8-23-90
00 8097

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

Aug. 8/23/90

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP #9G3797/FAP #0H05594 - Quinclorac; Application for an Experimental Use Permit and Temporary Tolerance for the Use of FACET 50 WP Herbicide in/on Rice (EPA ID # 7969-EUP-25) **(EXPEDITED REQUEST)**

Tox. Chem. No.: 325A
Project No.: 0-1835
Case No.: 194449
Submission No.: S380950

FROM: William B. Greear, M.P.H. William B Greear 7/10/90
Review Section II, Toxicology Branch I
Health Effects Division (H7509C)

TO: Vickie Walters/Robert J. Taylor, PM Team #25
Herbicide-Fungicide Branch
Registration Division (H7505C)

THRU: Marion P. Copley, D.V.M., Section Head,
Review Section II, Toxicology Branch I
Health Effects Division (H7509C)

I. Conclusions:

The toxicological data base is adequate and will support the Experimental Use Permit (EUP) for use in/on rice and the associated temporary tolerances.

II. Requested Action:

Under a cover letter dated August 23, 1990, Bob Rohde of the BASF Corporation has submitted additional, requested information on three toxicological studies which were found to be deficient by Toxicology Branch I (TBI) as indicated in TBI's memorandum of August 10, 1990. The information is necessary in order to complete the toxicological data base required to support an EUP with associated temporary tolerances. The studies are as follows:

83-3 Report on the Study to Determine the Prenatal Toxicity of Reg. No. 150 732 in Rats after Oral Administration (gavage). Dr. J. Hellwig. May 12, 1987. BASF Reg. Doc. No. 87/0167. pp. 284. MRID 41063524

10-5

1

84-2 Report on the Study of Reg. No. 150 732 in the AMES Test (Standard Plate Test with Salmonella typhimurium) dated May 4, 1984. Dr. rer. nat. J. Engelhardt. BASF Reg. Doc. No. 84/0156. pp 26. MRID 41063527

84-4 Report on the Evaluation of Reg. No. 150 732 (ZNT No. 84/150) In Vitro Rat Primary Hepatocyte Unscheduled DNA Assay. Maria A. Cifone. June, 1986. BASF Reg. Doc. No. 86/0135. pp. 24. MRID 41063531

III. Consideration:

Each study will be listed followed by 1) TBI's initial comments specifying the deficiencies in the study, 2) BASF's response to the deficiencies and 3) TBI's conclusions as to the acceptability of the response and final assessment of the study.

Study #1: 83-3 Report on the Study to Determine the Prenatal Toxicity of Reg. No. 150 732 in Rats after Oral Administration (gavage). Dr. J. Hellwig. May 12, 1987. BASF Reg. Doc. No. 87/0167. pp. 284. MRID 41063524

TBI's Comment:

Because of the absence of supporting data regarding the concentration and stability of dosing solutions, the NOEL and LEL could not be determined and the study is Core-Supplementary.

BASF's Response:

An analytical report dated 3/13/85 signed by Pawliczek indicates that dosing solutions with target concentrations of 438, 2920 and 8760 mg/100 ml had mean values of "501, 2.919 and 8.761%" when analyzed 3 days after preparation. A second report for the period 3/12 - 3/15/85 gave mean values of 486.3, 2906.8 and 8526.5 mg/100g for target concentrations of 488, 2920 and 8760 mg/100 ml. (The signature with date was illegible).

TBI's Conclusion:

[TBI believes that an error was made in the first analytical report in that the target concentration reported to be 438 mg/100 ml was probably 488 mg/100 ml as indicated by the mean analytical concentration of 0.501%.] The two reports adequately define the concentrations of the dosing solutions and indicate that the test substance in 0.5% carboxymethlycellulose is stable for at least 3 days. TBI's concerns are satisfied.

2

The study is therefore upgraded to Core-Minimum. The NOEL and LEL are as follows:

NOEL (maternal toxicity) = 146 mg/kg
LEL (maternal toxicity) = 438 mg/kg (reduced food consumption; increased water intake and mortality)

NOEL (developmental toxicity) = 438 mg/kg (HDT)

Study #2: 84-2 Report on the Study of Reg. No. 150 732 in the AMES Test (Standard Plate Test with Salmonella Typhimurium) dated May 4, 1984. May 4, 1984. Dr. rer. nat. J. Engelhardt. BASF Reg. Doc. No. 84/0156. pp 26. MRID 41063527

TBI's Comment #1:

The author should justify use of the high (30%) S-9 concentration in the S-9 mix or repeat the study with the recommended S-9 concentration (4%).

BASF's Response:

The high concentration of S-9 in the S-9 mix is in accord with Tox. Method No. 005 of the Ecological and Toxicological Association of the Dyestuffs manufacturing industry and has been in use at the testing laboratory for a decade. Studies conducted on pesticides using this protocol have been accepted worldwide and by EPA/TSCA/FIFRA. In addition, positive controls used in each study demonstrated that the concentration of S-9 in the S-9 mix is capable of activating promutagens.

TBI's Comment #2:

The purity of the test material was not provided. In addition, analytical data to support the actual concentration was not provided.

BASF's Response:

The test material used was from batch N 32 which had a purity of 96.5% which was confirmed by reanalysis in 1989. No concentration control analyses are performed in vitro short-term mutagenicity tests like the Ames test. Usually, cytotoxicity is used as a measure for sufficient exposure of the test system to the test material. Although, significant bacterio-toxicity was not demonstrated, there was reduced

his- background growth without S-9 mix in TA 1537 and with S-9 mix in TA 100 indicating that borderline bacterio-toxicity was achieved. The stability of the test material in the test system environment (aqueous) and in the solvent (DMSO) was proved after 48 and 24 hours, respectively.

TBI's Conclusion:

The test material was stored at ambient conditions after receipt on October 13, 1989. When reanalyzed on December 13, 1989 the mean analytical concentration of the test material was 97.0% compared to a theoretical concentration of 96.5%.

The background growth was reduced with S-9 mix, in TA 100 when compared to the negative control (DMSO) with S-9 mix. (The values obtained were 96 and 132 revertants per plate, respectively.) The his- background growth appeared to be comparable for the test material and negative control for TA 1537 without the S-9 mix.

The concentration of the test material at 0.1% in DMSO was 100.5 to 101.2% of the theoretical concentration after 24 hours at room temperature. The concentration of the test material in aqueous solution at 23°C for a period of 48 hours was 100.0 - 100.6% of the theoretical concentrations of 31.6 to 31.8 mg/l.

TBI's Conclusion:

BASF's response is acceptable. The study is therefore upgraded to "Acceptable".

84-4 Report on the Evaluation of Reg. No. 150 732 (ZNT No. 84/150) In Vitro Rat Primary Hepatocyte Unscheduled DNA Assay, Maria A. Cifone, June, 1986. BASF Reg. Doc. No. 86/0135 pp. 24. MRID 41063531

TBI's Comment:

The study is not fully acceptable because of the lack of information on the purity of the test material and supporting analytical data to confirm the actual concentration.

BASF's Response:

The test material was from batch N 32 which had a purity of 96.5% which was confirmed by reanalysis in 1989. No concentration control analyses are performed in in vitro short-term tests like the UDS assay. Usually, cytotoxicity is used as a measure for significant exposure to the test

4

material. Cytotoxicity was clearly demonstrated which indicates that the cells were exposed to the test material. The stability of the test material in the test system environment (aqueous) and in the solvent (DMSO) was proved after 48 and 24 hours, respectively.

TBI's Conclusion:

The data provided by BASF is identical with that provided for the Ames test regarding the concentration and stability of the test material. Cytotoxicity was clearly demonstrated in the UDS assay.

BASF's response is acceptable. The study is therefore upgraded to "Acceptable".

IV. Other: The Data Evaluation Reports for the rat teratology (MRID #41063524; BASF #87/0167), gene mutation - Ames (MRID #41063527; BASF #84/0156) and other genotoxic effects - UDS #41063531; 87/0167) studies can be found in a separate memorandum PP #9F3778 /FAP #9H5583; Proj. #9-1764A; W. B. Greear; September, 1990.