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

008586

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

August 28, 1991

MEMORANDUM

SUBJECT: PP #9F3755/FAP #0H5594: Quinclorac - The Use of FACET® Herbicide on Rice - Submission of Additional Data on a 2-Generation Reproduction Study (BASF #88/0321)

Shaughnessy No.: 128974
Tox Chem. No.: 325A
Project No.: 1-1530
MRID No.: 419100-01

FROM: William B. Greear, M.P.H. William B. Greear 8/28/91
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Health Effects Divison (H7509C)

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THRU: Marion P. Copley, D.V.M., Section Head Marion Copley 8/28/91
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I. CONCLUSIONS:

The 2-generation reproduction study (BASF #88/0321; 7/21 88) is upgraded to Core-Minimum Data and satisfies the Guideline Requirements for a 83-4 2-Generation Reproduction Study.

II. REQUESTED ACTION:

Under a cover letter dated June 12. 1991, Bob Rohde of the BASF Corporation has submitted additional data on food consumption and individual clinical observations as a supplement to the original 2-generation reproduction study.

III. DISCUSSION:

The sponsor has responded to several deficiencies noted in the 2-generation reproduction study in two-separate submissions

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[Proj. Nos. 1-1323 (6/15/91) and 1-1530(6/12/91)]. The items are discussed below:

Report on the Reproduction Study with Registration No. 150-732 in Rats; Continuous Dietary Administration Over Two Generations (Two Litters in the First and One Litter in the Second Generation (BASF #88/0321, 7/21/88)).

Proj. No. 1-1323, (BASF #91/5037, May 14, 1991; MRID # 418742-01)

Dynamac Comment No. 1: The sponsor should submit data on the stability of test material in the diet.

BASF Response: In a 4-week feeding study in rats, the stability of the test material at a level of 40 ppm in the diet was demonstrated when stored over a 30-day period at room temperature. All "concentration control" analyses were provided in the initial submission.

TB-I Response: The 30-day stability analysis of the diet containing 40 ppm of the test material is adequate in lieu of data determined for the concentrations that were actually used in the study. The concentration of quinclorac in the 40 ppm mixture was 41.3 ppm at 30 days. The data on the "concentration control" analyses are not meaningful with respect to stability analysis without further explanation such as the length of storage, if any.

Dynamac Comment No. 2: Culling of litters on day 4 postpartum was not conducted.

BASF Response: The study was conducted according to EPA/FIFRA and OECD Testing Guidelines. EPA/FIFRA guidelines recommend culling whereas OECD guidelines do not. The rearing of litters without culling does not compromise the scientific or regulatory validity of the study.

TB-I Response: TB-I agrees.

Dynamac Comment No. 3: The sponsor should have submitted individual animal data on food consumption with a statistical analysis of the data.

BASF Response: Individual animal data (in the form of tables) for food consumption during the premating period (males 70 days; females 98 days) are herein submitted. There are minor and rare deviations between

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the mean values presented here. These deviations are directly related to the method by which missing values were handled in the summation. Missing values were estimated via linear interpolation. During the period between premating and gestation, the method for recording data was changed from a magnetic tape recording system to a manually recording system.

All individual food consumption data have been included in the raw data (German, no translation) but are not presented in the report. However, EPA/FIFRA does not specify as to when and how often food consumption should be measured in a two-generation study. In addition, food consumption values taken during the later phase of the lactation period give no real information since pups already start to eat the diet.

TB-I Response: The food consumption data for both premating periods are acceptable and adequately reflect the results that were summarized in the initial submission. TB-I will examine the individual animal data during gestation and lactation when it is submitted in the appropriate form. It is noted that a statistical analysis of these data was not submitted. However, this is a minor deficiency that will not impact on the acceptability of the study.

Dynamac Comment No. 4: Clinical observation and data were not presented.

BASF Response: All relevant clinical findings were discussed in the report of the two-generation study. BASF is currently in the process of translating and tabulating the individual clinical findings. The data will be forwarded to EPA in 4 to 6 weeks.

TB-I Response: TB-I will examine the data when they are made available.

Dynamac Comment No. 5: The study was conducted according to OECD GLPs and not EPA GLPs.

BASF Response: All relevant study data will be retained for longer periods than those specified by EPA.

TB-I Response: BASF's response is acceptable.

Proj. No. 1-1530 (BASF #91/10229, May 16, 1991; MRID # 419100-01)

The sponsor has submitted individual animal data on clinical signs and on food consumption of females during gestation and lactation (English translation). The data are acceptable and adequately reflect the results summarized in the original study.

Summary: The study is upgraded to Minimum Data and it satisfies the requirement for a 2-generation reproduction study.

Results: Doses: 0, 1000, 4000 and 8000 ppm (0, 40, 160 and 480 mg/kg/day)
Route: Oral in the diet. Strain: Wistar [Chbb-THOM(SPF)]
Maternal NOEL = 4000 ppm (160 mg/kg/day).
Maternal LEL = 12000 ppm (480 mg/kg/day) based on reduced body weights.
Develop. NOEL = 4000 ppm (160 mg/kg/day).
Develop. LEL = 12000 ppm (480 mg/kg/day) based on reduced pup viability and pup weight, and delay in development, i.e., pinna unfolding and eye opening)

[Note: This memorandum is in place of a supplemental DER and the results and Doc. No. should be entered on the one-liners with the new BASF Nos.(date)/MRID Nos.: 91/5037 (5/14/91)/418742-01; 21/10229 (5/14/91)/419100-01 . The original review reported in Doc. No. 008161.

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