DATA EVALUATION RECORD - SUPPLEMENT

XDE-570 (FLORASULAM)

Study Type: Non-guideline; Supplementary Metabolism Study in Rats

Work Assignment No. 4-1-128 T (MRID 46808303)

Prepared for
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See TXR # 0054348 for previous DER

This supplement contains:

- New cover page
- New executive summary

STUDY TYPE: Non-guideline; supplementary metabolism study in rats

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

TEST MATERIAL (RADIOCHEMICAL PURITY): XDE-570 (Florasulam; 98.5%)

SYNONYMS: *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: Hansen, S.C. (1997) XDE-570: distribution and metabolism of ^{14}C-labeled XDE-570 in selected tissues at plasma Cmax and C½max and in the bile following oral administration in Fischer 344 rats. The Toxicology Research Laboratory, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI. Laboratory Project ID: HET DR 0312-6565-029, September 29, 1997. MRID 46808303. Unpublished.

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

EXECUTIVE SUMMARY: In a metabolism study (MRID 46808303), [^{14}C]-XDE-570 (Florasulam; 98.5% radiochemical purity; Lot No. B734-21) in a suspension of 0.5% Methocel™ cellulose ethers was administered to 3 Fischer 344 rats/sex/time point as a single gavage dose at 10 or 500 mg/kg bw. Animals were killed at Tmax or T½max (0.5-4 h postdose). Tissue samples, carcass, and final cage wash were analyzed for radioactivity. Additionally, 3 males were fitted with indwelling bile-duct cannulas prior to dosing. Bile was periodically sampled, and urine and feces were collected for a 24 hour interval. The animals were killed 24 hours postdose, and blood, skin, carcass, and gastrointestinal tract/ingesta samples were collected. Data were reported for 2 animals in this group. [^{14}C]-XDE-570 was uniformly labeled in the aniline ring for each of these test groups. The stated purpose of this study was to provide additional information on the absorption, distribution, metabolism, and excretion of the test compound to support registration in Japan.

Total recovery was 98.7% in the bile duct cannulated group and 77.8-94.8% in the other test groups. The highest concentration of radioactivity was found in the kidney (570 µg-eq/g). On a percentage of the dose basis, excluding the carcass and GIT/ingesta, the blood, kidneys, liver, and skin had relatively high amounts of radioactivity; however, the radioactivity isolated in the skin may have been due to urinary contamination. Excluding the skin, the amount (% dose) isolated was generally highest in the blood, but all amounts were low (0.5-5.0% dose), regardless of dose, time point, or sex. Parent accounted for >91% of the radioactivity in the kidney, liver, and blood for each dose, time point, and sex. At 24 hours postdose, biliary excretion accounted for only 1.0% of the administered dose, while urinary excretion (81.0% dose) accounted for the majority of the dose. The remaining administered radioactivity in the bile duct cannulated test group was isolated in the feces (3.9% dose), tissues, GIT/ingesta, and carcass (8.3% dose), and final cage wash (4.6% dose). There were no sex-related differences in the metabolism or pharmacokinetics of the test compound.

This study is classified as **acceptable/non-guideline**. An acceptable metabolism study (MRID 46808301) was concurrently submitted.

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