11-6-92

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Risk Assessment for Permanone® 40MFG Concentrate (EPA Reg. No. 4816-552). DP No. 177983.

FROM: Stephanie Willett, Chemist SW 11/4/92
Registration Section
Chemical Coordination Branch
Health Effects Division (H7509C)

ABK. 11/6/92

THROUGH: Esther Saito, Acting Branch Chief ECS 11/6/92
Chemical Coordination Branch
Health Effects Division (H7509C)

TO: George LaRocca/Theresa LeMaster, PM Team 13
Registration Division (H7505C)

Roussel Uclaf has proposed to amend the registration of Permanone® 40 MFG Concentrate, which contains permethrin as the active ingredient. Permanone is to be factory applied to fabrics such as tents, shelters, truck coyers, awnings, hunting blinds, and netting at a rate of 1.25 g/$m^2$. OREB has provided an exposure assessment of the proposed label (see 10/26/92 memo of John Tice, DP183488). The toxicity data base is sufficient for HED to provide a risk assessment for the proposed use (see 9/15/92 memo of J. Doherty).

CONCLUSIONS

- The HED Peer Review Committee on Carcinogenicity has classified permethrin as a Group Cq carcinogen. The estimate of unit risk, $Q_1^*$, is $1.84 \times 10^{-2}$ mg/kg/day.
- The added cancer risk resulting from exposure to permethrin from proposed use of Permanone® 40 MFG is estimated to be $1.3 \times 10^{-6}$.



1

DISCUSSION

The proposed use of Permanone® 40 MFG concentrate was reviewed by OREB (see memo attached). Note that this review supersedes a previous review dated 10/8/92 by John Tice. According to this evaluation, the average daily dermal exposure to permethrin resulting from the proposed use is estimated to be 0.002 mg/kg bw/day. This estimate was not corrected for dermal penetration. Inhalation exposure is not a concern due to the low vapor pressure of permethrin.

The added cancer risk to persons handling materials treated with Permanone® 40 MFG may be estimated as follows:

$$\text{RISK} = \text{EXPOSURE} \times Q_1^*$$

EXPOSURE (LADD) = daily exposure x duration of exposure x absorption
= 0.002 mg/kg/day x 35 yr/70 yr x .07
= $7.0 \times 10^{-5}$ mg/kg/day

The dermal absorption estimate of 7% is based on (1) a rabbit dermal absorption study where 30 to 70% of permethrin was found to be absorbed (see TOX database), and (2) rabbit skin is 10 to 15 time more permeable than human skin.

Thus;

$$\text{RISK} = 7.0 \times 10^{-5} \text{ (mg/kg/day)} \times 1.84 \times 10^{-2} \text{ (mg/kg/day)}$$
$$= 1.3 \times 10^{-6}$$

Attachments: (1) J. Tice memo dated 10/26/92
(2) J. Doherty memo dated 9/15/92

cc: A. Kicoalski, Caswell File 652BB, S. Willett

Attachment 1

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

Revised

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

OCT 26 1992

**MEMORANDUM**

**SUBJECT:** Revised Permanone Fabric Treatment Exposure Evaluation

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

**TO:** Albin Kocialski, 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: D183488

Pesticide Chemical Code: 109701 (permethrin)

EPA Reg. No.: 4816-552 (Permanone 40 MFG Concentrate)

EPA MRID No.: 42280000-01

PHED: NO

**REFERRED TO CCB FOR RISK ASSESSMENT**

## I. INTRODUCTION:

Background/Purpose:

This review amends the Oct 8, 1992 review "Permanone Fabric Treatment Exposure Evaluation", DP Barcode D177983. Shortly after the registrant received this review, they noticed that the label did not reflect the correct application rate to treated fabric. The prior review contains a qualitative exposure assessment to fabric treated at the rate of 0.125 grams permethrin /$m^2$ (0.0125 mg/$cm^2$). The correct rate is 1.25 grams of permethrin/$m^2$ or 0.125 mg/$cm^2$. All other aspects of the label and use remain the same.

## II. DETAILED CONSIDERATIONS:

### A. Use:

The proposed uses remain the same. The uses results in minimal occasional contact with the active ingredient. Exposures will be estimated for persons handling treated tent material for 8 hrs. a day.

### 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 FCC mouse study using the dose-related increase in combined lung adenomas and /or carcinomas observed in females.

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

RfD

The RfD approved by the Agency RfD Committee is 0.05 mg/kg/day based on the FCC 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 end points 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

Numerous exposure reviews were completed for various use patterns. The table below lists the use patterns, maximum fabric concentration at application, and yearly exposures.

| Use Pattern/Application Rate | Max fabric concern-traction $mg/cm^2$ | Adult annual exp. mg/kg/day |
|---|---|---|
| Military use on clothing to repel or kill ticks/chiggers/ and mosquitos. 630 mg of permethrin are applied to clothing, 110 mg applied to mosquito netting and assumed to be in contact to treated clothing 365 days a yr. Curt Lunchick review 7/31/91. | 348 mg/17420 $cm^2$ = 0.02 | 0.0056 |
| Civilian use tick and insect repellent. Clothes treated every other day for 183 days. Evaluated by Curt Lunchick, 10/25/89, reevaluated on 12/12/90 (treatment changed to once a week for two months). | 0.01666 | 4.0 reevaluated to 0.00036 |
| Impregnated cotton balls used in pet rodent cages to control mites. Three balls handled per week by a child. J. Tice 7/17/92 | n/a | 0.00038 |
| Industrial carpet treatment applied at 0.3 mg ai/gram of wool. J. Tice, 4/17/92 | n/a | 0.0028 |

D. Detailed Exposure Calculations

**INHALATION**

In the data package submitted by the registrant, MRID # 42280001-01, Fairfield American calculated the equilibrium vapor concentration of permethrin. The calculations indicate the concentration at 70°F would be $7.8 \times 10^{-3}$ mg/m$^3$. With permethrin's low vapor pressure of $1.30 \times 10^{-13}$ Torr, inhalation is not a primary concern.

**DERMAL**

To calculate dermal exposure, the following assumptions are made:

- an individual's hands are in contact with treated fabric 8 hrs. a day for 220 work days a year.
- the surface area in contact with the treated material is 820 cm$^2$ (area of both hands,(Sub. Part U).
- canvas material is treated at the maximum label rate and there is no degradation of product over time.
- exposed handlers have an average body weight of 70 kg.
- exposures are not corrected for dermal penetration.

With a fabric concentration of 0.125 mg/cm$^2$, and 820 cm$^2$ of hands exposed, the theoretical maximum daily exposure will be 102.5 mg permethrin. Using the information that 4% of the permethrin migrates (in 7 days, 168 hours) from the treated fabric to the skin[1]; then 4% / 168 = 0.024% transfer per hour. Using the following formula, the maximum daily exposure then becomes:

*(Maximum daily exposure)* * *(Hourly Transfer Rate)* * *(8Hr Day)* = *Daily Exposure*

102.5 mg * 0.00024 * 8 hrs = 0.197 mg permethrin per day.

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[1] Migration of Permethrin from Impregnated Military Fabrics as Measured in Rabbits, Dated 11/30/88; MRID #407668-13.

The acute daily exposure is then calculated as 0.197 mg/70 kg or 0.003 mg/kg bw.

The annual average daily exposure is calculated as:

$$\frac{(\textit{DailyExposure}) * (220\ \textit{Days Exposed})}{365\ \textit{Days Per Yr}}$$

or (0.003 mg/kg * 220 days)/ (360 days) = 0.002 mg/kg bw/day.

## III. CONCLUSIONS:

OREB's conservative quantitative assessment for persons in contact with treated tent/tarp fabric, 8 hrs a day for 220 working days is as follows:

- acute daily exposure is 0.003 mg/kg bw.
- annual average daily exposure is 0.002 mg/kg bw/day.

Again note these estimates are not corrected for dermal penetration.

cc: George LaRocca, RD
Correspondence File
Permethrin File (109701)

Attachment 2

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA ID #004816-00552. Permethrin: Permanone 40 MFG Concentrate - request to amend label to include fabric treatment in the production of tents, shelters, truck covers, awnings, nettings, etc..

TOX CHEM No.: 652BB
PC No.: 109701
Barcode: D177983 (D182579)
Submission No.: S416902

FROM: John Doherty 9/15/92
Section IV, Toxicology Branch I
Health Effects Division (H7509C)

TO: Flora Chow, Section Head
Reregistration Section
Chemical Coordination Branch
Health Effects Division (H7509C)

THROUGH: Marion Copley, DVM, Section Head 9/15/92
Section IV, Toxicology Branch I
Health Effects Division (H7509C)

## I. CONCLUSION

The coordination of this proposed use of permethrin with exposure is deferred to Chemical Coordination Branch of Health Effects Division.

The product is currently registered. A copy of the Free Standing Toxicity Summary for permethrin is attached.

## II. ACTION REQUESTED

The Fairfield American Company is requesting to amend the label of their product Permanone 40 MFG Concentrate (EPA Reg. No.: 4816-552) to include use on fabrics such as tents and other materials.

III. Toxicology Branch Comments

1. No record of the review of the labelling is available in Toxicology Branch Files. TB-I defers to Registration Division for confirmation that the product was reviewed and that the signal word and precautionary statements are appropriate for this registered product.

# FREE STANDING TOXICITY SUMMARY - PERMETHRIN

**Toxicity Data Base:** Permethrin [Data provided jointly from the FMC and ICI Corporations, the Burroughs-Wellcome Co and/or the US Army.]

Tox Chem Number: 652BB
PC Number: 109701

| Series. Study Type | Study Available | Comment on study or significant finding[2] | Document Number[3] |
|---|---|---|---|
| 81-1. Acute oral - rats | A | Tox. Cat. III-IV | 1570 |
| 81-2. Acute Dermal - rabbits | A | Tox. Cat. IV | 1570 |
| 81-3. Acute inhalation - rats | A | Tox. Cat. IV | 5/10/76 |
| 81-4. Primary eye - rabbits | A | Tox. Cat. IV | 1570 |
| 81-5. Primary dermal - rabbits | A | Tox. Cat. IV | 1570 |
| 81-6. Dermal sensitization - guinea pig | A | Not a sensitizer (U.S.Army study). | 7624 |
| 81-7. Delayed neurotoxicity - hen | No | Not applicable | |
| 81-8. Special neurotoxicity - rat | No | Requirement pending. See also 82-7. | |
| 82-1a. Subchronic oral - rodent | 3 | NOEL/LEL = 100/500 ppm. Liver effects. NOEL = 20/100 ppm. Liver effects. NOEL/LEL = 20/100 ppm. Liver effects. | |
| 82-1b. Subchronic oral - nonrodent | A | NOEL/LEL = 50/364 mg/kg/day (capsule). CNS activity, liver and body weight effects. | |
| 82-2. 21-day dermal | A | NOEL = 1.0 gm/kg/day (HDT). U.S. Army study. | 1570 |
| 82-3. 90-day dermal | No | | |

| | | | |
|---|---|---|---|
| 82-4. 90-day inhalation - guinea pig<br><br>90-day inhalation - dogs<br><br>90-day inhalation - rat | S<br><br>S<br><br>S | NOEL > 500 ug/l/day (HDT)<br><br>NOEL > 500 ug/l/day (HDT)<br><br>NOEL/LEL = 250/500 ug/l/day. Tremors, convulsions, liver effects.<br><br>All are U.S. Army studies. | 1570 |
| 82-5. 90-day neurotoxicity - hen | No | Not applicable. | |
| 82-6 | | | |
| 82-7. Neurotoxicity screen rats<br><br>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.<br><br>No morphological lesions at 600 ppm (21 days feeding). NOEL < 4000 ppm for tremors, deaths at 9000 ppm. | 5946<br><br>8163 |
| 83-1a. Chronic feeding - rat | | See 83-5. | |
| 83-1b. Chronic feeding - nonrodent | 2 | NOEL/LEL = 5/100 mg/kg/day (capsule). Liver effects.<br><br>NOEL > 250 mg/kg/ay (HDT). | 3403 |
| 82-2a. Oncogenicity - rat | | See 83-5. | |
| 82-2b. Oncogenicity - mouse<br><br>[3 studies considered acceptable, one considered invalid] | A | NOEL/LEL = 100/250 ppm. Liver effects.<br><br>NOEL/LEL = 20/500 (males) and 2500/5000 ppm (females). Liver effects. Positive for lung and liver tumors.<br><br>NOEL ≥ 250 mg/kg/day (HDT). Considered positive for lung tumors at 250 mg/kg/day. | 8163 |
| 83-3a. Developmental toxicity - rat | A | NOEL/LEL = 50/150 mg/kg/day for both maternal and developmental toxicity (decreased fetal weight). | 8344 |



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| | | | |
|---|---|---|---|
| 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. Liver effects in pups. BOdy tremors in parents at 1000 and 2500 ppm and in pups at 2500 ppm.<br><br>NOEL > 180 mg/kg/day (HDT). | 8163 |
| 83-5. Combined chronic/onco - rat | 3 | NOEL < 500 ppm. Liver effects.<br><br>NOEL/LEL = 20/100 ppm. Liver effects. Equivocal for lung adenomas.<br><br>NOEL/LEL = 10/50 mg/kg/day. Liver effects. | 8163 |
| 84-2. Gene mutation | A | Ames test: Not mutagenic | |
| 84-2. Chromosome aberration | No | | |
| 84-2. Other mechanism genetic toxicity. | No | Unscheduled DNA systhesis: Not mutagenic | 8761 |
| 85-1. Metabolism - rata and dogs. | A | Several studies define absorption, excretion and retention of labelled permethrin. | 1660<br><br>7524 |
| 85-2. Domestic animal safety | | See formulations. | |
| 85-3. Dermal Absorption - rabbits | S | [U.S. Army study indicates 30-70% absorption.] | |
| 85-. Nerve function/operant behavior | No | Requirement pending | |

[1] 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 ACCEPTABLE 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 no date or document number, consult the one liners 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 $1.84 \times 10^{-2}$ (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.

6. Dermal penetration.

The U.S. Army has submitted a study which indicates 30 - 70% of permethrin may be absorbed through rabbit skin. This study is considered SUPPLEMENTARY and additional data are required to better establish the rate of penetration of permethrin through the skin. According to Robert Zendzian, pharmacologist HED, the dermal penetration factor of 3 to 7% is currently recommended for estimating human absorption of permethrin. This is based on human skin being about 1/10 as permeable as rabbit skin.