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)

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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-diflurophenyl)-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 Unpublished.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.

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.