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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAY 15 1990

MEMORANDUM

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PROPACHLOR - NUMEROUS WAIVER REQUESTS IN RESPONSE TO REGISTRATION STANDARD

TO: HUNDEMANN
PRODUCT MANAGER (74)
REGISTRATION DIVISION (H7505C)

FROM: LINDA L. TAYLOR, PH.D. Linda Lee Taylor 5/7/90
TOXICOLOGY BRANCH II, SECTION II
HEALTH EFFECTS DIVISION (H7509C)

THRU: K. CLARK SWENTZEL K. Clark Swentzel 5/7/90
SECTION II HEAD, TOXICOLOGY BRANCH II
HEALTH EFFECTS DIVISION (H7509C)

MARCIA VAN GEMERT, PH.D. Marcia van Gemert 5-7-90
CHIEF, TOXICOLOGY BRANCH/HFAS/HED (H7509C)

WILLIAM L. BURNAM
DEPUTY DIRECTOR, HED (H7509C) 5/7/90

REGISTRANT: MONSANTO AGRICULTURAL COMPANY
CHEMICAL: 2-CHLORO-N-ISOPROPYLACETANILIDE
SYNONYM: PROPACHLOR, RAMROD
PROJECT NO.: 0-1057
CASWELL NO.: 194
RECORD NO.: 262620
IDENTIFYING NO.: 524-310
MRID NO.: NOT APPLICABLE
ACTION REQUESTED: BILL BURNAM REQUESTED A BEAN SHEET FOR NUMEROUS WAIVER REQUESTS MADE BY MONSANTO. PLEASE EXPEDITE PROCESSING THESE REQUESTS.

COMMENT: IN A LETTER DATED APRIL 3, 1985, THE REGISTRANT POINTED OUT SEVERAL "ERRORS" IN THE GUIDANCE DOCUMENT FOR REREGISTRATION OF PROPACHLOR. THIS MEMO RESPONDS ONLY TO THOSE REGARDING TOXICOLOGY.

WITH REGARD TO THE REQUESTS FOR CHANGES IN DUE DATES FOR REQUIRED STUDIES, THE DEADLINES REQUESTED HAVE ALREADY PAST AND, IN MOST CASES, THE STUDIES HAVE BEEN SUBMITTED. THEREFORE, NO COMMENT ON CHANGES IN DUE DATES WILL BE MADE.

1) UNDER 3. A., THE REGISTRANT STATED THAT ACUTE INHALATION AND 90-DAY INHALATION STUDIES ARE INCORRECTLY REQUESTED, AND VARIOUS REASONS FOR THIS DETERMINATION WERE DISCUSSED.

TB II RESPONSE: AN ACUTE INHALATION STUDY WAS SUBMITTED (REPORT DATED 5/12/86; SUBMITTED 10/9/86; STUDY # BD-85-122; ACCESSION/MRID #265531; FORWARDED TO

TB II 2/16/90) AND IS CURRENTLY UNDER REVIEW. THE TEST MATERIAL IS RAMROD 4L 42.5 % PROPACHLOR. AN ACUTE INHALATION STUDY ON THE TECHNICAL PRODUCT IS A REQUIREMENT, AND A WAIVER CANNOT BE GRANTED. IT IS UNCLEAR TO THIS REVIEWER WHY THE 90-DAY STUDY WAS LISTED AS A REQUIREMENT; HOWEVER, THIS MAY HAVE BEEN LISTED AS A REPLACEMENT STUDY FOR THE IBT 90-DAY INHALATION STUDY THAT WAS INVALID. TB II HAS NO WORKER-EXPOSURE INFORMATION WITH WHICH TO DETERMINE WHETHER FURTHER INHALATION TESTING IS NEEDED. FROM THE AVAILABLE INFORMATION, A 90-DAY INHALATION STUDY IS NOT A REQUIREMENT AT THIS TIME.

2) UNDER 3. B., IT IS STATED THAT THE GUIDANCE DOCUMENT REQUIRED A DERMAL SENSITIZATION STUDY IN RABBITS.

TB II RESPONSE: THERE IS A DERMAL SENSITIZATION STUDY ON PROPACHLOR IN THE GUINEA PIG, WHICH WAS RECEIVED BY THE AGENCY IN DECEMBER, 1984 AND ACKNOWLEDGED IN THE DOCUMENT. IT IS NOT CLEAR TO THIS REVIEWER WHY A STUDY IN RABBITS WAS REQUESTED. A WAIVER OF THIS REQUIREMENT CAN BE GRANTED. THE GUINEA PIG STUDY ON PROPACHLOR FULFILLS THIS DATA REQUIREMENT.

3) UNDER 3. C., THE REGISTRANT STATED THAT A 90-DAY DERMAL STUDY WAS INCORRECTLY LISTED AS REQUIRED AND INDICATED THAT PROPACHLOR DOES NOT MEET THE CRITERIA FOR SUCH A STUDY. ADDITIONALLY, AS NOTED BY THE REGISTRANT, A 21-DAY DERMAL STUDY SHOULD HAVE BEEN CONDITIONALLY REQUIRED FOR PROPACHLOR.

TB II RESPONSE: TB II CONCURS WITH THE REGISTRANT. INFORMATION REGARDING WORKER EXPOSURE IS NEEDED BEFORE TB II CAN DETERMINE WHETHER A 21-DAY DERMAL STUDY IS REQUIRED.

4) UNDER 3. D., THE REGISTRANT STATED THAT AN AMENDMENT SHOULD BE MADE REMOVING THE ADDITIONAL RABBIT TERATOLOGY STUDY AS A REQUIREMENT.

TB II RESPONSE: ALTHOUGH THERE IS A RABBIT TERATOLOGY STUDY AVAILABLE (ACCESSION NO. 255758), IT DOES NOT FULFILL THE DATA REQUIREMENT FOR SUCH A STUDY. THE STUDY IS CLASSIFIED: SUPPLEMENTARY SINCE NO NOEL FOR DEVELOPMENTAL TOXICITY WAS OBSERVED; THE STUDY MUST BE REPEATED.

5) THE REGISTRANT REQUESTED THAT THE IN VITRO CYTOGENETIC DAMAGE STUDY NOT BE A REQUIREMENT AND THAT THE DOMINANT LETHAL STUDY BE MADE A CONDITIONAL REQUIREMENT PENDING THE OUTCOME OF OTHER MUTAGENIC STUDIES.

TB II RESPONSE: THERE ARE TWO ACCEPTABLE MUTAGENICITY STUDIES AVAILABLE AT THIS TIME ON PROPACHLOR (GENE MUTATION STUDY AND A CHROMOSOMAL ABERRATION ASSAY). THE UDS ASSAY IS CLASSIFIED AS UNACCEPTABLE, PENDING SUBMISSION OF DATA ON WHETHER THE PROPACHLOR USED WAS TECHNICAL GRADE. THE RAT BONE MARROW CYTOGENETIC ASSAY IS UNACCEPTABLE PENDING JUSTIFICATION OF THE DOSE LEVELS UTILIZED. IT IS NOT APPARENT TO THIS REVIEWER WHY THESE TWO STUDIES WERE SPECIFICALLY REQUESTED, UNLESS THEY WERE REPLACEMENT STUDIES FOR IBT DATA. SINCE REPRESENTATIVE TESTS WITHIN EACH OF THE THREE CATEGORIES HAVE BEEN PERFORMED, PENDING SUBMISSION OF INFORMATION TO UPGRADE THOSE CLASSIFIED UNACCEPTABLE, NO FURTHER MUTAGENICITY TESTING IS REQUIRED AT THIS TIME.

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6) THE REGISTRANT STATED THAT A GENERAL METABOLISM STUDY WAS INCORRECTLY LISTED AS REQUIRED, SINCE THERE ARE EXTENSIVE DATA IN THE LITERATURE THAT ADEQUATELY DESCRIBE THE METABOLISM OF PROPACHLOR.

TB II RESPONSE: THIS REQUIREMENT IS NOT INCORRECT, SINCE METABOLISM INFORMATION IS REQUIRED WHEN CHRONIC DATA ARE REQUIRED. HOWEVER, IT IS NOTED THAT THE REGISTRATION STANDARD STATED THAT: "ADDITIONAL PROTOCOL DATA FOR THE GENERAL METABOLISM STUDY IN MAMMALS ARE REQUIRED", WHICH SUGGESTS TO THIS REVIEWER THAT METABOLISM DATA WERE AVAILABLE, BUT THAT CLARIFICATION WAS NEEDED AS TO HOW THE STUDY WAS PERFORMED. THE DATA (PUBLISHED STUDIES) MENTIONED HAVE BEEN SUBMITTED (FORWARDED TO TB II 2/16/90) AND ARE CURRENTLY UNDER REVIEW.

7) THE REGISTRANT STATED THAT A DOMESTIC ANIMAL SAFETY STUDY WAS INCORRECTLY LISTED AS REQUIRED.

TB II RESPONSE: SINCE PROPACHLOR IS NOT LABELED FOR SUCH USE, A STUDY IS NOT REQUIRED.