DP Barcode: D229055

OCT 3 1996

Case: 031340

MEMORANDUM

Subject: EPA File Symbol/EPA Reg. No.: 432-TOA/Aqua Permanone; Submission of Supplementary Information for Registration -- Missing Items from Earlier Review

From: Carol E. Glasgow, Ph.D., Toxicologist Carol
Precautionary Review Section
Registration Support Branch (7505W)
Registration Division (7505C)

To: George LaRocca, PM 13
Insecticide-Rodenticide Branch
Registration Division (7505C)

Applicant: AgrEvo Environmental Health
95 Chestnut Ridge Road
Montvale, NJ 07645

FORMULATION FROM LABEL:

Active Ingredient (s):	% by weight
Permethrin	20.0
Piperonyl butoxide, technical	20.0
Inert ingredient(s)	60.0

BACKGROUND: AgrEvo submitted additional information on three studies (acute dermal toxicity, primary eye and dermal irritation) on Aqua Permanone as required in a November 16, 1995 Agency letter. Original studies performed by MB Research Laboratories, Inc. and reviewed by Mrs. Lucy Markarian of PRS on 8/9/95. She rated the acute oral toxicity **Acceptable**, the acute inhalation and the dermal sensitization as **Unacceptable** and three studies **Supplementary** for lack of the following information:

acute dermal toxicity:	areas of application in measured units; the amount of test material applied per cm^2; thickness of gauze used for covering the application site
primary eye irritation:	method of evaluation, i.e., source of light and/or if magnification used
primary dermal irritation:	site and description of patch including thickness of patching material; confirmation of the size of application site; if the test material was applied to the skin directly; a description of the semi-occlusive dressing.

On April 22, 1996, AgrEvo submitted MB Research Laboratories, Inc.'s response with the information Mrs. Markarian had said was missing.

RECOMMENDATION: RSB/PRS findings are as follows:

The acute inhalation toxicity and dermal sensitization studies are **Acceptable**. See also previous review of D227078 for the **Supplementary** studies.

However, although the acute inhalation study meets the minimum MMAD, it is right on the borderline. With only 1 pre-trial study to evaluate aerosol generation, it is possible that other modifications might have been made to ensure the size of the MMAD at a lower level. The same is also true for the chamber humidity. This value is higher than desired, and as the product is a liquid, it is possible the humidity could not have been further decreased and still maintain the concentration, but an explanation for this would aid the evaluator. Nor were positive control animal weights reported in the dermal sensitization study. Animal bodyweight gain helps the researcher and the reviewer tell if the animals are healthy.

TOXICITY PROFILES

Acute oral toxicity	III	Acceptable
Acute dermal toxicity	IV	Acceptable
Acute inhalation toxicity	IV	Acceptable
Primary eye irritation	IV	Acceptable
Primary dermal irritation	IV	Acceptable
Dermal sensitization	No	Acceptable

LABELING: The signal word is "Caution," because of the III rating for acute oral toxicity. The following language should be included in the label:

INGREDIENT LABELING:

Contains Petroleum Distillate.

SIGNAL WORD: CAUTION

PRECAUTIONARY STATEMENTS:

Harmful if swallowed. Wash thoroughly with soap and water after handling.

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF SWALLOWED: Call a physician or Poison Control Center. Do not induce vomiting. Do not give anything by mouth to an unconscious person. Avoid alcohol.

The proposed label should contain the following guidance:

May pose an aspiration pneumonia hazard.

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DATA EVALUATION REVIEW FOR ACUTE INHALATION TOXICITY (§81-3)

Product Manager: 13 **Reviewer**: Carol Glasgow, Ph.D.
MRID No.: 440644-01 **Report Date**: May 28, 1996
Testing Laboratory: Stillmeadow Incorporated
Report No.: 2784-96
Author(s): Jerry Bennick
Species: HSD:Sprague-Dawley rat
Weight: males: 298 - 359 g, female: 220 - 260 g
Age: young adult
Sex: 5 males, 5 females
Source: Harlan Sprague Dawley, Inc., Houston, Texas
Test Material: RUC # 1320 (Aqua-Permanone 20-20) R96-135; white liquid
Quality Assurance (40 CFR §160.12): Included, acceptable

Summary:

1. **LC_{50}(mg/L)**: >2.87
2. **Toxicity Category**: IV
3. **Classification**: Acceptable

Procedure (Deviation from §81.3): Animals quarantined 5 days. Only one pre-screening trial was performed for deciding correct generation mechanism to reach appropriate particle size. Animals weighed before exposure on day of dosing and on days 7 and 14. Rats exposed to test substance for 4 hours with no food or water. Clinical observations taken every half-hour during exposure, upon chamber removal and daily thereafter. All animals necropsied.

Exposure conditions: chamber: temperature (68 - 71 °F), humidity (90 - 91 %) recorded every 30 minutes during exposure with a Taylor wet bulb/dry bulb hygrometer; ambient temperature (72 ± 5 °F), humidity (30 - 80%)

Exposure chamber: 500 L nose-only stainless-steel, dynamic flow

Particle size analysis performed and measured with an Andersen cascade impactor twice during exposure at a flow rate of 28.3 L/min for a duration of 1 minute.

Analytic samples taken once per hour from the breathing zone of animals during each exposure and measured with a Bausch & Lomb Spectronic 2000

Aerosol generated by 1/4" JSS atomizer (Spraying Systems Inc.), then elutriating the resulting aerosol through a 91 L baffling chamber, diluting with filtered air and drawing into exposure chamber.

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Air flow maintained at 22 L/min recorded every 30 minutes during exposure, with a rate of 11.8 air changes per hour, and was sufficient to maintain oxygen content at 19%. $T_{99} = 23$ min.

Results: No deaths occurred in this study, LC_{50} >2.87 mg/L, MMAD ranged from 3.855 - 4.077 μ, GSD from 1.916 - 2.189 μ. Clinical signs included activity decrease and piloerection in all rats from chamber removal through days 1 and 2. body weights in 1 male and 4 females decreased between days 0 and 7, and the other female lost weight in the following week, although not back to her original weight. No unusual findings at gross necropsy.

DATA EVALUATION REVIEW FOR DERMAL SENSITIZATION (§81-6)

Product Manager: 22 **Reviewer**: Carol Glasgow, Ph.D.
MRID No.: 440644-02 **Report Date**: June 17, 1996
Testing Laboratory: Stillmeadow Incorporated
Report No.: 2785-96
Author(s): Janice O. Kuhn, Ph.D., D.A.B.T.
Species: Hartley albino guinea pigs
Weight: males: 304 - 399 g, females: 310 - 376 g
Age: young adult
Sex: 12 males, 12 females
Source: SASCO, Inc., Madison, WI
Test material: RUC # 1320 (Aqua Permanone 20-20) Lot#: NB96: 130-52; white liquid
Positive Control: 1-chloro-2,4-dinitrobenzene: induction 1% w/v in 80% ethanol; challenge 0.45% w/v in acetone
Quality Assurance (40 CFR §160.12): Included, acceptable
Method: Buehler

Summary: **1. Toxicity Rating**: Non-sensitizer

2. Classification: Acceptable

Procedure (Deviation from §81.6): Animals acclimated 5 days. Four guinea pigs (2 M, 2 F) used to screen for the highest non-irritating concentration for treatment and challenge. Animals clipped on back of trunk and 4 sites on each animal were used for testing -- 2 on each side. Test material at 100%, 75%, 50% and 25% v/v concentrations in deionized water were tested. Induction and challenge dose of 100% chosen for 10 test animals (5M, 5F). On the day before each treatment, animals were clipped on back of trunk to expose 8 x 10 cm on each animal. Test substance (0.4 mL) introduced under a Coverlet dressing (3.8 x 5 cm gauze over adhesive patch), then overwrapped with clear polyethylene film and the animal placed in a restrainer. Animals removed from chambers and wrappings and patches removed after 6 hours exposure. Inductions performed on days 1, 8 and 15. Scoring was performed for all animals at 24 hours after treatment, and at 48 hours after the first induction and challenge treatments. Test substance challenge was 2 weeks after last induction on a virgin spot on the test animals, with 10 naive controls (5M, 5F). Body weights taken on days 0 and 28. **(Positive control animal weights not reported during this study.)** Scoring system included in study report.

Results: One male and one female developed erythema grades of 0.5 on the first induction at 24 hours, and a different male had 0.5 grade erythema at 24 hours challenge. No other effects seen on either test or naive control animals. Weight gain in animals adequate and positive control acceptable.

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