#MSD/ISB

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

DEC 5 1988

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: ID #352-366: Request for A Six-month Extension for Methomyl In A Livestock Metabolism Study. (DEB #4531)

FROM: W. T. Chin, Ph. D., Chemist
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Dietary Exposure Branch
Health Effects Division (TS-769)

THRU: Philip V. Errico, Section Head
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TO: Dennis Edwards, PM #12
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Registration Division (TS-767)

and

Toxicology Branch
Health Effects Division (TS-769)

BACKGROUND

According to the Agency's 3/30/87 3(c)(2)(B) letter, E. I. Du Pont de Nemours & Co. has to submit additional metabolism data of methomyl, methyl N-[[(methylamino)-carbonyl]oxy] ethanimidothioate, from food-producing animals in 18 months (before 9/30/88) including the identification of unknown metabolites in the cyclohexane soluble fraction from the goat liver as reported in AMR 22-80 (MRAD #63418). In addition, an EPA's call-in requested Du Pont to submit a cattle feeding study, before April, 1990, for the determination of the magnitude of secondary residues in livestock commodities. To met these requirements, Du Pont decided to conduct the scheduled cattle feeding study, but using ^{14}C-methomyl with the hope to met both requirements on time with one trial. However, due to the contractor's unanticipated scheduling problems, Du Pont requests a six-month extension, from 9/30/88 to 3/30/89.

RECOMMENDATION

In accordance with the guidance specified in PR Notice 85-5 on the Agency's policy for the granting of time extension for submitting required data, DEB has no objection to the six-month extension request for submitting additional methomyl metabolism and residue data from 9/30/88 to 3/30/89. However, DEB recognizes that the granting of a time extension request is an administration decision of the Registration Division.

DETAILED CONSIDERATIONS: Du Pont's 9/28/88 cover letter indicates:

1. According to EPA's 3/30/87 3(c)(2)(B) letter, Du Pont was requested to submit additional data within 18 months (before 9/30/88) on metabolism of methomyl in goat, specifically addressing the identity of unknown metabolites in the cyclohexane soluble fraction from the liver as reported in AMR 22-80 (MRID #00063418). Du Pont has proposed an in vitro goat hepatocyte metabolism study. However, EPA indicated that this might not be sufficient in replacing the requested goat metabolism study.

2. EPA's call-in requested a cattle feeding study, due April, 1990, to determine the magnitude of secondary residues in livestock commodities. The second phase of this data call-in is on schedule for April, 1990.

3. In lieu of repeating the goat metabolism study, Du Pont decided to conduct the scheduled cattle feeding study using ^{14}C labeled methomyl. This could provide sufficient data for both livestock metabolism and residue data.

4. Du pont unexpectedly found approximately 13 grams of freeze-dried goat liver from the original ^{14}C-methomyl goat metabolism study reported in AMR 20-80. Du Pont will use this sample to confirm the absence or presence of acetamide and to identify the unknown metabolites using new techniques and equipment that were not available in 1980.

5. Because of the contractor's unanticipated scheduling problems, the cattle feeding study did not start on time. Therefore, Du Pont requests a six-month time extension until 3/30/89. At that time, Du Pont will submit (1) liver metabolism data from the ^{14}C cattle feeding study; and (2) the characterization of the cyclohexane soluble metabolites from the original goat liver sample.

OTHER CONSIDERATIONS

The petitioner submitted the following two documents to describe the on-going studies:

1. Protocol: To Determine the Possible Bioaccumulation of Methomyl In Lactating Dairy Cows (Du Pont Study No. AMR-898-87, 3/9/88).

The first purpose of this study is to determine the magnitude of methomyl residues in edible tissues and milk generated from 12 lactating dairy cows treated with ^{14}C-methomyl at 0, 1X (= 8 ppm), 3X and 10X dose levels for 28 days. The second purpose is to study the metabolism of methomyl in livestock animals. Since this protocol was prepared for the trial proposed between January and February, 1988, it should have been officially reviewed. DEB concludes that this protocol was designed in accordance with EPA's Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry (§171-4) and considers it adequate for the proposed purposes.

2. Methodology: Determination of Acetamide (Methomyl Metabolite) in Cow Tissues (Ref.: CRP NB E45350 139-42, 8/2/88)

The purpose for developing this method is to determine acetamide in cow tissues during the above-mentioned cattle feeding study. It is a capillary GC method equipped with a NPD detector. The detection limit of this method is approximately 0.1 ppm acetamide. Using this method, the presence of naturally occuring acetamide in cow tissues was confirmed by GC/MS. Examples of calculation and GC chromatograms are adequately submitted. DEB considers this method adequate for the expected purpose.

Because these are on-going studies, DEB will not further comment on the content of these documents, but will place them in DEB's files.

cc: R.F., Circu., W.T.Chin and PMSD-ISB

RDI: P.V.Errico(12/2/88), R.D.Schmitt(12/2/88)
TS-769: RCB: CM#2, RM812,557-4352, W.T.Chin,wc(12/5/88)