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OVERVIEW

MESOTRIONE (ZA1296) 7/18/2000

Study Type: Non-Guideline; 90 Day Dietary Study in Rats to Investigate Selective Non-Ocular Toxicity End Points

Work Assignment No. 2-01-52I (amend 1) (MRID 44505021)

Prepared for

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OVERVIEW

STUDY TYPE: Correlation of dose with selective non-ocular toxicity endpoints
OPPTS Number: N/A OPP Guideline Number: non-GDL

DP BARCODE: D259369 SUBMISSION CODE: S541375
P.C. CODE: 122990 TOX. CHEM. NO.: None

TEST MATERIAL (PURITY): Mesotrione (95.1% a.i.)

SYNONYMS: ZA1296; 2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione; 2-(4-mesyl-2-nitrobenzoyl)-cyclohexane-1,3-dione

CITATION: Brammer, A. (1995) ZA1296: 90 Day Dietary Study in Rats to Investigate Selective Non-Ocular Toxicity End Points. Central Toxicology Laboratory, Cheshire, UK, Laboratory Report No: CTL/T/2887; Study No: PR0990, August 1, 1995. MRID 44505021. Unpublished.

SPONSOR: Zeneca AG Products, Wilmington, Delaware

Executive Summary: The objective of this study (MRID 44505021) was to investigate the dose-response relationship for body weights and organ weight changes in male Alpk:AP$_f$SD rats. Male Alpk:AP$_f$SD rats (12/group) were fed diets containing mesotrione (95.1% a.i., Batch P11) at 0, 10, 20, 50, or 125 ppm (equivalent to 0, 0.9, 1.7, 4.3, or 10.7 mg/kg/day) for 90 days.

Clinical signs, body weights, food consumption, and kidney and liver weights were measured and/or recorded. Ophthalmoscopic exams were performed on all survivors prior to termination. Necropsies were performed at termination or upon the event of premature death.

Results of toxicological concern of this special study are presented as an attachment to this overview (Study Report Tables 6, 9, 10, and 11, pages 29 and 35 through 38). No treatment-related mortalities occurred. There were no differences of toxicological concern in body weights, body weight gain (as calculated by the reviewers), or food consumption. Gross necropsy results were not reported.

Opaque eyes were observed during clinical examinations in all treatment groups (3-9/12 each treated vs 0/12 controls). At ophthalmoscopic exam, the incidence of slight to marked hazy opacity or slight to marked opacity was increased in the all treatment groups (7/24, 12/24, 9/22,

and 18/24 eyes examined in the 10, 20, 50, and 125 ppm groups, respectively, vs 1/24 controls). Corneal vascularization was also observed in all treatment groups (2/24, 8/24, 8/22, and 14/24 eyes examined in the 10, 20, 50, and 125 ppm groups, respectively, vs 0/24 controls). Ghost vascularization of the cornea was observed in the 10 (1/24 eyes examined vs 0/24 controls) and 50 (1/22) ppm animals. Food utilization was decreased in the 125 ppm group during weeks 9-13 (↓13%, $p \leq 0.05$).

Adjusted (to body) kidney weights were increased ($p \leq 0.01$) at termination in all treatment groups (↑8-10%), but not dose-dependently. Absolute kidney weights were increased only in the 50 ppm group (↑7%, $p \leq 0.05$). Adjusted liver weights were also increased ($p \leq 0.01$) non-dose-dependently in all treatment groups (↑12-14%). Absolute liver weights were increased ($p \leq 0.05$) in the 10 and 50 ppm groups only (↑9-11%).

In conclusion, treatment with mesotrione at 10, 20, 50, or 125 ppm caused dose-dependent changes in corneal opacity and corneal vascularization. Changes in adjusted (to body) kidney and liver weights occurred in all treatment groups, but these changes were not dose-dependent. There were no changes of toxicological concern in body weights.

ATTACHMENT

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