SUBJECT: Thiabendazole, 2-(4-Thiazolyl)-benzimidazole, 0.1 ppm tolerance on soybeans. Mertect 340-F registration.

DATE: September 2, 1975

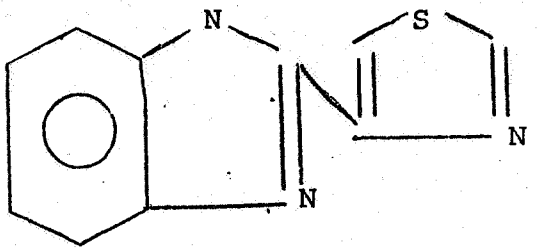
FROM: TB

TO: PM 21

Chemistry Branch OCT 2 1975

Petition No.: 5F1646 Registration No: 618-75 Merck Co.

Chemical Formula:



Formulation of Mertect 340-F:

	Percent by weight
Active Ingredient:	
2-(4-thiazolyl)-benzimidazole.....	42.28
Inert Ingredients:.....	[redacted]

INERT INGREDIENT INFORMATION IS NOT INCLUDED

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Conclusion:

1. Tolerance: Based on the extensive toxicity data on this product the tolerance of 0.1 ppm on soybeans can be supported, CB considerations permitting. (see rationale below; very important)
2. Registration: TB objects to the registration of Mertect-340-F. The registrant must submit dermal LD_{50} data.

Toxicological evaluation:

1. Tolerance: The toxicity data is submitted in a descriptive form without actual test results. These summaries are listed on the attached "Tolerance Toxicology Summary" sheet. At present there is only one life-time oral exposure study done on this product and a mutagenic evaluation is also missing. This product like any other will be subject to registration, at which time these defficiencies will have to be rectified or resolved. In the meantime however the tolerance on soybeans can be granted since the contribution of additional residues to the human diet can be virtually ruled out and tolerances exist on a number of actual diet items including milk. Furthermore the product shows very little toxic effects with NEL not less than 40 mg/kg/day. The product has also a long time use as ant-helmintic drug in man and animal. Since TB cannot conclude that the new requirements under Sect. #3 can be waived, even on a temporary basis (that is until the product is called in for reregistration) we defer our conclusion to Dr. Rogoff.

A translation of a French article "Embryotoxic properties in the rat, and residues in cattle and sheep, of three anthelmintics, derivates of benzimidazole" Bull. Soc. Sci. Vet. et Med. 76: 147-154 (1974) is attached to section C of this petition. It was shown, that only carbamate substituted benzimidazoles were embryotoxic and teratogenic for the rat but not thiabendazole. Thiabendazole, in fact, was used as a negative control, a dose of 80 mg/kg/day fed during the gestation period (day 8-15) was neither embryotoxic nor teratogenic, the carbamate substituted products on the other hand showed as much as 95% resorption and 100% anomalies of fetuses, at lower exposure levels.

2. Registration:

The toxicity data in support of the registration are also furnished in a narrative form (with exception of the oral LD50). Since the irritation of eyes and skin is minimal we can accept this type of evidence. Dermal Toxicity data (LD50) are, however, missing and we need evidence that the formulation is (also) not toxic via the dermal route. See TB objection.

Reto Engler
Toxicology Branch
Registration Division

cc: CB, EEEB, Branch File PP# 5F1646
Reg. No. 618-75

R/D Init: O.E. Paynter 9/2/75

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