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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

652-BB
CASWELL FILE

OCT 03 1992

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Risk Assessment for Pounce - Label Amendments

TO: Linda Arrington/George LaRocca, PM 13
Registration Division (H7505C)

FROM: Flora Chow, Acting Section Head *Flora Chow 30 Sept 92*
Reregistration Section
Chemical Coordination Branch
Health Effects Division (H7509C)

THROUGH: Esther Saito, Acting Chief *ES*
Chemical Coordination Branch
Health Effects Division (H7509C)

HED Project No.: 1-0027 and 1-0279
Submission No.: S384191, S384283,
S384280, S384278,
S385719, S385722,
S385728, S385732
Caswell No.: 652BB

FMC Corporation has proposed to amend the registrations of its POUNCE (permethrin) products to include use on pistachios, broccoli and cauliflower. In conjunction with this, FMC has petitioned for increased tolerances to accommodate the new uses. TB-1 has reviewed the toxicity data base, and a summary has been provided (attachment: Doherty memo). OREB has conducted an exposure assessment based on the proposed use (attachment: Tice memo). HED is now providing a worker risk assessment based on this information.

CONCLUSION

- o The HED Peer Review Committee on Carcinogenicity classified permethrin as a Group Cq carcinogen; the estimate of unit risk, Q_1^* , is 1.8×10^{-2} (mg/kg/day)⁻¹.
- o Based on worst-case assumptions, the extra cancer risk to workers (mixer/loader/applicators) using permethrin on pistachios, broccoli or cauliflower is estimated to be 3.3×10^{-4} .

DISCUSSION

The use of permethrin on pistachios, broccoli and cauliflower as proposed for three FMC "Pounce" products has been reviewed by OREB. OREB evaluated application methods (airblast, ground boom and aerial) that would be appropriate for the proposed uses. Based on this evaluation, OREB expects worker exposure to be less than 13 mg/kg/year for an individual serving as mixer, loader and applicator.

Risk characterization. The extra cancer risk to a worker may be calculated from the maximum potential exposure of 13 mg/kg/year. This exposure represents a combined dermal and inhalation exposure, and also represents a worst-case scenario because 100% absorption would be assumed.

Estimates of the extra cancer risk is calculated from the following equation:

$$\text{Extra risk} = \text{LADD} \times Q_1^*$$

where:

$$\text{LADD} = \frac{13 \text{ mg/kg/yr}}{365 \text{ days}} \times \frac{35}{70} \times \text{Absorption}$$

$$\text{Absorption} = 1.00$$

$$\text{and } Q_1^* = 1.84 \times 10^{-2} \text{ (mg/kg/day)}^{-1}$$

The extra risk to workers using permethrin on pistachios, broccoli or cauliflower is calculated to be 3.3×10^{-4} .

Attachment:

Doherty memo (23 Oct 1991)
Tice memo (27 July 1992)

cc: M. Copley
J. Doherty
J. Tice



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OCT 23 1991

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Permethrin: Risk assessment associated with increased application rates on pistachios, broccoli and cauliflower,

TOX CHEM No.: 652BB
TOX PROJECT No.: 1-0027 and 1-0279
SUB. No.: S-284191 and S-385728.

FROM: John Doherty *John Doherty 10/23/91*
Section IV, Toxicology Branch I
Health Effects Division (H7509C)

TO: Flora Chow *Marion Copley 10/23/91*
Chemical Manager
Science Analysis and Coordination Branch
Health Effects Division (H7509C)

THROUGH: Marion Copley, DVM, Section Head
Section IV, Toxicology Branch I
Health Effects Division (H7509C)

THROUGH: Karl Baetcke, Ph.D.
Chief
Toxicology Branch I
Health Effects Division (H7509C)

Attached are the labels for the products POUNCE 3.2 EC Insecticide, POUNCE 25 WP Insecticide and POUNCE WSB containing permethrin, a copy of the toxicity data base summary for permethrin and a memo for these HED projects from TB-I. The FMC Corporation is requesting to increase the usage rate for these products on pistachios, broccoli and cauliflower. Please forward the above product labels to OREB for exposure assessment. In addition, please review the attached labels and supporting information and provide a risk assessment for the proposed changes in usage rates for both the applicators and for dietary exposure.

82-4. 90-day inhalation - guinea pig	S	NOEL > 500 ug/l/day (HDT)	1570
90-day inhalation - dogs	S	NOEL > 500 ug/l/day (HDT)	
90-day inhalation - rat	S	NOEL/LEL = 250/500 ug/l/day. Tremors, convulsions, liver effects. All are U.S. Army studies.	
82-5. 90-day neurotoxicity - hen	No	Not applicable.	
82-6			
82-7. Neurotoxicity screen rats Special study to assess for particular pyrethroid neurotoxicity. Note: new Guidelines require additional study types.	S	NOEL/LEL 100/200 mg/kg/day. Increased irritability. Possible morphological changes at 400 mg/kg/day. No morphological lesions at 600 ppm (21 days feeding). NOEL < 4000 ppm for tremors, deaths at 9000 ppm.	5946 8163
83-1a. Chronic feeding - rat		See 83-5.	
83-1b. Chronic feeding - nonrodent	2	NOEL/LEL = 5/100 mg/kg/day (capsule). <u>Liver effects</u> . NOEL > 250 mg/kg/ay (HDT).	3403
82-2a. Oncogenicity - rat		See 83-5.	
82-2b. Oncogenicity - mouse [3 studies considered acceptable, one considered invalid]	A	NOEL/LEL = 100/250 ppm. <u>Liver effects</u> . NOEL/LEL = 20/500 (males) and 2500/5000 ppm (females). <u>Liver effects</u> . Positive for <u>lung</u> and <u>liver</u> tumors. NOEL ≥ 250 mg/kg/day (HDT). Considered positive for <u>lung</u> tumors at 250 mg/kg/day.	8163
83-3a. Developmental toxicity - rat	A	NOEL/LEL = 50/1150 mg/kg/day for both maternal and developmental toxicity (decreased fetal weight).	8344

83-3b. Developmental toxicity - rabbit	A	Maternal toxicity LEL < 600 mg/kg/day (equivocal body weight gain). NOEL/LEL for developmental toxicity 600/1200 mg/kg/day.	8344
83-4. Multi generation reproduction - rat	2	NOEL < 500 ppm. <u>Liver effects</u> in pups. Body tremors in parents at 1000 and 2500 ppm and in pups at 2500 ppm. NOEL > 180 mg/kg/day (HDT).	8163
83-5. Combined chronic/onco - rat	3	NOEL < 500 ppm. <u>Liver effects</u> . NOEL/LEL = 20/100 ppm. <u>Liver effects</u> . Equivocal for lung adenomas. NOEL/LEL = 10/50 mg/kg/day. <u>Liver effects</u> .	8163
84-2. Gene mutation	A	Not mutagenic	
84-2. Chromosome aberration	No		
84-2. Other mechanism genetic toxicity.	No		
85-1. Metabolism - rata and dogs.	A	Several studies define absorption, excretion and retention of labelled permethrin.	1660 7524
85-2. Domestic animal safety		See formulations.	
85-3. Dermal Absorption	S	[U.S. Army study indicates 30-70% absorption.]	
85-. Nerve function/operant behavior	No	Requirement pending	

A = Acceptable study satisfies the data requirement. S = a SUPPLEMENTARY study containing useful information is available but additional data are required. Number = more than one study containing useful information has been presented. No = no acceptable or useful study has been provided.

² Consult DER for additional details. Only significant toxicity at the LEL is presented.

³ The document number for the DER is given but in some cases when no document number is available the date of the review is given. If not date or document number, consult the one linres for further study

identification.

Special Toxicology Issues and Problems.

1. Labelling. There are no specific labelling and precautionary statements required based on the toxicity of technical permethrin. The label signal word and precautionary statements should be governed by the toxicity studies with the formulations.

2. Carcinogenicity.

The HED Peer Review Committee classified permethrin (as of September 18, 1989) as a Group C carcinogen (possible human carcinogen) and recommended that quantitative risk assessments be performed based on the FMC mouse study using the dose-related increase in combined lung adenomas and/or carcinomas observed in females.

The Q_1^* based on the FMC mouse study for lung and liver tumors is 1.84×10^{-2} (mg/kg/day).

3. RfD.

The RfD approved by the Agency RfD Committee is 0.05 mg/kg/day based on the FMC 2-year rat feeding study with a NOEL of 5 mg/kg/day and a safety factor of 100.

4. Non carcinogenic risk assessment.

There are no other specific toxicity endpoints besides carcinogenicity and RfD as indicated above.

5. Mutagenicity/genetic toxicity comments.

The mutagenicity/genetic toxicity data base is considered incomplete and is being revised and updated.



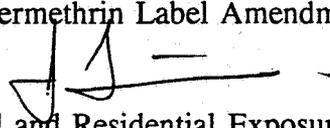
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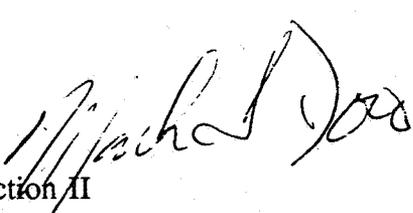
OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Review of Permethrin Label Amendments

FROM: John Tice 
Occupational and Residential Exposure Branch
Health Effects Division (H-7509-C)

TO: Flora Chow, Section Head
Chemical Coordination Branch
Health Effects Division (H-7509-C)

THRU: Mark I. Dow, Ph.D., Section Head 
Special Review and Registration Section II
Occupational and Residential Exposure Branch
Health Effects Division (H-7509-C)

Larry Dorsey, Acting Chief 
Occupational and Residential Exposure Branch
Health Effects Division (H-7509-C)

Please find below, the OREB review of:

DP Barcode: D178180

Pesticide Chemical Code: 109701 Permethrin

EPA Reg. No.: Pounce, 279-3014 (3.2 EC), 279-3083 (WSB), 279-3051 (WP)

EPA MRID No.: NONE

Review Time: 3.5 DAYS

PHED: NO

REFERRED TO CCB FOR RISK ASSESSMENT

I. INTRODUCTION:

Background/Purpose:

This review examines the potential increase in exposure to workers (M/L/A) from six separate label amendments to three FMC permethrin products. Table 1 summarizes the requested changes:

Table 1

PRODUCT	PISTACHIOS	BROCCOLI/ CAULIFLOWER
POUNCE 25 WP 279-3051	Double season max. rate to 1.6 lb ai/acre	Increase max. use rate to 0.2 lb ai/A. Season max. unchanged at 0.8 lb/yr.
POUNCE 3.2 EC 279-3014	Double season max. rate to 1.6 lb ai/acre	Increase max. use rate to 0.2 lb ai/A. Season max. unchanged at 0.8 lb/yr.
POUNCE WSB 279-3083	Double season max. rate to 1.6 lb ai/acre	Increase max. use rate to 0.2 lb ai/A. Season max. unchanged at 0.8 lb/yr.

II. DETAILED CONSIDERATIONS:

A. Use:

The above named products currently use the requested rates (and higher season maximum rates) for other crops. Specifically, the labels currently list other nut crops with the max use rate of 0.4 lb ai/acre with season maximum of 2.0 lb ai/acre. The highest application rate registered is for cotton which is applied at 0.2 lb ai/acre with a season max of 3.0 lb ai/acre. As such, the application rates requested are within the bounds of currently registered use rates for these products.

B. TOXICOLOGY CONCERNS

Carcinogenicity

The HED Peer Review Committee classified permethrin (Sep 18, 1989) as a Group C carcinogen (possible human carcinogen) and recommended that quantitative risk assessments be performed based on the FMC mouse study using the dose-related increase in combined lung adenomas and /or carcinomas observed in females.

The Q_1^* based on the FMC mouse study for lung and liver tumors is 1.84×10^{-2} (mg/kg/day).

RfD

The RfD approved by the Agency RfD Committee is 0.05 mg/kg/day based on the FMC 2-yr rat feeding study with a NOEL of 5/mg/kg/day and a safety factor of 100.

Non-carcinogenic risk assessment

There are no other specific toxicity endpoints besides carcinogenicity and RfD discussed above.

Mutagenicity/genetic toxicity

The mutagenicity/genetic toxicity data base is considered incomplete and is being revised and updated.

C. PRIOR EXPOSURE REVIEWS

A review by David Jaquith dated 20 July 1989 Titled, "Preliminary Exposure Estimates for Permethrin", looked at the highest agricultural exposure rates for all permethrin products. Typical exposures were calculated, using surrogate data, for air-blast application to peaches, ground boom application to cotton and, aerial application to cotton. Each scenario evaluated results at a higher yearly use rate than the rate requested (1.6 lb ai/A/year). The exposure assessments are attached and summarized in Table 2.

TABLE 2

SCENARIO	Annual Dermal Exposure (mg/kg/yr)		
	MIX/LOAD	APPLY	TOTAL
Airblast / peaches 3.0 lbs ai/A/year	0.8 ¹	5.6	6.4
Ground boom / cotton 3.0 lbs ai/A/year	9.6 ¹	3.5	13
Aerial / cotton 3.0 lbs ai/A/year	9.6 ^{1,2}	0.11	--

1. A liquid formulation is assumed. Wettable powder formulations will yield slightly different values.
2. A work crew is assumed to treat one farm per day, 15 times per year. Commercial applicators may treat more than one farm per day.

D. Detailed Exposure Calculations

See D. Jaquith's detailed exposure discussions attached to this review.

III. CONCLUSIONS:

The worst exposure estimated from the application rate of 3.0 lbs ai/A/yr on cotton yields a yearly exposure of 13 mg/kg/yr for a person mixing, loading and applying permethrin. This exposure assessment results in an annual exposure of 0.035 mg/kg/day. Note that this exposure is based on the following assumptions:

- Individual workers weigh 70 kg,
- exposure represents material deposited on the skin, it does not factor inhalation exposure or dermal penetration.

OREB expects worker exposures (from the proposed label changes) to result in less exposure than estimated exposures stated above. Specifically, the exposures anticipated for the pistachio maximum season rate of 1.6 lb ai/A/yr (air blast) is expected to be less than the air blast application to peaches at the rate of 3.0 lb ai/A/yr. Additionally, the application rate of 0.2 lb ai/A to broccoli/cauliflower with a season maximum of 0.8 lb ai/A/yr is expected to yield less exposure than the ground boom or aerial application to cotton at the maximum rate of 3.0 lb ai/A/yr.

Attachment

CC: Correspondence File
Permethrin File (109701)

Appendix B. Exposure to Permethrin During Airblast Application to Peaches.

Assumptions: Average peach orchard is 20 acres (1).
Applied at maximum rate of 0.4 lbs ai/A/day.
Applied at maximum annual rate of 3.0 lbs ai/A/year
Application requires 2.7 hours per day, one day per application (1).
Applicator wears short sleeve shirt, long pants, no gloves.
Mixer/loader wears long sleeve shirt, long pants, and gloves.

Applicator Exposure:

$$\begin{aligned} \text{Days per year} &= \frac{3.0 \text{ lb ai/A/season}}{0.4 \text{ lb ai/A/day}} \\ &= 8 \text{ days/season} \end{aligned}$$

$$\begin{aligned} \text{Annual Exposure time} &= 8 \text{ days/season} \times 2.7 \text{ hrs/day} \\ &= 22 \text{ hrs/season} \end{aligned}$$

Using a linear equation derived from surrogate data (2) the annual exposure of a 70 kg applicator is:

$$\begin{aligned} \text{Annual Exposure} &= (4.8 \times 0.4 \text{ lb ai/A} + 16) \times 22 \text{ hrs/year} \times 1/70 \text{ kg} \\ &= 5.6 \text{ mg/kg/yr} \end{aligned}$$

Mixer/loader exposure (liquid formulation):

Lbs ai handled per year:

$$\begin{aligned} \text{Lb ai/yr} &= 20 \text{ Acres} \times 3.0 \text{ lb ai/A/year} \\ &= 60 \text{ lb ai/year} \end{aligned}$$

Using surrogate data from NDEB's database (3):

$$\begin{aligned} \text{Annual Exposure (mg/kg/year)} &= 60 \text{ lb ai/year} \times 0.93 \text{ mg/lb ai} \times 1/70 \text{ kg} \\ &= 0.8 \text{ mg/kg/year} \end{aligned}$$

If the same individual performs both tasks:

$$\begin{aligned} \text{Total Annual Exposure (mg/kg/year)} &= 5.6 \text{ mg/kg/year} + 0.8 \text{ mg/kg/year} \\ &= 6.4 \text{ mg/kg/year} \end{aligned}$$

Appendix C. Exposure to Permethrin During Ground Boom Application to Cotton.

Assumptions: Average cotton field is 241 acres (4).
 Applied at maximum rate of 0.2 lbs ai/A/day.
 Applied at maximum annual rate of 3.0 lbs ai/A/year
 Application requires 6 hours per day, during which
 81 acres are treated (4).
 Applicator wears a long sleeve shirt, long pants, no
 gloves.
 Mixer/loader wears long sleeve shirt, long pants,
 and gloves.

Applicator Exposure:

$$\text{Days per Application} = \frac{241 \text{ Acres}}{\text{Application}} \times \frac{1 \text{ day}}{81 \text{ Acres}}$$

$$3.0 \text{ days/application}$$

$$\text{Maximum Applications per season} = \frac{3.0 \text{ lb ai/A/season}}{0.2 \text{ lb ai/A/application}}$$

$$= 15 \text{ applications/season}$$

$$\text{Annual Exposure time} = \frac{15 \text{ applications}}{\text{season}} \times \frac{3 \text{ days}}{\text{Application}} \times \frac{6 \text{ hrs}}{\text{day}}$$

$$= 268 \text{ hrs/season}$$

Using surrogate data from NDEB's database (3) the annual exposure would be:

$$\text{Annual Exposure} = 268 \text{ hrs/year} \times 4.6 \text{ mg/hr} \times \frac{0.2 \text{ lb ai/A}}{1.0 \text{ lb ai/A}} \times \frac{1}{70} \text{ kg}$$

(mg/kg/year)

$$= 3.5 \text{ mg/kg/year}$$

Mixer/loader exposure (liquid formulation):

Maximum Lbs ai handled per year:

$$\text{Lb ai/yr} = 241 \text{ Acres} \times 3.0 \text{ lb ai/A/year}$$

$$= 723 \text{ lb ai/year}$$

Using surrogate data from NDEB's database (3):

$$\text{Annual Exposure} = 723 \text{ lb ai/year} \times 0.93 \text{ mg/lb ai} \times \frac{1}{70} \text{ kg}$$

(mg/kg/year)

$$= 9.6 \text{ mg/kg/year}$$

Appendix C (Continued). Exposure to Permethrin During Ground Boom Application to Cotton.

If the same individual performs both tasks:

$$\begin{aligned} \text{Total Annual Exposure} &= 3.5 \text{ mg/kg/year} + 9.6 \text{ mg/kg/year} \\ & \text{(mg/kg/year)} \\ &= 13 \text{ mg/kg/year} \end{aligned}$$

Appendix D. Exposure to Permethrin During Aerial Application to Cotton.

Assumptions: Average cotton field is 241 acres (4).
 Applied at maximum rate of 0.2 lbs ai/A/day.
 Applied at maximum annual rate of 3.0 lbs ai/A/year
 Pilots are exposed for 4.5 hours per day, during which
 241 acres are treated (4). NDEB notes that a commercial
 pilot may treat more than 1 farm on a given day.
 Mixer/loader wears long sleeve shirt, long pants,
 and gloves.

Pilot Exposure:

$$\begin{aligned} \text{Maximum Applications per season} &= \frac{3.0 \text{ lb ai/A/season}}{0.2 \text{ lb ai/A/application}} \\ &= 15 \text{ applications/season} \end{aligned}$$

$$\begin{aligned} \text{Annual Exposure time} &= \frac{15 \text{ applications}}{\text{season}} \times \frac{4.5 \text{ hrs}}{\text{day}} \\ &= 68 \text{ hrs/season} \end{aligned}$$

using surrogate data from NDEB's database (5) the annual exposure would be:

$$\begin{aligned} \text{Annual Exposure} &= 68 \text{ hrs/year} \times 0.08 \text{ mg/nr} \times \frac{0.2 \text{ lb ai/A}}{1.0 \text{ lb ai/A}} \times \frac{1}{70} \text{ kg} \\ &= 0.11 \text{ mg/kg/year} \end{aligned}$$

Mixer/loader exposure (liquid formulation):

Maximum Lbs ai handled per year:

$$\begin{aligned} \text{Lb ai/yr} &= 241 \text{ Acres} \times 3.0 \text{ lb ai/A/year} \\ &= 723 \text{ lb ai/year} \end{aligned}$$

Using surrogate data from NDEB's database (3):

$$\begin{aligned} \text{Annual Exposure} &= 723 \text{ lb ai/year} \times 0.93 \text{ mg/lb ai} \times \frac{1}{70} \text{ kg} \\ &= 9.6 \text{ mg/kg/year} \end{aligned}$$

REFERENCES

- (1) Memorandum from E.N. Pelletier (BUD) to D. Severn (EAB), titled "Report on Use Practice Data Relative to Daily Dinocap Exposure", dated 4 May 1984.
- (2) Reinert, J.C. and Severn D.J. (1985) Dermal Exposure to Pesticides - The Environmental Protection Agency's Viewpoint. IN:Dermal Exposure Related to Pesticide Use - Discussion of Risk Assessment R.C. Honeycutt, G. Zweig, and N.N. Ragsdale Eds, ACS Symposium 272, American Chemical Society, Washington, D.C.
- (3) Lunchick, C., G. Burin, J.C. Reinert, and K.E. Warkentien (1989) The Environmental Protection Agency's Use of Biological Monitoring Data for the Special Review of Alachlor. IN:Biological Monitoring for Pesticide Exposure, R. G. M. Wang, C.A. Franklin, R.C. Honeycutt, and J.C. Reinert Eds, ACS Symposium 382, American Chemical Society, Washington, D.C.
- (4) Memorandum from W. Gross (BUD) to D. Jaquith (EAB) titled "Transmittal of Application Exposure Information for Use of Monocrotophos on Cotton", dated 22 April 1985.
- (5) Lunchick, C. (1987) Draft Testimony for Dinoseb Cancellation Hearings.
- (6) Memorandum from K. Warkentien (EAB) to G. LaRocca (RD) titled "Inhalation Exposure for Permethrin", dated 29 April 1987.