DATA EVALUATION RECORD - SUPPLEMENT

XDE-570 (FLORASULAM)

Study Type: OPPTS 870.3700b [' 83-3b]; Developmental Toxicity Study in Rabbits

Work Assignment No. 4-1-128 J (MRID 46808233)

Prepared for
Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Pesticides Health Effects Group
Sciences Division
Dynamac Corporation
1910 Sedwick Road, Bldg 100, Ste B.
Durham, NC 27713

Primary Reviewer
Michael E. Viana, Ph.D., D.A.B.T.
Signature: _____
Date: _____

Secondary Reviewer
John W. Allran, M.S.
Signature: _____
Date: _____

Program Manager:
Michael E. Viana, Ph.D., D.A.B.T.
Signature: _____
Date: _____

Quality Assurance:
Mary L. Menetrez, Ph.D.
Signature: _____
Date: _____

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EPA Reviewer: Karlyn J. Bailey **Signature:** _____
Registration Action Branch 2, Health Effects Division (7509P) **Date:** _____
Work Assignment Manager: Myron Ottley, Ph.D. **Signature:** _____
Registration Action Branch 3, Health Effects Division (7509P) **Date:** _____

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See TXR # 0054348 for previous DER

This supplement contains:

- New cover page
- New executive summary

STUDY TYPE: Prenatal Developmental Toxicity Study - Rabbits; OPPTS 870.3700b [§83-3b]; OECD 414.

PC CODE: 129108 **DP BARCODE:** D331116
TXR#: 0054348

TEST MATERIAL (PURITY): XDE-570 (99.3% a.i.)

SYNONYMS: Florasulam; *N*-(2,6-Difluorophenyl)-8-fluoro-5-methoxy(1,2,4)triazolo (1,5-*c*)pyrimidine-2-sulfonamide; XR-570; XRD-570; DE-570

CITATION: Zablotny, C. L., and E. W. Carney (1997) XDE-570: oral gavage teratology study in New Zealand White rabbits. The Toxicology Research Laboratories, The Dow Chemical Company, Midland, MI. Laboratory Project Study ID: 960022, August 12, 1997. MRID 46808233. Unpublished.

SPONSOR: Dow AgroSciences Canada, Inc., 2100-450 1 St. SW, Calgary, AB, Canada

EXECUTIVE SUMMARY: In a developmental toxicity study (MRID 46808233), XDE-570 (Florasulam; 99.3% a.i.; Lot No. 940714) in aqueous 0.5% methylcellulose was administered daily via oral gavage to 20 naturally mated New Zealand White rabbits/group at a dose volume of 4 mL/kg at dose levels of 0, 50, 250, or 500 mg/kg/day from gestation day (GD) 7-19. On GD 28, all surviving does were killed and a limited necropsy was performed. The liver, kidneys, and gravid uterus were removed and weighed, and the fetuses were delivered by cesarean section and examined.

One 250 mg/kg/day doe aborted on GD 22, and one 500 mg/kg/day doe aborted on GD 17. Prior to aborting, both animals displayed decreased fecal output, body weight loss, and markedly lower food consumption. At necropsy, the 500 mg/kg/day doe was found to have findings indicative of pneumonia, which was most likely due to deposition of the test substance in the lungs. One 500 mg/kg/day doe was found dead on GD 19; the cause of death was attributed to a ruptured esophagus with atelactic lungs, with thoracic adhesions and hydrothorax present.

No treatment-related effects were observed on mortality, clinical signs, body weights, body weight gains, food consumption, organ weights, or gross pathologic examinations in the animals that survived to scheduled termination.

The maternal LOAEL was not observed. The maternal NOAEL is 500 mg/kg/day.

There were no premature deliveries or complete litter resorptions, and no effects of treatment on the numbers of litters, live fetuses, dead fetuses, or resorptions (early), or on gestation index, fetal body weights, sex ratio, post-implantation loss, or gravid uterine weights. There were no treatment-related external, visceral, or skeletal findings.

The developmental LOAEL was not observed. The developmental NOAEL was 500 mg/kg/day.

This study is classified **acceptable/guideline (OPPTS 870.3700b)** and satisfies the guideline requirements for a developmental toxicity study in the rabbit. Although the animals were not dosed to the limit dose, a preliminary developmental toxicity study in rabbits (MRID 46808232) was performed and indicated that a dose of 600 mg/kg/day probably would have exceeded the maximum tolerated dose and resulted in excessive maternal death. Therefore, selection of the high dose (500 mg/kg/day) used in this study was considered reasonable. Additionally, while this study did not dose the animals for the recommended interval (implantation through the day prior to cesarean section), it must be noted that this study was performed prior to the adoption of the current guidelines (OPPTS 870.3700, August, 1998).

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