Supplement to Document No. 007865 - DER for MRID No. 41026603: Embryotoxicity and Teratogenicity Study in Sprague Dawley Rats (Imazalil Sulphate ® 27180). This supplement provides an Executive Summary to upgrade the original DER.

EPA Reviewer: Abdallah Khasawinah, Ph.D., Date _____
Reregistration Branch 4 (7509C)
EPA Secondary Reviewer: Sanjivani Diwan, Ph.D., Date _____
Reregistration Branch 4 (7509C)

DATA EVALUATION RECORD

STUDY TYPE: Prenatal Developmental Study - Rat; OPPTS 870.3700 [§83-3a]

DP BARCODE: D262725 SUBMISSION CODE:S548748
P.C. CODE: 111901 TOX. CHEM. NO.:497AB

TEST MATERIAL (PURITY): Imazalil Sulphate (R27180)

SYNONYMS: None reported

CITATION: Gillardin, JM and Van Cauteren, H, 1988. Embryotoxicity and Teratogenicity in Sprague-Dawley Rats. Study number 2003/88-05. Research Department, Laboratories Janssen, France. July 5, 1988. MRID 41026603. Unpublished.

SPONSOR: Janssen Pharmaceutica N.V., 2340 Beerse, Belgium

EXECUTIVE SUMMARY:

In a developmental toxicity study (MRID 41026603), imazalil sulphate (99.9% purity) was administered to 24 Sprague-Dawley rats/dose by oral gavage in aqueous solutions at dose levels of 0, 40, 80 or 120 mg/kg/day from days 6 through 16 of gestation.

Maternal toxicity was observed at all dose levels as evidenced by significantly decreased mean food consumption (9.8%, 17.1% and 18.7%, for the low, mid and high doses, respectively) during the dosing period. Mean body weights on gestation day 17 were significantly decreased for the mid (3.5%) and high (4.6%) dose groups compared to the control group. The mean body weight gain for the low dose group and the control group was comparable. For the high dose group, mean body weight on gestation day 22 (6.2%) and mean corrected body weight gain (19%) for gestation days 1-22

were significantly decreased compared to the control group. **The maternal toxicity LOAEL is 40 mg/kg/day, based on decreased mean food consumption. The maternal toxicity NOAEL is <40 mg/kg/day (LDT).**

Developmental toxicity was manifested by a dose-related significant decrease in mean fetal weights in the mid (7.1%) and high (17.9%) dose groups compared to the controls. Other toxic effects were reported in the high dose group. These were: a significantly decreased mean litter size (11.2 vs 13.9 for the control), a significantly decreased number of live fetuses/litter (11.1 vs 13.8 for the control group), a significantly increased number of resorbed fetuses/litter (3.7 vs 0.4 for the control group). An increase in the number of fetuses (but not litters) with rudimentary extra ribs(6/247 vs 0/333 for the control group) was noted in the high dose group. This was found to be litter effect (See page 26) and therefore was not considered to be treatment related. The litter incidence for rudimentary extra ribs was 2/22 for the high dose group and 0/24 for the control group. No other treatment related effects were reported. **The developmental toxicity LOAEL is 80 mg/kg/day, based on decreased mean fetal weights. The developmental toxicity NOAEL is 40 mg/kg/day.**

This developmental toxicity study in the rat is classified as **acceptable** and **satisfies** the guideline requirement for a developmental toxicity study [870.3700 (83-3)] in rats.

COMPLIANCE: Signed and dated GLP, Quality Assurance, Data Confidentiality, and Flagging statements were provided.

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SignOff Date:	2/8/00
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