MEMORANDUM

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

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TO: J. Ellenberger/R. Whiters, 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.


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

62-8: Solubility. A study (MRID# 409473-01) was conducted to
determine the solubility of thia bendazole (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 cali-
bration.

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

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

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.

62-10: 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 solu-
tions 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 transi-
tions 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, thiacarbendazol 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 thiacarbendazol.

No positive reactions were observed as a result of the impact testing of thiacarbendazol from a drop height of 10 inches, and no exotherm was observed at a temperature ≤ 300°C by differential scanning calorimetry (DSC).

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

DEB concludes no further information is needed for this topic.

CONCLUSIONS

1. Data on the solubility of thiacarbendazol 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 thiacarbendazol 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 thiacarbendazol. 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), Thiacarbendazol Subject File, R. Schmitt, ISB/PMSD (E. Eldredge).