

OVERVIEW

MESOTRIONE (ZA-1296)

7/18/2002

Study Type: Non-Guideline; 7-Day ZA1296 Rat Study

Work Assignment No. 2-01-52A (amend 1) (MRID 44505113)

Prepared for

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Mesotrione (ZA1296)

7-day systemic exposure in rats (non-GDL)

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Overview

STUDY TYPE: 7-Day Rat Study
OPPTS Number: N/A

OPP Guideline Number: N/A

DP BARCODE: D259369
P.C. CODE: 122990

SUBMISSION CODE: S541375
TOX. CHEM. NO.: None

TEST MATERIAL (PURITY): Mesotrione (93.3 and 95.1% w/w)

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

CITATION: Hall, M.G., (1996) ZA1296: Systemic Exposure Following Dietary Administration.
Central Toxicology Laboratory, Cheshire, UK, Laboratory Report No:
CTL/L/7179, June 10, 1996. MRID 44505113. Unpublished.

SPONSOR: Zeneca AG Products, Wilmington, Delaware

EXECUTIVE SUMMARY: The objective of this study (MRID 44505113) was to assess the differences in systemic exposure from treatment with two different batches of mesotrione (ZA1296; Batch P8 [93.3% w/w] and Batch P11 [95.1% w/w]) administered for 7 days in the diet to male AlPk:APfSD rats (18/group) at levels of 1, 40, 25, 1250, or 5000 ppm. Exposure was compared from measurements of mesotrione in urine and blood plasma and from the dosing effect on plasma tyrosine concentrations. Total food consumption (for days 1 through 7) was also determined. Each parameter was determined on 3 rats/dose/batch.

The total amount of food consumed by each group was similar; there appeared to be no differences in palatability between the test diets. Systemic exposure comparisons based on urinary excretion of mesotrione and its effect on plasma tyrosine concentrations showed no significant differences between Batch P8 and P11. There was a linear increase in area under the curve (AUC) and the maximum observed plasma concentrations ($C_{p_{max}}$) with increasing dose for both Batch P8 and Batch P11. A comparison of the AUC and the $C_{p_{max}}$ of Batch P8 with Batch P11 suggested that at dose levels >1000 ppm, higher systemic exposure of Batch P11 may occur.

From the information provided, it was not clear whether or not the two batches of mesotrione were tested concurrently and whether or not the same animals were used to test the two batches

of test material. The results of this special study are presented as an attachment to this overview (study report Figures 1 through 4, pages 8-11).

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