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DATA EVALUATION RECORD - SUPPLEMENT

XDE-570 (FLORASULAM)

Study Type: OPPTS 870.6200 [§82-7a], Chronic Neurotoxicity Screening Battery in Rats

Work Assignment No. 4-01-128 F (MRID 46808228)

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
David A. McEwen, B.S.

Signature: _____
Date: _____

Secondary Reviewer
Stephanie E. Foster, 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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XDE-570 (FLORASULAM)/129108

OPPTS 870.6200/DACO 4.5.13/OECD None

EPA Reviewer: Karlyn J. Bailey Signature: _____

Registration Action Branch 2, Health Effects Division (7509P) Date: _____

EPA Secondary Reviewer: 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: Chronic Neurotoxicity – Feeding Study in Rats; OPPTS 870.6200 [' 82-7];
OECD None.

PC CODE: 129108**DP BARCODE:** D331116**TXR#:** 0054348**TEST MATERIAL (PURITY):** XDE-570 (Florasulam; 99.3% a.i.; Lot # 940714)

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

CITATION: Shankar, M.R. and K.A. Johnson (1996) XDE-570: Chronic neurotoxicity in Fischer 344 rats. The Toxicology Research Laboratory, The Dow Chemical Company, Midland, MI. Laboratory Project Study ID: DR-0312-6565-019N, September 25, 1996. MRID 46808228. Unpublished.

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

EXECUTIVE SUMMARY - In a chronic neurotoxicity study (MRID 46808228), XDE-570 (Florasulam; 99.3% a.i.; Lot # 940714) was administered to 10 young adult Fischer 344 rats/sex/dose in the diet at dose levels of 0, 10, 125 (females only), 250, or 500 (males only) mg/kg/day (time-weighted average test substance intake was 0, 8.6, 216, and 460 mg/kg/day in males and 0, 9, 113, and 266 mg/kg/day in females) for 12 months. Neurobehavioral assessment (functional observational battery [FOB] and motor activity testing) was performed in all rats at pre-dosing and at 3, 6, 9, and 12 month post-dosing. At study termination, auditory function (auditory brainstem response) was evaluated in 5 rats/sex/dose from the control and high-dose animals (500 mg/kg/day males and 250 mg/kg/day females). After completion of the auditory function examination, a neuropathological examination of perfusion-fixed central and peripheral nervous system tissues was conducted using these control and high-dose animals. All animals were subjected to a gross necropsy at termination. Positive control data were provided.

XDE-570 (FLORASULAM)/129108OPPTS 870.6200/DACO 4.5.13/OECD None

There were no compound-related effects on mortality, clinical signs, food consumption, FOB parameters, motor activity, and gross or neuropathology observed at any dose. Organ weights were not provided; however, in the concurrently performed 2-year dietary chronic toxicity/oncogenicity study (MRID 46808236), brain weight was unaffected after 12 and 24 months of treatment.

At 500 mg/kg/day, body weights were decreased ($p < 0.05$) by 9-15% in the males at 6, 9, and 12 months. Additionally, body weight gains were decreased by 61-67% at 3-12 months and overall (0-12 months) gains were decreased by 27% compared to controls. Food consumption was similar to controls in these animals.

No treatment-related effects were observed at 250 mg/kg/day and below in either sex.

No evidence of neurotoxicity was observed at any dose in either sex.

The systemic LOAEL is 500 mg/kg/day, based on decreased body weight and body weight gain in males. The systemic NOAEL is 250 mg/kg/day.

The neurotoxicity LOAEL was not observed. The neurotoxicity NOAEL is 250 mg/kg/day, the highest dose tested in females.

This study is classified as **acceptable/guideline** and satisfies the guideline requirement for Test Guideline OPPTS 870.6200 for a chronic neurotoxicity feeding study in the rat.

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