterova, Standards for Carbathion in the Working Zone, Air. Hyg. Sanit. 34 (5), 191-196 (1969).) There were major problems with the Nesterova study, making it inappropriate for use in risk assessment. However, at the time, it was the only acute inhalation study examining eye irritation. Subsequent to the OEHHA evaluation, an eye irritation study was conducted using human subjects, and this study is described in detail in the RCD. This study demonstrated an acute NOEL of 220 ppb (660 mg/m^3) in the air for eye irritation in humans. The parameters that were measured were changes in eye-blink rate, Likert scale (subjective estimation of eye irritation), redness of eyes, visual acuity, and tear production. The NOEL (220 ppb), is based on blink rate increases and Likert scale at the next highest dose of 800 ppb, and is for exposure of human subjects over 1 to 8 hours. The intensity or rate of these effects did not increase with increasing exposure time over the 1 to 8 hour time period. It was concluded that the level of irritation would also not be expected to change from 8 to 24 hours. Therefore, the same NOEL can be used for 8, 16, or 24 hours. This was the lowest relevant acute NOEL. Since the effect, eye irritation, is not a systemic effect, relative breathing rates are not applicable.

A 90-day rat inhalation study (exposure 4 hours per day, 5 days per week) is used to generate the critical subchronic NOEL of 1.0 ppm (3 mg/m^3) for decreased body weight gain, increased water consumption, and decreased serum protein. The equivalent human child NOEL is 150 ppb (450 ug/m^3).

Applying the conventional uncertainty factor of 10 for results based on human studies (10-fold uncertainty factor intraspecies uncertainty) to the acute NOEL of 220 ppb results in an acute screening level of 22 ppb (66 ug/m^3). In their comments, however, OEHHA proposed a "24-hour acute screening level of 6.6 ug/m^3 (2.2 ppb) for methylisothiocyanate (MITC). Our review of the human study upon which the DPR proposed value of 66 ug/m^3 is based indicated several problems with the study, including using only healthy adults, eye only exposure instead of inhalation, and some problems with the selection of controls. While we do not consider the Nesterova (1969) study using cats, rats and mice to be satisfactory for risk assessment, we do not

want to discount the lower NOAELs measured in animals for eye and respiratory irritation. In addition, respiratory symptoms were reported in humans exposed to MITC levels below the proposed DPR acute screening level during the 1991 metam spill at the Cantara Loop near Dunsmuir, California. Therefore we propose that an additional uncertainty factor be applied to the proposed screening level of 66 ug/m^3 to account for sensitive individuals, such as persons with asthma. Therefore, we propose an acute screening level of 6.6 ug/m^3." For the purposes of generating a screening level for this project, OEHHA's recommendation will be followed and a 24-hour **acute screening level of 2.2 ppb (6.6 ug/m^3)** will be used. However, this does not indicate a change in DPR's approach in the RCD. The SRP peer review will consider the relevance of these various acute studies, as well as the appropriate uncertainty factors to apply.

Applying the conventional uncertainty factor of 100 for results based on animal studies to the subchronic NOEL of 150 ppb (450 ug/m^3) results in a **subchronic screening level of 1.5 ppb (4.5 ug/m^3)**.

Attachment

cc: Paul Gosselin
       Gary Patterson
       Joyce Gee

Table 1. Screening levels and recommended responses.

Analyte	No Observable Effect Level	Screening Level	Ambient Air Concentration[a]	Recommended Response[b]
Telone	Acute (24 hour) 14,000 $\mu g/m^3$	140 $\mu g/m^3$ (30 ppb)	< 140 $\mu g/m^3$	Not necessarily a health concern. No immediate response. May still merit further analysis.
			≥ 140 $\mu g/m^3$	Not necessarily a health concern. However, initiate a more refined analysis. If the concentration exceeds 1400 $\mu g/m^3$, immediately explore the need for mitigation measures.
	Subchronic 9,100 $\mu g/m^3$	91 $\mu g/m^3$ (20 ppb)	< 91 $\mu g/m^3$	Not necessarily a health concern. No immediate response. May still merit further analysis.
			≥ 91 $\mu g/m^3$	Not necessarily a health concern. However, initiate a more refined analysis. If the concentration exceeds 910 $\mu g/m^3$, immediately explore the need for mitigation measures.
Chloro-picrin	Acute (24 hour) Not Available[b]	10 $\mu g/m^3$ (2 ppb)	< 10 $\mu g/m^3$	Not necessarily a health concern. No immediate response. May still merit further analysis.
			≥ 10 $\mu g/m^3$	Not necessarily a health concern. However, initiate a more refined analysis. If the concentration exceeds 100 $\mu g/m^3$, immediately explore the need for mitigation measures.
	Subchronic Not Available[b]	1.0 $\mu g/m^3$ (0.2 ppb)	< 1.0 $\mu g/m^3$	Not necessarily a health concern. No immediate response. May still merit further analysis.
			≥ 1.0 $\mu g/m^3$	Not necessarily a health concern. However, initiate a more refined analysis. If the concentration exceeds 10 $\mu g/m^3$, immediately explore the need for mitigation measures.

Methyl Bromide	Acute (24 hour) 82,000 µg/m³	82 µg/m³ (21 ppb)	< 82 µg/m³	Not necessarily a health concern. No immediate response. May still merit further analysis.
			≥82 µg/m³	Not necessarily a health concern. However, initiate a more refined analysis. If the concentration exceeds 820 µg/m³, immediately explore the need for mitigation measures.
	Subchronic 27,000 µg/m³	27 µg/m³ (7 ppb)	< 27 µg/m³	Not necessarily a health concern. No immediate response. May still merit further analysis.
			≥ 27 µg/m³	Not necessarily a health concern. However, initiate a more refined analysis. If the concentration exceeds 270 µg/m³, immediately explore the need for mitigation measures.
MITC	Acute(24 hour) 660 µg/m³	6.6 µg/m³ (2.2 ppb)	< 6.6 µg/m³	Not necessarily a health concern. No immediate response. May still merit further analysis.
			≥ 6.6 µg/m³	Not necessarily a health concern. However, initiate a more refined analysis. If the concentration exceeds 66 µg/m³, immediately explore the need for mitigation measures.
	Subchronic 450 µg/m³	4.5 µg/m³ (1.5 ppb)	< 4.5 µg/m³	Not necessarily a health concern. No immediate response. May still merit further analysis.
			≥ 4.5 µg/m³	Not necessarily a health concern. However, initiate a more refined analysis. If the concentration exceeds 45 µg/m³, immediately explore the need for mitigation measures.

a. Ambient air concentrations will be averaged as described in section 7.1 of the Fumigant Sampling and Analysis Plan.

b. A more refined analysis could include, but not be limited to atmospheric dispersion modeling, more air monitoring, and a more refined risk analysis. Mitigation measures could include, but not be limited to permit conditions, statewide regulations, and label changes.

c. See memorandum text for discussion.

MINI MEMO

TO: Lisa Ross

FROM: Jay Schreider

DATE: December 7, 1999

SUBJECT: RESPONSES TO OEHHA'S COMMENTS ON SCREENING LEVELS

General Comments

1.   Based on discussion during the November 18 TAG conference call as well as on OEHHA's comments, the original tiered approach has been changed and now reflects OEHHA's suggestions. Only acute and subchronic screening values are included, since, as OEHHA notes, chronic exposures are probably not relevant to the current monitoring program.

2.   Unless otherwise noted, the acute values are for 24 hours. This is now more clearly delineated.

3.   The default parameters and calculations are now included and more clearly explained.

Specific Comments

A. Methyl Bromide

1.   For the purposes of generating a screening level for this project, OEHHA's recommendation of an uncertainty factor 1,000 (instead of 100) will be taken and a 24-hour acute screening level of 21 ppb (82 ug/m^3) will be used. However, this does not indicate a change in DPR's approach in the RCD, which will be addressed in the peer review. For consistency, this factor is also used for the subchronic values; however, again, this does not indicate a change in DPR's approach in the RCD, which will be addressed in the peer review.

2.   The correction has been made.

3.   As now noted in the document, the NOAEL of 40 ppm is based on developmental toxicity. Since the NOEL from this study is based on effects in the fetus from exposure of an adult, it may not be appropriate for deriving a human equivalent NOEL for children.

B. Methylisothiocyanate

1.   For the purposes of generating a screening level for this project, OEHHA's recommendation of an additional uncertainty factor of 10 will be taken and a 24-hour acute screening level of 2.2 ppb (6.6 ug/m^3) will be used. However, this does not indicate a change in DPR's approach in the RCD. The SRP peer review will consider the relevance of these various acute studies, as well as the appropriate uncertainty factors to apply.

2.   DPR feels that it is important to adjust for differences in breathing rates between experimental animals and humans. This factor is not taken into account by the interspecies uncertainty factor, which is primarily intended to adjust for differences in sensitivity. DPR's approach with inhalation is consistent with adjusting for different consumption rates when evaluating dietary exposure. Therefore, the screening level will remain at 1.5 ppb rather than the OEHHA suggested 1 ppb.

3.   As noted previously, the screening level document does not include chronic values.

C. Telone

No response needed.

D. Chloropicrin

1. & 2. The document now uses OEHHA's recommended 24-hour REL of 10 ug/m^3.

3.   No response needed.

Department of Pesticide Regulation

dpr

Paul E. Helliker
Director

MEMORANDUM

Gray Davis
Governor

Winston H. Hickox
Secretary, California
Environmental
Protection Agency

TO: Randy Segawa
Environmental Monitoring Branch

FROM: Jay Schreider, Ph.D.
Medical Toxicology Branch

DATE: October 26, 2001

SUBJECT: UPDATE ON FUMIGANT SCREENING LEVELS

In response to questions raised by various participants of the last conference call, I am providing the following information.

1. **Description of Screening Levels**: There has been discussion regarding the most appropriate ways to describe the screening levels. Perhaps the best wording would be that used in the Fumigant Sampling and Analysis Plan and in the appendix of the plan describing the fumigant screening levels and their derivation. The documents have been publicly available and on our web site for over two years and represent a general, though not necessarily unanimous, consensus of the Technical Advisory Group (TAG). This appendix consisted of a November 29, 1999 memorandum from myself to Lisa Ross, which presented the fumigant screening levels and incorporated the comments of member of the TAG. That document stated:

    "A measured air level that is below the screening level for a given fumigant would not be considered to represent a significant health concern and would not generally undergo further evaluation, but also should not automatically be considered "safe." DPR, in consultation with the TAG, may choose to evaluate further any environmental levels that are below the screening levels. By the same token, a measured level that is above the screening level would not necessarily indicate a significant health concern, but would indicate the need for a further and more refined evaluation. Significant exceedances of the screening levels could be of health concern and would indicate the need to explore the imposition of mitigation measures. This framework was also suggested by OEHHA in their memorandum."

2. **Methyl Bromide**: At the time the November 29, 1999 memorandum was written and the screening levels derived, the DPR risk assessment on methyl bromide was undergoing review by the National Academy of Sciences (NAS). OEHHA, in their comments suggested that an additional uncertainty factor of 10 be included to account for the potential increased sensitivity of children. Since the NAS peer review was not completed, I incorporated the additional factor of 10 suggested by OEHHA for the purposes of reaching consensus. Since that time, the NAS review has been concluded. In that review, NAS was asked among other things to review the endpoints that DPR selected and whether an additional 10-fold factor was appropriate. The NAS agreed with the toxicological endpoints selected by DPR and

clearly stated that the additional 10-fold factor was not appropriate. Therefore, I think it is appropriate to remove the additional factor, raising the screening levels by a factor of 10.

3. MITC:

- Since the November 29 memorandum, DPR has prepared a health evaluation of MITC for the Toxic Air Contaminant (TAC) Program. As part of the TAC program, there is an exhaustive review of the available toxicology information. This evaluation has been finalized for submission to the Science Review Panel. As a result of this review, a different inhalation study was selected for evaluating subchronic exposure to MITC in the air. The selected study was a 4-week Wistar rat inhalation study conducted according to a 6 hour per day, 5 day per week exposure regimen. The NOEL, normalized to 24 hours per day, 7 days per week, is 300 ppb for nasal epithelial atrophy, inflammation, and clinical signs. Since these effects were judged to be due to the irritation of the MITC, rather than systemic toxicity, air concentration is most important (rather than the amount of material absorbed), and the NOEL is not adjusted to address differences in breathing rates. The resulting Reference Exposure Level (REL) developed in the document is 3.0 ppb (9.0 ug/m^3). This is the screening level value that should be now used to evaluate subchronic exposure to air levels of MITC.

- The acute screening level (2.2 ppb, 6.6 ug/m^3) generated in November 29 memorandum was based on the results of a human study, but incorporated an additional uncertainty factor of 10 at the request of OEHHA to address sensitive individuals, such as persons with asthma. The TAC document uses an acute REL of 22 ppb (66 mg/m^3). Therefore, the screening level of 2.2 ppb (6.6 ug/m^3) should be considered quite health protective. Another consideration for the acute screening value was that it was based on 8 hours exposure to humans, but the data indicated that the effect did not change between 1 and 8 hours of exposure. Therefore, the 8-hour value could arguably be used to evaluate a 24-hour air level. The 8-hour value should certainly be used to evaluate a measured 8-hour air level.

- Since chronic exposure was not being monitored, the November 29, 1999 memorandum only presented screening levels for acute and subchronic toxicity. In the TAC document, a chronic REL of 0.3 ppb (0.9 ug/m^3) was derived by applying an additional uncertainty factor of 10 to the subchronic REL. This could be used as a default screening level for chronic exposure.