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MEMORANDUM

SUBJECT: REVISED Margins of Exposure for Worker and Residential/Bystanders During Soil Applications of Metam Sodium

FROM: Deborah McCall, Acting Head
Special Review Section
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

TO: Jay Ellenberger, Branch Chief
Accelerated Reregistration Branch
Special Review and Reregistration Division (7508W)

and

Jack Housenger, Branch Chief
Special Review Branch
Special Review and Reregistration Division (7508W)

THROUGH Debra Edwards, Branch Chief
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

Attached are the revised Margins of Exposure (MOEs) for occupational and residential/bystander exposures to metam sodium during soil applications. This revision became necessary when different short and intermediate term toxicity endpoints were established by the Less-then-Lifetime Committee (LTL) in January 1995 for methyl isothiocyanate (MITC), the principle decomposition product and metabolite of metam sodium. This assessment estimates the short and intermediate term risk to workers: mixer/loaders and applicators, and residents who reside downwind from field applications. If you have any questions please

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contact D. McCall at 308-2718.

Attachment

cc: Larry Dorsey, Stephanie Irene, Steven Knott, Mike Ioannou, Tim McMahon, Mike Beringer

I. BACKGROUND

HED completed a worker and residential/bystander risk assessment in June of 1994 for metam sodium which included the hydrolysed products methyl isothiocyanate (MITC) and carbon disulfide (CS_2). Metam sodium is a non-selective preplant fumigant for control of weeds, soil borne diseases, and nematodes infesting field and vegetable crops. The 35 formulated metam sodium products are water miscible. When metam sodium is mixed with water during use it hydrolyses to form MITC and CS_2.

The June 1994 risk assessment indicated that the toxicology database for MITC had several studies currently under review in HED. Upon completion of those studies, the MITC toxicology database was re-evaluated by the Less-Than-Lifetime Committee (LTL) in January 1995. The LTL Committee determined the short and intermediate term toxicity endpoint for MITC to be based on a 90-day inhalation study. [The 1994 risk assessment was based on a developmental toxicity study.] This addendum will update the worker and residential/bystander risk assessment for methyl isothiocyanate.

II. HAZARD IDENTIFICATION

A. *Toxicology* Endpoint for Short and Intermediate Term Exposure

MITC was tested in a 90-day rat subchronic inhalation study. MITC was administered to rats by the inhalation route for 12-13 weeks (MRID # 412214-07). Three groups of 10 rats/sex/dose received nose-only inhalation exposure at 0, 3.16, 30.67 or 137.13 μg/L for 4 hours/day, 5 days/week. The dose levels from the 4 hour exposure were extrapolated to 6 hour exposure as recommended by the Subdivision F guidelines. The 6 hour extrapolated levels were 0, 2.1, 20.6, or 91.9 μg/L. Effects at the high dose were apathy, salivation, nasal discharge, and stimulated vocalization. The high dose animals exhibited decreased body weight and food intake/food efficiency and increased water intake plus alterations in clinical chemistry values. The NOEL is 2.1 μg/L (2.4 mg/kg/day) and the LOEL is 20.6 μg/L. The LOEL is based on decreased body weight and food efficiency and blood protein values accompanied by increased water intake.

III. EXPOSURE ASSESSMENT

The Occupational and Residential Exposure Branch (OREB) completed a worker and residential/bystander exposure assessment for metam sodium in May 1994 which included MITC. The exposure assessment was based on two Mixer/Loader/Applicator studies (MRID #'s 429684-02 and 429684-01). This addendum will use the same exposure estimates and assumptions as in OREB's May 1994 assessment (A. Mehta, May 5, 1994). Also, it should be noted that 1994 OREB exposure assumptions were based on a female body weight (60 kg) and ventilation rate and these values were not changed in this addendum.

Although metam sodium probably has no measurable vapor pressure since it is a salt, a solution of metam sodium has a vapor pressure of 21 mm Hg at 25°C. Metam sodium is very stable at a pH greater than 8.8. The commercial metam sodium formulation consists of 32.7% of the active ingredient in water, which is stable at a buffered pH of about 10 (Amvac, 1991; Herbicide Handbook, 1983). Metam sodium is not stable at a pH below 7 and readily hydrolyses.

In the M/L/A exposure studies both the mixer/loader and applicator wore long-sleeved shirts and long pants. In addition, mixer/loaders wore rubber boots, goggles, respirators, and chemical-resistant gloves while working with metam sodium as required on the label. Applicators were provided with goggles, respirators, and chemical-resistent gloves to wear at their discretion.

Inhalation exposure to metam sodium is assumed to be negligible because metam sodium readily degrades to MITC, CS_2, and other products. As the handler loads metam sodium into the applicator tank or sprinkler system, water is simultaneously added. As indicated above, the physical and chemical properties of metam sodium cause it to have a short half-life when it comes in contact with air and water. The potential exposure under the current use conditions to both handlers and residents/bystanders would be to the MITC and CS_2 not metam sodium.

The primary route of exposure for MITC is inhalation, and HED assumes that absorption is 100%. The toxicity endpoint for MITC is derived from an 90-day inhalation study in rats. The number of hours the mixer/loader is exposed is 0.5 hr/day, and the applicator is exposed 8 hrs/day. OREB assumed residents/bystanders are exposed for 24 hours/day.

Workers may receive some dermal exposure to metam sodium. However, HED assumes dermal exposure to be minimal to handlers since the surface of human skin has an acidic environment with pH in the range of 4.5 - 6, metam sodium is expected to undergo transformation to its degradates after it comes into contact with human skin. No dermal exposure is expected for the residents/bystanders.

The MOEs were calculated after converting the inhalation NOEL from an air concentration value to a dose expressed in mg/kg/day. The equation is as follows:

$$\text{Dosage (mg/kg/d)} = \frac{AF * VT * f * C * t}{BW}$$

AF - absorption factor = 1.0, assuming 100% retention
VT - tidal volume (mL) = 1.84 mL or 1.84×10^{-6} m^3
f - respiratory rate in breathes per minute = 117
C - atmospheric concentration (mg/m^3) = 2.1 mg/m^3
t - 24 hours x 60 minutes hour = 1440 minutes/day
BW - body weight of test animal (rat) = 0.270 kg

The NOEL of 2.1 mg/m^3 was converted to 2.4 mg/kg/day by the following equation:

$$\frac{1.0 \times (1.84 \times 10^{-6}\ m^3) \times 117/\text{minute} \times 2.1\ mg/m^3 \times 1440\ \text{minutes}}{0.270\ kg}$$

$$= 2.4\ mg/kg/day$$

IV. RISK CHARACTERIZATION

The revised MOE's were derived based on a NOEL of 2.4 mg/kg/day from a 90-day rat inhalation study. The LTL Committee determined this study to be appropriate for assessing risk from short and intermediate term exposures to MITC. Tables 1 and 2 contain the exposure estimates and the revised MOEs. Risk estimates should be considered conservative as they were calculated assuming the maximal application rate of 318 lbs ai/treated acre.

TABLE 1: Bystander/Residential Exposure Estimates to MITC using Downwind Sampling Data

Sample Interval (hrs)	Soil Type	Distance (meters)	Exposure (mg/kg/day) Females	MOE (NOEL[A] = 2.4 mg/kg/day)
0-24	Loamy sand	5.0	183×10^{-3}	13
0-24	Loamy sand	25.0	165.6×10^{-3}	14
0-24	Loamy sand	125.0	114.8×10^{-3}	21
0-24	Loamy sand	500.0	22.14×10^{-3}	108

[Exposure data were extracted from the Worker and Residential Exposure Assessment of Metam Sodium, A. Mehta, May 5, 1994, pg 14, see Attachment A.]

[A] The NOEL of 2.1 mg/m^3 was converted to 2.4 mg/kg/day.

Margin of Exposure = NOEL ÷ Exposure

TABLE 2: MITC Handler MOE's for Each Application Method

Application Method	MIXER/LOADER		APPLICATOR	
	Adjusted Exposure (mg/kg/day)[A] Females	MOE[B]	Exposure (mg/kg/day)[A] Females	MOE[B]
Shank Injection	2.61×10^{-3}	920	1.32×10^{-1}	18
Rotary Tiller Injection	3.62×10^{-3}	663	7.69×10^{-2}	31
Solid Set Sprinkler (chemigation)	3.52×10^{-3}	682	1.14×10^{-1}	21
Center Pivot Sprinkler (chemigation)	1.63×10^{-3}	1472	1.15×10^{-2}	209

[Exposure data were extracted from the Worker and Residential Exposure Assessment of Metam Sodium, A. Mehta, May 5, 1994, pg 9, see Attachment A.]

[A] The number of hours the Mixer/Loader is exposed is 0.5 hr/day.

The exposure value presented in the table has been adjusted for time. The exposure value was multiplied by 0.5 to adjust for the hours exposed for the mixer/loader, and by 8 (hrs/day) for the applicator.

[B] The NOEL of 2.1 mg/m^3 was converted to 2.4 mg/kg/day.

Margin of Exposure = NOEL ÷ Exposure

V. STRENGTHS AND UNCERTAINTIES OF THE RISK ASSESSMENT

The worker and residential/bystander risk assessment contains uncertainties that are the result of data gaps and/or lack of scientific knowledge. Standard assumptions were used to estimate worker and residential/bystander risks including inter-species extrapolation.

The MOEs are presented in Tables 1 and 2. The conversion of µg/L (air concentration) to a mg/kg/d basis adds some uncertainties due to fact that HED has to assume a ventilation rate, overall mean body weight and extrapolate for time.

Risk estimates should be considered conservative as they were calculated assuming the maximal application rate of 318 lbs ai/treated acre; therefore, it is possible that risks would be lower for applications made using a lower rate. The residential/bystander MOE's were calculated for only one application method, i.e. the solid set sprinkler chemigation and should be considered conservative since they represent a worse case scenario. No data are available for the other three application methods.

VI. CONCLUSIONS

Risk estimates for both the MITC worker and residential population have been updated with revised toxicity endpoint. Exposures to the MITC are primarily via the inhalation route. The residential/bystander MITC MOEs at the four distances range from 13 to 108. The MITC mixer/loader MOEs were all above 100 for all 4 application methods. The MITC applicator MOEs were below 100 for the 3 of the 4 applicator types.

It is worth noting that in the first worker exposure study, 2 of the 10 applicator replicates during shank injection, were taken in a positive pressure charcoal filtered enclosed tractor cab. Exposure estimates using those 2 replicates were approximately 30% lower. However in the second study, 5 of the 10 replicates were measured in a charcoal filtered enclosed cab; and, again 2 out of the 5 replicates provided lower exposure estimates. Although currently there is no Enclosed Cab Tractor Standard that requires manufacturers to meet certain performance criteria, the use of this mitigation technique must be encouraged as it has the potential of greatly reducing exposure to MITC. The present label according to the WPS guidance on metam sodium, requires handlers to wear respirators if they are not in an enclosed cab; however, compliance regarding this PPE requirement is known to be low.

VII. REFERENCES

A. Mehta/HED. Worker and Residential Assessment of Metam Sodium. Memorandum to T. Myers/SRRD (May 5, 1994).

A. Mehta/HED. Worker and Residential/Bystander Risk Assessment of Metam Sodium during Soil Applications. Memorandum to J. Ellenberger and J. Housenger/SRRD (June 22, 1994).

Toxicology Endpoint Selection Document/HED. Methyl Isothiocyanate. February 21, 1995.

cc: S. Irene
L. Dorsey
S. Knott
M. Ioannou
T. McMahon
RCAB chemical file
Electronic file
Caswell file