

DATA EVALUATION RECORD

STUDY 1

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CHEM 102001                      Thiophanate-methyl                      §161-1

FORMULATION--00--ACTIVE INGREDIENT  
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STUDY ID 40095507

Nomura, O. 1986. Thiophanate-methyl: Hydrolysis. Laboratory Project ID EC-67. Unpublished study performed by Nippon Soda Co., Ltd., Kanagawa, Japan, and submitted by Pennwalt Corporation, Philadelphia, PA.

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STUDY ID 92186016

Soeda, Y. 1990. Phase 3 summary of MRID 40095507; thiophenate-methyl - Hydrolysis. Project EC-67. Prepared by Nippon Soda Co., Ltd., Kanagawa, Japan, and submitted by Pennwalt Corporation, Philadelphia, PA.

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DIRECT REVIEW TIME - 8  
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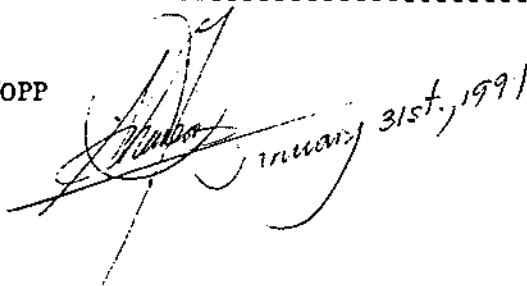
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January 31st, 1991

CONCLUSIONS:

Degradation - Hydrolysis

1. This study can be used to fulfill data requirements.
2. Thiophanate-methyl was stable at pH 5 and hydrolysed with half-lives of 36 and 0.7 days at pH 7 and 9, respectively, in sterile buffered solutions that were incubated in the dark at 22 C for 35 days. Two degradates, methyl 2-benzimidazolylcarbamate (MBC) and methyl N-[2-(thioureido)phenylaminocarbonothioyl]carbamate (AV-1951), were

identified in both the pH 7 and 9 solutions. The hydrolytic stability of thiophanate-methyl decreases with increasing pH.

From studies conducted at higher temperatures (45 and 65 C), it was shown that the hydrolysis rate of thiophanate-methyl was dependent on temperature, with the compound becoming less stable as the temperature increases.

3. This study is acceptable and fulfills EPA Data Requirements by providing information on the hydrolysis of thiophanate-methyl at pH 5, 7, and 9.
4. No additional information on the hydrolysis of thiophanate-methyl is required at this time.

#### METHODOLOGY:

Thiophanate-methyl (purity 99.6%, Nippon Soda), dissolved in acetone, was added at 10 ppm to sterile aqueous buffered solutions adjusted to pH 5 (0.05 M phthalate), pH 7 (phosphate, molarity unknown), or pH 9 (0.05 M borate). Aliquots of each test solution were placed in duplicate 50-mL Erlenmeyer flasks that were stoppered and maintained in the dark at 22 C. The pH 5 solutions were sampled at 0, 7, 14, 24, 31, and 35 days posttreatment. The pH 7 solutions were sampled at 0, 6, 10, 13, 20, and 33 days posttreatment. The pH 9 solutions were sampled at 0, 26, 48, 75, and 96 hours posttreatment.

Duplicate aliquots (5 uL) of each test solution were analyzed directly by HPLC using a solvent system of 40% acetonitrile in pH 3 phosphate buffer solution and UV detection (280 nm). The method detection limit was 0.004 ppm. Thiophanate-methyl and its degradates were quantified by comparing their peak heights to those of reference standards.

#### DATA SUMMARY:

Thiophanate-methyl (purity 99.6%), at 10 ppm, was stable at pH 5 and degraded with registrant-calculated half-lives of 36 and 0.7 days at pH 7 and 9, respectively, in sterile buffered solutions that were incubated in the dark at 22 C. In the pH 5 solution, thiophanate-methyl was an average of 9.81 ppm at 35 days posttreatment (Table 2). In the pH 7 solution, the thiophanate-methyl concentration declined to 5.96 ppm at 33 days posttreatment (Table 5). In the pH 9 solution, thiophanate-methyl declined to 4.72 ppm at 26 hours posttreatment and then to 0.65 ppm at 96 hours (Table 8). Two degradates,

methyl 2-benzimidazolylcarbamate (MBC) and

methyl N-[2-(thioureido)phenylaminocarbonothioyl]carbamate (AV-1951),

were identified in both the pH 7 and 9 solutions at all sampling intervals except immediately posttreatment. In the pH 7 solution, maximum average concentrations of MBC and AV-1951 were 2.86 and 0.81 ppm, respectively, at 33 days posttreatment (Table 5). In the pH 9 solution, MBC was a maximum of 5.87 ppm at 96 hours and AV-1951 was a maximum of 2.64 ppm at 75 hours posttreatment (Table 8). During the study, total thiophanate-methyl residues decreased from 9.77-10.06 ppm to 9.01-9.81 ppm (Tables 2, 5, and 8).

COMMENTS:

1. In order to identify possible degradates of thiophanate-methyl, a preliminary experiment was conducted. Thiophanate-methyl (purity 99.6%) was added at 30 mg to 500 mL of pH 5, 7, and 9 aqueous buffered solutions (described previously) that were subsequently incubated in the dark at 65 C for 4 days (pH 5), 4 hours (pH 7), or 2 hours (pH 9). Based on HPLC, TLC, and EI-MS analyses, three degradates were identified: MBC, AV-1951, and 2-aminobenzimidazole (2-AB). The data from this preliminary experiment were used for identification of possible degradates in the definitive study.
2. The pH 5 and 9 buffer solution concentrations were calculated by the Dynamac reviewer to be 0.05 M based on information provided in Table 1 of the registrant's study report (MRID 40095507). Sufficient information was not provided to determine the concentration of the pH 7 buffer solution. However, the concentrations of the buffer solutions were reported to be 0.01 M in the registrant's summary (MRID 92186016). Since more detailed information was provided in the study report, the concentrations calculated from Table 1 were reported in this review.
3. Additional data were provided for the hydrolysis of pH 5, 7, and 9 solutions incubated in the dark at 45 or 65 C. These data were not reviewed since the temperatures are not within the range of normal environmental temperatures. The half-lives for thiophanate-methyl at these temperatures are listed in Table 12.
4. The study author (Arrhenius equation) calculated half-lives of thiophanate-methyl at 25 C by interpolating the data obtained for the pH 5, 7, and 9 solutions incubated at 22, 45, or 65 C. Calculated half-lives at 25 C are listed in Table 12.
5. For the pH 5 solution, the study author calculated a half-life of 1179 days ( $2.83 \times 10^4$  hours) at 22 C. This statistical estimation is of limited value because the calculation involves extrapolation considerably beyond the experimental time limits of the study. Data are often incapable of accurately predicting trends outside of their range because small differences are magnified and reactions which appear linear may, in fact, be curvilinear. Therefore, the

calculated half-life value for the pH 5 hydrolysis solution was not included in the Data Summary section of this review.

6. The actual measured pH values for the buffer solutions at the initiation of the experiment were 5.03, 7.05, and 9.03 (Table 1). The study author stated that during the dark incubation, the pH values of the solution were not changed and no microbial contamination was observed.
7. The solubility of thiophanate-methyl in distilled water was reported to be 21.8 ppm at pH 5.2 and 25 C.