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Supplement to TXR No. 002308-DER for MRID No. 00077127. Developmental Toxicity Study in Rats. This supplement provides a revised Executive Summary to upgrade the original DER.

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Reregistration Branch 1, Health Effects Division (7509C) **Date** 12/8/04
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Reregistration Action Branch 1, Health Effects Division (7509C) **Date** 12/9/04

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DATA EVALUATION RECORD

STUDY TYPE: Developmental Toxicity Study in Rats OPPTS 870.3700a [§83-3a]

PC CODE: 120301 **DP BARCODE:**D294560

TXR No.: 0052174

TEST MATERIAL (PURITY): Thidiazuron (99.4% a.i.)

SYNONYMS: SN 49537; N-phenyl-N'-(1, 2, 3-thiadiazol-5-yl) urea

CITATION:

MRID No. 00077127
Reprotox GmbH (1981) Thidiazuron (SN 49 537): Teratology Study in the Rat: Reprotox Order No. 536/A. Rev. final rept. (Unpublished study received May 29, 1981 under 2139-122; submitted by Nor-Am Agricultural Products, Inc., Naperville, Ill.; CDL: 070129-C)

SPONSOR: Nor-Am Agricultural Products

EXECUTIVE SUMMARY:

In a developmental toxicity study (MRID No. 00077127), 25 presumed pregnant Wistar Han 78 strain rats per group were administered thidiazuron (purity: 99.4%; batch/lot No.: 271006B) by oral gavage in Myrj 53 solution at doses of 0, 25, 50, 100 or 300 mg/kg/day on gestation days (GD) 6-15, inclusive.

On GD 19, dams were sacrificed and examined grossly. The ovaries and uteri were excised and the number of corpora lutea, live young, resorptions, fetal weights and the incidence of external fetal abnormalities were recorded. Approximately 2/3 of the litters were examined for skeletal abnormalities and the 1/3 were examined for visceral abnormalities. Uteri were examined for evidence of implantation. Dams were observed daily and weighed on days 0, 6, 15 and 19 of pregnancy.

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Maternal Toxicity

No dams died during the course of the study. No clinical observations of toxicity were noted. A slight decreased mean body weight gain (87% of controls) was observed in the females of the 300 mg/kg/day group. The absolute maternal weight decrease was marginal (6%) but the weight loss persisted even after termination of treatment (day 15) (Table 1). Although maternal toxicity was only marginal at 300 mg/kg/day, the previous study (MRID No. 00077126) also showed significant decreased mean body weight gain (90% of controls) at 250 mg/kg/day and a frank maternal toxicity (mortality and reduced body weights) at 900 mg/kg/day. Therefore, the two studies taken together, the maternal LOAEL in this study was considered to be 300 mg/kg/day based on slightly reduced body weight gains.

The maternal LOAEL was 300 mg/kg/day based on reduced body weight gains. The maternal NOAEL was 100 mg/kg/day.

Developmental Toxicity

There were no differences between the control group and the all treated groups for number of litter size, rate of implantation, and pre- and post-implantation losses. Mean fetal weights and mean litter body weights were significantly decreased in the 300 mg/kg/day group (Table 1). There were no treatment-related external, visceral, or skeletal malformations.

The developmental LOAEL was 300 mg/kg/day based on decreased fetal body weights. The developmental NOAEL was 100 mg/kg/day.

This study is classified **acceptable/guideline (OPPTS 870.3700b)** and satisfies the requirements for a developmental study in the rat.

TABLE 1: Selected mean maternal body weights, litter weights, and fetal weights (g)

GD	0	15 mg/kg/day	40 mg/kg/day	120 mg/kg/day
Absolute Body Weights (g)				
0	218	224	214	212
6	250	250	247	243
15	290	286	282	275
19	326	322	313	306 (94%) [a]
Litter weights (g)				
	18.6	19.7	18.1	16.7 (90%) [a]
Fetal weights (g)				
	2.23	2.29	2.24	2.08* (93%) [a]

[a] Number in parentheses is per cent of control; calculated by reviewer.

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