UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

CHS#

385

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MEMORANDUM

SUBJECT: Mobay Requests for Data Substitutions and Time Extensions of Data Requirements for Trichlorfon

FROM: Herbert S. Harrison, Chief
Insecticide-Rodenticide Branch
Registration Division

TO: Douglas D. Campt, Director
Registration Division

BACKGROUND:

On July 19, 1984, the Agency mailed its Reregistration Guidance Package for Trichlorfon. The document was issued for manufacturing-use only products. There are eleven registered manufacturing use products involving five registrants. Only Mobay has submitted data to support the Standard.

Requests for Data Substitutions and Time Extensions

1. 90-Day feeding Study in the Rat (82-1)

The registrant has requested to substitute this data with data from their 2-year rat chronic feeding study. A time extension from June 1987 to March 1989 (the date the 2 year rat sudy will be completed) would also be necessary.

2. 90-Day Feeding Study in the Dog (82-1)

The registrant has requested to substitute this data, with data from their ten-year monkey feeding study. A time extension from June 1987 to December 1987 (the date, the ten-year monkey study will be completed) would also be necessary.

CONCURRENCES								
SYMBOL	TS-767	TS-767						
SURNAME	W. Miller	HHH						
DATE	2/6/86	2/6/86						

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*U.S. GPO : 1985-467-853

4 pages

3. 90-Day Dermal Rabbit (82-3)

The registrant has requested to substitute the 21-day dermal study since the 90-day study is only required, if the use involves purposeful dermal application or there is prolonged human exposure. Neither of these conditions occur from the recommended use patterns for trichlorfon.

4. 90-Day Inhalation Rat (82-4)

The registrant indicates that this study is only required when repeated inhalation is likely to occur at toxic levels. None of the labeled uses for trichlorfon products involve inhalation exposure that is likely to be toxic.

5. Combined 2-year Rat Chronic Feeding and Oncogenicity (83-1 and 83-2)

The registrant has requested an extension from June 1987 to March 1989. Three rat chronic feeding studies were previously submitted to EPA but were inadequate to satisfy regulatory data requirements because of procedural and reporting deficiencies. During preliminary work, in January 1985, on their trichlorfon mouse oncogenicity study, the registrant found that trichlorfon is not stable in rodent feed at room temperatures for a whole week. The registrant believes this extension request is justified on the basis that they only recently learned of the diet stability problem. Moreover, since they are now aware of the diet stability problem they plan to conduct confirming stability studies using the rats diet prior to intiating the study.

6. 2-year Chronic Feeding Study Dog (83-1)

The registrant has requested to substitute the data from a ten-year monkey feeding study. A time extension from June 1987 to December 1987 would also be required. The registrant believes this study should be an acceptable substitute for a chronic study in the dog. The duration of the study, ten-years is more than adequate to establish the chronic effects of trichlorfon. Furthermore, toxicity data in a non human primate is at least as useful for predicting effects on humans as data from dogs would be, if not more so. The final report from this monkey study should be available in December 1987. The monkey study was underway well before the registration standard was written and the registrant prefers not to adjust the protocol at this late date.

7. Oncogenicity Study in the Mouse (83-2)

The registrant has requested an extension from June 1987 to May 1988. The registrant believes this extension is entirely justified since their initiation of this study was delayed due to their findings from the 2-year chronic rat feeding study that trichlorfon is not stable at room temperature in the diet. This finding has necessitated additional feed stability work prior to initiating the study to assure that the diets of the animals were correctly prepared and stored.

Evaluation of Data Substitution and Extension Requests by HED/TB

1. TB recommends accepting the 90-day feeding study in the rat as part of the 2-year chronic rat feeding study.

2. TB has received an interim report on the Trichlorfon monkey study. Data provided in this submission should be adequate to determine subchronic effects and a NOEL for the required non-rodent species. TB does not usually review interim reports but rather the final report when submitted.

3. TB agrees that the 90-day dermal requirement can be replaced with a 21-day dermal study.

4. TB agrees that the 90-day inhalation is not required, because repeated inhalation exposure at toxic levels would not be expected. Additionally, TB has already reviewed a three week inhalation study in rats and determined that the study was valid.

5. TB notes the difficulties encountered with ingredient stability in an older rat feeding study. TB notes that the rat chronic feeding study will be combined with the oncogenicity study.

6. TB agrees that the 10-year monkey feeding study would adequately substitute for the non-rodent (dog) long-term feeding study.

7. TB notes the difficultuies encountered with ingredient stability in the older mouse oncogenicity study.

RECOMMENDATION:

Based on the registrant's justification and TB's concurrence, it is recommended that the requested data substitutions and time extensions be granted.

We hereby request that you concur with this recommendation.

CONCUR_____

DO NOT CONCUR_____

DATE_____