CONCLUSIONS:

Degradation - Hydrolysis

1. This study is acceptable and partially fulfills EPA Data Requirements for Registering Pesticides by providing information on the rate of hydrolysis of malathion in sterile aqueous buffered solutions at pH 5, 7, and 9, and on the identification of malathion degradates.

Since there is the possibility that the major malathion degradates (malathion monoester, ethyl hydrogen fumarate, and diethyl thiosuccinate) may be of environmental concern, additional hydrolytic data are required on the rate of hydrolysis of those degradates in sterile aqueous buffer solutions.
INTRODUCTION

Malathion is a non-systemic broadspectrum insecticide and acaricide registered for use to control aphids, spider mites, scale insects, and other sucking and chewing insects on terrestrial food crop, terrestrial nonfood, greenhouse food crop, greenhouse nonfood, aquatic food crop, aquatic nonfood, forestry, and indoor use sites. Single active ingredient formulations include dust, emulsifiable concentrate, oil solutions, and wettable powder.
2. EFGWB concludes that malathion is stable to hydrolysis at pH 5 and not stable at pH 7 and 9, since the study indicates that malathion hydrolyzed in sterile aqueous buffered solutions with calculated half-lives of 107 days at pH 5, 6.21 days at pH 7, and 11.8 hours at pH 9 incubated at 25 ± 1°C in the dark. The main degradates formed at pH 7 and 9 were monoethyl-[(dimethoxy phosphoro-thiolythio]-butanediolate (malathion monoester); (e)-2-butenedioic acid, monoethyl ester (monoethyl fumarate); and 2-thiobutanedioic acid, diethyl ester (diethyl thiosuccinate).

METHODOLOGY: Not applicable since no new study was submitted.

DATA SUMMARY: Taken from DER of EFGWB #90609 dated 3/2/90:

The author reported that recovery of radioactivity, based on the amount determined at Day 0, ranged from 90.5 to 101.9% (Tables 4-6).

The author reported that the calculated half-lives and rate constants at pH 5, 7, and 9 were respectively, 107 days, 0.00027 hour⁻¹; 6.21 days, 0.00463 hour⁻¹; and 11.8 hours, 0.0587 hour⁻¹ (Tables 1-3 and Figures 4-6). The half-life and rate constant at each pH level was calculated using a linear regression of the data according to the first-order rate equation: ln(C/Co) = -kt.

The author reported that hydrolysis at pH 5 proceeded too slowly to produce any products at a concentration >10% of the initial parent malathion (Table 7). However, malathion monocarboxylic acid ethyl ester, ethyl hydrogen fumarate and diethyl thiosuccinate (see Table of Compounds for structure of major products of malathion hydrolysis) were formed in the pH 7 and 9 solutions at concentrations >10% of the original malathion concentration (Tables 8 and 9 and page 6/66).

Radiolabeled components remaining at the origin of the TLC plates of the pH 7 experiment in some instances were >10% of the initial malathion concentration. The author reported that mass spectral analysis of this material showed a mixture of acidic components which were predominately diethyl thiosuccinate.

Figure 24 shows the pathway, as proposed by the author, for the formation of the hydrolysis products of malathion.

REVIEWER’S COMMENTS:

In a previous report (EFGWB, 3/2/90), the study "Malathion (AC 6,601): Hydrolysis Study" (MRID 40941201), was deemed to be scientifically sound, but did not meet Subdivision N guidelines because:

1. Sample calculations were not provided.

In response to this comment, the registrant has provided sample calculations. EFGWB accepts this response as resolving the original comment.
2. It was not specified whether samples were stored before analysis, and, if stored, sample storage stability data were not provided.

The registrant reported that the samples were analyzed immediately after collection, so storage stability data are not required. EFGWB accepts this response as resolving the original comment.

3. Information was not provided on how \(^{14}\text{C}\) residues adhering to the vessel walls were determined.

The registrant responded that during the hydrolysis study, aliquots of the test solutions were incubated in individual LSC vials, which were drained when sampled. The vial walls were then rinsed with methanol, liquid scintillation cocktail was added to the vials containing the methanol rinsate, and the "wall extracts" were radioassayed. EFGWB accepts this response as resolving the original comment.

4. Information was not provided on the pH of the test solutions at each sampling interval, or on how the initial pH was adjusted.

The registrant responded that the quantities of acid and base used to adjust the pH of the buffer solutions were not recorded. A table reporting the pH of samples at each sampling interval before and after adjustment was provided (Table I, see attached). The pH of the pH 5 buffer solution ranged from 4.70 to 5.16, the pH 7 buffer from 6.94 to 7.25, and the pH 9 buffer from 8.79 to 9.02. The pH adjustments are minor, and it is unlikely that the small fluctuations in pH and solution volume affected the behavior of malathion. EFGWB accepts this response as resolving the original comment.

5. The rate of decline of the major degradates was not determined.

EFGWB notes that to the registrant's credit, neither Subdivision N guidelines nor the SEP for Hydrolysis require that the rate of decline of the major degradates be determined; only determination of the rate of decline of the parent compound and the identification all degradates comprising >10% of the applied are required.

In response to the request for additional information, the registrant stated that the decline of the hydrolytic degradates of malathion (malathion monoester, monoethyl fumarate, diethyl thiosuccinate, malathion diacid, and malathion monoacid) was not addressed because little or no decline of these compounds was noted during the experiments. This is an accurate statement, since only diethyl thiosuccinate in the pH 7 solution and malathion monoester and monoethyl fumarate in the
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pH 9 solution appear to have begun to decrease at the final sampling intervals.

EFGWB does not accept this response as resolving the original comment, since further information on the decline of malathion degradates cannot be satisfied with the data in the present hydrolysis study. Additional hydrolysis experiments of longer duration or using the specific malathion degradates, as noted above, as the test substance will be needed to satisfy EFGWB concerns.
REPORTED RESULTS:

The author reported that recovery of radioactivity, based on the amount determined at Day 0, ranged from 90.5 to 101.9% (Tables 4-6).

The author reported that the calculated half-lives and rate constants at pH 5, 7, and 9 were respectively, 107 days, 0.00027 hour⁻¹; 6.21 days, 0.00463 hour⁻¹; and 11.8 hours, 0.0587 hour⁻¹ (Tables 1-3 and Figures 4-6). The half-life and rate constant at each pH level was calculated using a linear regression of the data according to the first-order rate equation: ln(C/Co) = -kt.

The author reported that hydrolysis at pH 3 proceeded too slowly to produce any products at a concentration >10% of the initial parent malathion (Table 7). However, malathion monocarboxylic acid ethyl ester, ethyl hydrogen fumarate and diethyl thiosuccinate (see Table of Compounds for structure of major products of malathion hydrolysis) were formed in the pH 7 and 9 solutions at concentrations >10% of the original malathion concentration (Tables 8 and 9 and page 6/66).

Radiolabeled components remaining at the origin of the TLC plates of the pH 7 experiment in some instances were >10% of the initial malathion concentration. The author reported that mass spectral analysis of this material showed a mixture of acidic components which were predominately diethyl thiosuccinate.

Figure 24 shows the pathway, as proposed by the author, for the formation of the hydrolysis products of malathion.

DISCUSSION:

EPGWS concludes that this study is scientifically sound. However, it does not satisfy the data requirement for this study for the following reasons:

1. Malathion, under the study presented here, hydrolysed to three major metabolites—malathion monoester, ethyl hydrogen fumarate, and diethyl thiosuccinate—that represents as much as 60 to 80% of applied malathion, at pH 7 and 9, respectively. However, the rate of decline and fate of these degradates is not discussed in the study.

Since there is the possibility that malathion monoester and some of the other hydrolysis products of malathion may be of environmental concern, the hydrolytic fate of these products must be addressed by the registrant before the study can be accepted as satisfying the data requirements.

2. More information is needed in relation to how much the pH of the solutions changed between pH measurements. Extreme changes
of pH either above or below the target pH values could have an impact on the rapidity of hydrolysis since it has been shown in this study that increasing pH resulted in increased hydrolysis.

3. There was no indication in the report how the radioactivity adhering to the vessel walls was determined. This information is needed to verify the material balance data reported.

4. Sample calculations should be provided to follow the mathematical equations used in the generation and analysis of the data contained in the report.

5. There was no information provided when samples were analysed in relation to when samples were collected. Storage stability data covering the length of time the samples were stored must be provided unless samples were analysed when taken.

6. EPGWB accepts this study as supplemental because of the noted deficiencies. The results of this study indicate that malathion is stable to hydrolysis at pH 5 and not stable at pH 7 and 9. While the study cannot be considered as satisfying the data requirement because of the deficiencies, the information needed to resolve the deficiencies is unlikely to change the conclusions drawn from the study.