

FREE SEARCH REVIEW

DATE: IN _____ OUT _____ IN 4/19/77 OUT 11/29/77 IN _____ OUT _____
FISH & WILDLIFE ENVIRONMENTAL CHEMISTRY EFFICACY

FILE OR REG. NO. 618-75

PETITION OR EXP. PERMIT NO. 6F1860

DATE DIV. RECEIVED _____

DATE OF SUBMISSION _____

DATE SUBMISSION ACCEPTED 3CID-28-Yes

TYPE PRODUCT(S): I, D, H, (F,) N, R, S _____

PRODUCT MGR. NO. 21 Wilson

PRODUCT NAME(S) Mertect 340-F

COMPANY NAME Merck

SUBMISSION PURPOSE New Use (soybeans)

CHEMICAL & FORMULATION Thiabendazole (2-(4-Thiazolyl) benzimidazole)

- 1.0 Introduction
- 1.1 Thiabendazole, Mertect
- 1.2 Percent Active: 42.28

Flowable Formulation

- 1.3 This is a resubmission for use on soybeans and a reply to a letter from EPA of 2/11/76. This submission has been in RD since 1973. Since then, many policy and personnel changes have occurred. A summary of this submission is warranted here so not to allow confusion via three groups (EC, PM, and Registrant). The first submission on 10/6/75, which was denied because EC data was either not referenced nor submitted. Of that review, protocol for EC data was submitted in March of 1976, and assessed by EC section personnel. We received a second submission for soybeans on 8/2/76--registration was denied for lack of (aged leaching, field soil, photodecomposition on soil surfaces, and effect of microbes on pesticides, sterile vs. nonsterile). On October 18, 1976, a letter was received from the registrant describing their views on the above deficiencies from a meeting in RD on 1/22/76 (we have a reply letter from EC section to that meeting). On March 30, 1977, we received from RD Director a request for an incremental risk analysis of thiabendazole for use on soybeans. This was completed on April 18, 1977. Lastly, we have a submission of protocol from the registrant for the deficiencies of 8/2/76, which is dated 2/8/77. We now have a resubmission (third time) that is dated 4/19/77. Pertinent policies for this review are Dr. Rogoff's memo to Mr. D. Campt of 8/12/77, and Mr. Johnson's memo of May 13, 1977.

- 2.0 Directions for Use

Soybeans: Apply Mertect 340-F at 6.0-10.0 fl. oz. per acre application in sufficient water for coverage. Make two applications per season, the first application at late flowering to early pod set and the second application two weeks later. Do not apply Mertect 340-F within 21 days of harvest. Do not tank mix with copper fungicides. Aerial applications should use a minimum of 5 gallons of water per acre.

2.1 Disposal

Do not apply when weather conditions favor drift. Keep out of lakes, ponds, or streams. Do not contaminate water by cleaning of equipment or disposal of wastes.

3.0 Discussion of Data

No new EC data submitted. Previously submitted data has not been validated per Dr. Rogoff's memo to Mr. Campt of 8/12/77.

4.0 Conclusions (General)

In view of the policy memo of Mr. Johnson to Mr. Campt to be implemented by RD personnel of May 13, 1977, the following scientific rationale is expressed:

A. Background--General Assumptions

The major mode of degradation is photolysis in H_2O (soil not established, although some argument is claimed that this is not a major route). The chemical is stable in H_2O , stable in soil ($t_{1/2}$ aerobically of ~403d, anaerobically ~279d), stable in plants (<2% degradative products), animal metabolism only adds glucuronide or ethereal sulfate to the intact structure (for excretion), it does not leach, bioaccumulate in fish, nor taken up into rotational crops (although soil photolysis products [if any] may negate these results/bioreactions. The mode of dissipation seems to be via bound residues (30-50%) in 15-30d. It also has high adsorption potential (low pH values). It is noteworthy that all soil-treated ranged in pH below 7.0 (4.8-6.8). The long $t_{1/2}$ in soil suggest two cases may be occurring: (1) The long delay (lag) in degradation suggests the compound is inherently resistant to attack (relatively few organisms in the soil have degradative ability) and the eventual degradation, at a slow rate, is either due to a long adaptation (inducement of enzymes) or to the emergence of mutants. (2) Little or no degradation implies that the compound may be utilized, although not necessarily in preference to other energy sources (one cannot discount the fact that facultative aerobic organisms may be utilizing the compound in the anaerobic pathways, low pH, or high adsorption).

Since the study showed very little $^{14}\text{CO}_2$ - evolved (0.4 to 7.0% after 157d); this precludes the emergence of mutants which would be rapidly growing (after formation) and evolving large amounts of CO_2 . The study was done in the dark precluding any help from phototrophs.

It is common knowledge that pesticide residues that adsorb to soil substantially preclude any/little biodegradation, and TBZ is highly adsorbed. The reason for this (little biodegradation) is that the substrate would be unavailable to microbial populations in sufficient quantity.

Since this chemical is a fungicide, it is doubtful any fungal interaction would contribute to the degradation and would in all probability be bacterial (also bacteria generally can outstrip filamentous fungi for sole carbon sources [in general]). These reactions may occur at a faster rate in conditions of increasing pH values (7 to 8.5 range).

B. Metabolism

Small trace amounts of Benzimidazole -2-carboximide have been found in soil. This may lead us to a start of the metabolism of TBZ. Chemoautotrophic and facultative aerobic organisms may cleave the [S] in the cyclopentadiene ring to form a mimic to tryptophan and eventually lead to indole, skatole type compounds, both of which are bacteriostatic in nature. Aerobically, this pathway would be different, either leading to catechol (via anthranilate) or to kynurenic acid. Since the aerobic pathway is much slower (soil metabolism) this route either does not occur or does not predominate. The formation of tryptophanase type enzymes is not available to a vast majority of microorganisms. (see metabolism chart--bacteria for details)

C. Theory

The chemical is inhibitory to bacteria at concentrations ~ 1.0 ppm. At concentrations of 10 and 20 ppm bacterial populations are effectively reduced (from $\sim 3.5 \times 10^6$ to < 10.0 in 2-7 days). The directions for use call for 6-10 fl oz/A, twice a year. This would put ~ 0.558 ppm/year at the highest rate recommended. Successive years of application could very well lead to loss of soil microbial functions (functional approach study would solve this).

4.1 Conclusions (specific)

Since the half-life in soil is 2400 days aerobically and leaching studies show TBZ not to leach, a (30 day) aged leaching study would not be needed. TBZ does not accumulate in fish, so that even if it did leach, ground water contamination hazard is minimal. Crop rotation studies show that TBZ is not taken up by rotational crops and we have a soil desorption study to show dissipation via bound residues (which can further be confirmed by adsorption, soil metabolism, and leaching data). We do not believe the field soil dissipation study is needed. Since the compound is stable in soil, both aerobically and anaerobically (with $^{14}\text{CO}_2$ evolved at 0.4-7.0 l/2 in 157d) an effects of microbes on pesticides study would only be supportive to the soil metabolism study at hand (in this case). In this case we would be interested in metabolic products of bacterial degradation and the effect on soil functions such as N_2 -fixation, etc.

We do believe that the photolysis on soil surface is needed because it may effect the leaching, dissipation, fish accumulation, and crop uptake (degradates may be unique). Since the registrant has satisfied the effect of pesticides on microbes (using the population approach) asking for the functional approach would be difficult, so we will ask it in a question form. This is further accentuated by the incremental ~~fish~~ ^{risk} analysis of May 30, 1977.

5.0 Recommendations

5.1 We do not concur with the proposed use on soybeans for TBZ.

5.2 The following data which are required (data gaps) were not made available or referenced.

- (1) Photolysis on soil surfaces.
- (2) Field soil study.
- (3) Aged leaching study.

- (4) Effects of microbes on pesticides, sterile vs. nonsterile. Of these four, we believe that with the data on hand, the characteristics of this chemical and scientific judgment the following is all that will be needed unless something unusual results from the study.

(a) Photolysis on soil surfaces.

PM NOTE - For further explanation see sections 4.1.

5.3 The following question needs to be answered;

- (1) What effect on soil functions (such as N₂-fixation, nitrification, cellulose, starch, pectin, and protein degradation) occur with successive (yearly treatment of TBZ).

PM NOTE - For further explanation see section 4.0(c).

5.4 PM NOTE - Registrant submitted acceptable protocol for photolysis on soil surfaces 8/23/77, so ^{we} do not feel that a protocol need be sent out, but a referral to this protocol submitted.

5.5 We note that the soils tested were all below pH 7.0. For uses that may be submitted in the future that utilize soils with pH values \geq 7.0, additional data may be required (adsorption, leaching, soil metabolism, dissipation, and crop uptake).

R E Ney
11/29/77

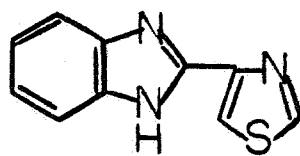
Robert F. Carsel
Environmental Chemistry Section
Efficacy and Ecological Effects Branch

Robert F. Carsel 12/12/77

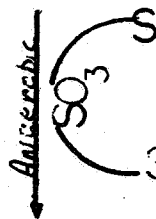
12/27/77 12/12/77

METABOLISM

Bacterial as proposed by EC Microbiologists
Speculatory, not confirmed by registrant data

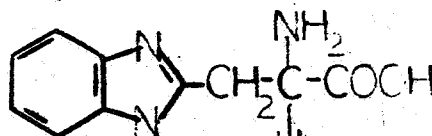


Thiabendazole

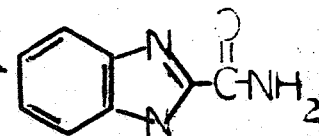


Organic Sulfur

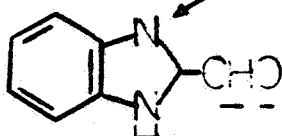
* Aerobic Minor if at all



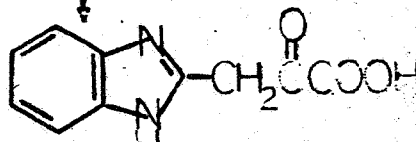
3-(2-benzimidazolyl)-alanine



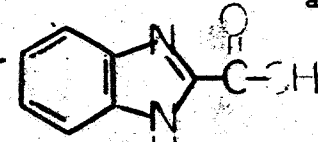
Benzimidazole-2-carb-
amide



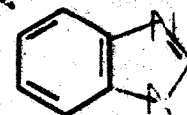
3-(2 benzimidazolyl)-aldehyde



3-(2 benzimidazolyl)-pyruvic



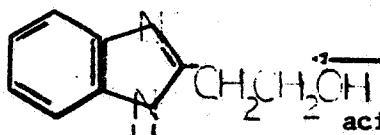
Benzimidazole-2-carboxylic acid



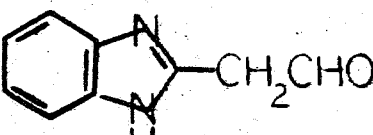
Benzimidazole

High adsorption of this compound may preclude any further breakdown

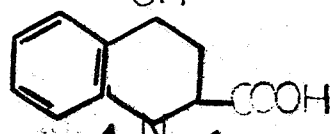
parent



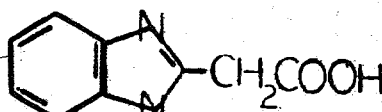
3-(2 benzimidazolyl)-propionic



3-(2 benzimidazolyl)-acetaldehyde)

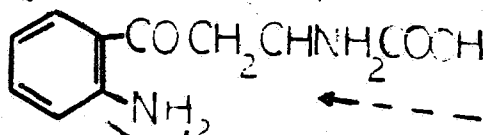


Kynurenine acid

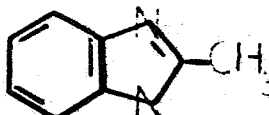


3-(2 benzimidazolyl)-acetic

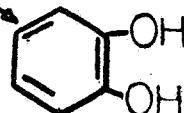
Anthracic Acid intermed.



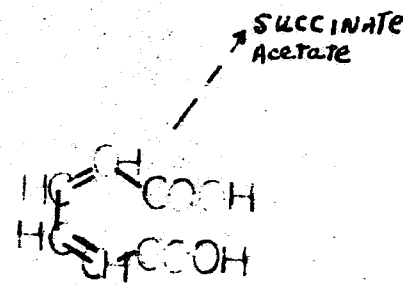
Kynurenine



Benzimidazole-2-methane



Catechol



→ SUCCINATE
Acetate

Sort Metk does NOT indicate

METABOLISM CHART

Thiabendazole

