849A UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Cobourly

001972

SUBJECT: 1) Experimental Use Permit for Mertect 340-F (Thiabendazole)
2) Temporary tolerances for thiabendazole on sugar beets at 6 ppm.
3) Temporary food additive tolerances for thiabendazole on the following processed food and feed items:

DATE: SEP 30 1975

FROM:

TO:

sugar beet, molasses	40 ppm
sugar beet, sugar	0.50 ppm
sugar beet, dry pulp	50 ppm

TO: Ms. Libby Zink

FROM: TB

Reg. #: 618-EUP

Petition #'s: 5G1649, 5H5098

Formulation:

Active Ingredient: 2-(4-thiazolyl)-benzimidazole (thiabendazole)..... 42.28%

Inert Ingredients:..... 57.72%

[redacted]

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Tolerated as an inert under 40 CFR 180.1001 (c)

EPA Form 1320-6 (Rev. 6-72)

Recommendations:

1) TB recommends in favor of the proposed tolerances for raw sugar beets and sugar beet sugar.

2) Final decision on the proposed feed tolerances must await CB's reply to TB's deferral as to whether existing meat and milk tolerances will adequately cover the secondary residues resulting from this use.

3) For the final tolerance carcinogenicity studies in the rat and mouse (with particular attention paid to thyroid effects) will be required.

4) Teratogenicity and mutagenicity will also be required for the final tolerance.

The following acute data relates to the Mertect 340F formulation (Reg. # 618-TL(75))

I. Acute Studies

A. Acute Oral LD50 (mouse) - 3.05 (2.23-4.17) g/kg

Toxic signs: ptosis, ataxia, decreased activity and respiratory rate, tremors, convulsions.

B. Primary Skin Irritation

The green stain included in the formulation (0.1 ml) made it difficult to observe any erythema when the occlusive bandages were removed after 24 hours. However, a slight edema was seen at 24 hours in both the intact and abraded sites. At 48 hours a very slight erythema and edema was observed at both sites. Within 5 days, scaling of the skin was observed at both sites, but no irritation was noted. At 14 days all sites appeared normal.

C. Primary Eye Irritation

The green color of the formulation (0.1 ml) made the 1-minute reading impossible. At 15 minutes, a moderate injection of the conjunctiva which persisted for 2 hours was noted in all animals. Eyes appeared normal at 24 hours.

II. Chronic Studies

A. 2-Year Dog Feeding Study (Woodard)
NEL: 20 mg/kg based upon decreased body weight.

B. 2-Year Rat Feeding Study (Woodard)
NEL: not assigned due to increased thyroid weights at lowest level fed (males).

C. 5-Generation Mouse Reproduction Study
NEL: 30 mg/kg based upon decreased body weight of offspring.

III. Human Ingestion

The maximum allowable human daily intake for thiabendazole (TBZ) has been calculated to be 0.1 mg/kg (4 ppm in the diet) (see Dr. Shibko's memo in FAP# 5A-1701).

A double-blind human study was submitted with PP#0G1001. Normal male adults were given 250 mg of thiabendazole daily for 24 weeks. No side reactions, or physical or clinical findings related to the compound were reported.

Using the above ADI of 0.1 mg/kg, this represents an acceptable intake of 6 mg/day for the average 60 kg man. Residues of thiabendazole at the proposed level of 0.5 ppm on beet sugar would result in an average daily intake of approximately 0.047 mg TBZ, well below the calculated allowable intake.

TB defers to CB as to whether existing meat and milk tolerances will adequately cover the secondary residues resulting from this use. The final decision regarding the safety of the proposed tolerances in animal feed must await CB's reply.

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cc: Branch Reading File

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DMReisa:gac 9/30/75