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

JUL 25 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No. 618-67. Thiabendazole.
§63-8, -10, -16 Data Submitted in Response to DCI.
DEB#: 5400 MRID#: 408355-02
HED#: 9-1534 409473-01, -02

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TO: J. Ellenberger/R. Whitters, PM Team 50
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BACKGROUND

PM Team 50 has sent to DEB for review the following three product chemistry studies submitted to the Agency by Merck & Co., Inc., in partial response to the EPA Comprehensive Generic Data Call-In (DCI) Notice on Thiabendazole of 3/24/88.

- (1) "Thiabendazole - Determination of Solubility", Ricerca Document No. 1959-88-0144-AS-001, November 15, 1988. Guideline Reference No. 63-8. MRID# 409473-01.
- (2) "Thiabendazole - Determination of Dissociation Constant", Ricerca Document No. 1959-88-0145-AS-001, November 15, 1988. Guideline Reference No. 63-10. MRID# 409473-02.
- (3) "Thiabendazole: Explosibility Tests of 2-(4-thiazolyl) benzimidazole", Laboratory Project ID: HERC No. 88-47, August, 1988. Guideline Reference No. 63-16. MRID# 408355-02.

These data are summarized below, followed by DEB's comments/conclusions.

DISCUSSION

63-8: Solubility. A study (MRID# 409473-01) was conducted to determine the solubility of thiabendazole (technical grade) in methanol; acetone; chloroform; ethyl acetate; toluene; hexane; and, water at pH 5, 7, and 9.

Replicate saturated solutions of thiabendazole in each organic solvent (reagent grade) and water (HPLC grade) were equilibrated in a 25°C water bath for fixed time intervals (90.5-91 and 113-114 hours), centrifuged, and the supernatants analyzed by liquid chromatography (HPLC), and quantified by external standard calibration.

At equilibration, technical thiabendazole is soluble in each of the solvents at the concentration listed below.

<u>Solvent</u>	<u>Solubility</u> <u>(mg/ml @ 25°C)</u>
Methanol	8.72
Acetone	2.90
Chloroform	2.36
Ethyl Acetate	2.13
Toluene	0.195
Hexane	0.004
Water, pH 5	0.030
Water, pH 7	0.028
Water, pH 9	0.028

The concentration reported is the average value (2-3 duplicates per time interval, two time intervals, for a total of n = 8-12).

DEB concludes no further information is needed for this topic.

63-10: Dissociation Constant. A study (MRID# 409473-02) was conducted to determine the dissociation constant of thiabendazole (99.4% purity).

Stock solutions of thiabendazole were prepared in buffered solutions of various pH (3-6 and 10-13) and scanned (350-205 nm) on a recording spectrophotometer to measure the UV absorbance.

It was determined thiabendazole exhibits two acid-base transitions which are detectable in aqueous solution. Transition I (responsible for pK_{1a}) occurs over the pH range of ca 3-6, at which thiabendazole is acting as a weak base. Transition II (responsible for pK_{2a}) takes place between pH 10-13, during which thiabendazole functions as a very weak acid.

To summarize, thiabendazole exhibits two dissociation constants. The first, pK_{a1} , was determined to be 4.73 (based on the average of 17 measurements); the second, pK_{a2} , was determined to be 12.00 (based on the average of 15 measurements).

DEB concludes no further information is needed for this topic.

63-16: Explosibility. A study (MRID# 408355-02) was conducted to determine the explosibility of thiabendazole.

No positive reactions were observed as a result of the impact testing of thiabendazole from a drop height of 10 inches, and no exotherm was observed at a temperature $\leq 300^{\circ}\text{C}$ by differential scanning calorimetry (DSC).

Since no positive reactions for thiabendazole were observed, testing was discontinued.

DEB concludes no further information is needed for this topic.

CONCLUSIONS

1. Data on the solubility of thiabendazole in various organic solvents and water (pH 5, 7, 9) have been provided. No further information is needed for this topic (Guideline Ref. No. 63-8, Product Chemistry Guidelines - Subdivision D).
2. It was determined thiabendazole exhibits two dissociation constants; the pK_{a} s were reported. No further information is needed for this topic (Guideline Ref. No. 63-10, Product Chemistry Guidelines - Subdivision D).
3. No positive reactions for explosibility were noted as a result of the impact testing and DSC of thiabendazole. No further information is needed for this topic (Guideline Ref. No. 63-16, Product Chemistry Guidelines - Subdivision D).

cc: M. Nelson, Reading File, Circulation (7), Thiabendazole Subject File, R. Schmitt, ISB/PMSD (E. Eldredge).

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