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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

Date: 31-May-2007

Subject: Florasulam. First Food Use Petition for the Establishment of Tolerances on the Raw Agricultural Commodities of Barley, Oats, Rye, Triticale, and Wheat. Summary of Analytical Chemistry and Residue Data. PP#6F7061

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40 CFR 180. Not established

Chemical Class: Sulfonanilide and triazolopyrimidine Herbicides

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5/31/07

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Executive Summary

Florasulam, N-(2, 6-difluorophenyl)-8-fluoro-5-methoxy[1, 2, 4]triazolo[1, 5-*c*]pyrimidine-2-sulfonamide, is a sulfonamide herbicide that is currently registered in Europe and Canada for use in cereal weed control. Florasulam is being developed in the U.S. for control of wild buckwheat, wild mustard, volunteer canola, field pennycress, common chickweed, shepherd's purse, bedstraw, and smartweed, when used in a post-emergent application in wheat, barley, oats, rye, and triticale. The mode of action at the cellular level involves the inhibition of the enzyme, acetolactate synthase (ALS).

Dow Agrosciences, LLC proposes the establishment of tolerances for residues of florasulam *per se* in/on the following commodities:

Barley grain	0.01 ppm
Barley forage	0.05 ppm
Barley hay	0.05 ppm
Barley straw	0.05 ppm
Oats grain	0.01 ppm
Oats forage	0.05 ppm
Oats hay	0.05 ppm
Oats straw	0.05 ppm
Rye grain	0.01 ppm
Rye forage	0.05 ppm
Rye hay	0.05 ppm
Rye straw	0.05 ppm
Triticale grain	0.01 ppm
Triticale forage	0.05 ppm
Triticale hay	0.05 ppm
Triticale straw	0.05 ppm
Wheat grain	0.01 ppm
Wheat forage	0.05 ppm
Wheat hay	0.05 ppm
Wheat straw	0.05 ppm

The end-use products are formulated as an emulsifiable concentrate with the following respective concentrations of the active ingredient (a.i.): 4.84% a.i., 0.58% a.i., 0.25% a.i., and 0.39% a.i. It may applied by either ground or aerial equipment at an application rate of up to 0.0045 pounds a.i. per acre per season. A pre-harvest interval (PHI) of 60 day is listed on the label. Livestock may not be allowed to graze for 7 days after application of florasulam. A plant-back interval of 3 months is listed on the label for field corn, pop corn, seed corn, sweet corn, and sorghum. A plant-back interval of 9 months is listed for alfalfa, canola, chickpea, soybean, dry bean, field pea, flax, lentil, potato, safflower, sugar beet, and sunflower. A 12-month plant-back interval is listed for other crops.

The nature of the residue in wheat is adequately understood. In an acceptable wheat metabolism study using two radiolabels and an application rate reflecting 10X, the parent was identified along with three metabolites. The metabolites were identified as the glucose conjugate of 4-OH phenyl florasulam, 4-OH phenyl florasulam, and 2-sulfonamide (See Figure 1 for chemical structures). The residue of concern in wheat for both tolerance expression and risk assessment is parent florasulam *per se* (D332983, K. Bailey, 5/31/2007).

The nature of the residue in livestock is adequately understood. The metabolism of florasulam in the laying hen and goat were similar. In both species, the majority of the radioactivity was found in the excreta. Most of the parent compound in goat and hen was eliminated unchanged with minor unknown metabolites at unquantifiable levels. No significant cleavage of the sulfonanilide bridge was observed. Radioactivity levels in tissues were low in the exaggerated rate metabolism studies. Therefore, for this petition no tolerances are required for livestock commodities. If in the future, uses are added which have livestock feed items this decision will be revisited.

Residues of florasulam as the N-methyl florasulam derivative were determined by capillary gas chromatography with mass selective detection (GC/MSD). This is a specific method that identifies/quantifies florasulam, the parent compound only. The limit of quantitation LOQ for florasulam was established at 0.01 ppm for grain and at 0.05 ppm for forage, hay, and straw. Radiovalidation of enforcement method was not conducted due to low radioactivity. The enforcement method will be submitted to BEAD/ACL for a petition method validation (PMV).

Tolerances are being proposed for wheat, oats, rye, barley, and triticale. Canadian and U.S. field trials were submitted for wheat, rye, barley, and oats. Residues of florasulam were below the LOQ for grain (0.01 ppm) and forage, hay, and straw (0.05 ppm). Field trials were not submitted for several of the required EPA regions but additional field trials were submitted for Canadian regions. Since residues were less than the LOQ, HED will allow the reduced dataset.

The supervised field trials indicated that residues of florasulam in grain of wheat, barley and oats were non quantifiable (<0.01 ppm), following a single foliar application at exaggerated rate (2 X the proposed maximum seasonal application rate). In addition, the metabolism studies in wheat, treated with ^{14}C-DE-570 at the exaggerated rate of 50 g a.i./ha (10X the proposed maximum seasonal rate), indicated very low radioactive residue levels (maximum of 0.002 ppm). HED concludes that it is unlikely that residues of florasulam in processed food/feed items will concentrate when treated according to the proposed use pattern (0.0045 lb a.i./acre). The proposed tolerance of 0.01 ppm for the raw agricultural commodity (RAC) will cover potential residues of florasulam in the processing commodities of wheat, barley and oats.

In the confined rotational crop study, florasulam was applied at a 1.5 X exaggerated application rate. Spring wheat, sunflower, cabbage and carrots were planted at 30 days after treatment (DAT) of soil. Spring wheat, sunflowers, cabbage and carrots were harvested at maturity i.e., 168 DAT (spring wheat and sunflowers), 195 DAT (cabbage), and 156 DAT (carrots). Each crop was separated into fractions as spring wheat (ears and straw), sunflower (heads and stems), cabbage (shoots) and carrot (leaves and roots). None of the fractions from rotational crops had total radioactive residues (TRRs) greater than 0.01 ppm. Therefore, no further attempt was made to characterize radioactivity. No tolerances for rotational crops are needed at this time.

Regulatory Recommendations and Residue Chemistry Deficiencies

Provided a revised Section F is submitted with correct raw agricultural commodity definitions and the correct spelling of the chemical name for florasulam, the residue chemistry database supports a conditional registration. The registration should be made conditional until successful completion of the PMV and submission of the analytical reference standard.

A human health risk assessment for florasulam is forthcoming.

Background

Florasulam, N-(2,6-difluorophenyl)-8-fluoro-5-methoxy[1, 2, 4]triazolo[1, 5-*c*]pyrimidine-2-sulfonamide, is a sulfonamide herbicide that is currently registered in Europe and Canada for use in cereal weed control. Florasulam is being developed in the U.S. for control of wild buckwheat, wild mustard, volunteer canola, field pennycress, common chickweed, shepherd's purse, bedstraw, and smartweed, when used in a post-emergent application in wheat, barley, oats, rye, and triticale. The mode of action at the cellular level involves the inhibition of the enzyme, acetolactate synthase (ALS).

TABLE A.1. Test Compound Nomenclature

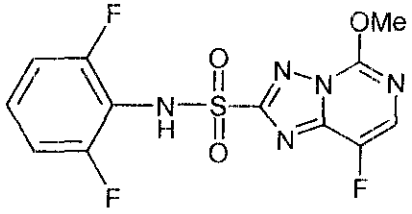
Compound	Chemical Structure
	
Common name	Florasulam
Company experimental name	DE-570 or EF-1343
IUPAC name	2', 6', 8-trifluoro-5-methoxy-*s*-triazolo [1,5-c]pyrimidine-2-sulfonanilide
CAS name	*N*-(2,6-difluorophenyl)-8-fluoro-5-methoxy[1, 2, 4]triazolo[1, 5-*c*]pyrimidine-2-sulfonamide
CAS #	145701-23-1
End-use product/EP	Florasulam Suspension Concentrate
Molecular Formula	$C_{12}H_8F_3N_5O_3S$
Molecular Mass	359.3

Figure 1. Chemical structures of identified metabolites.

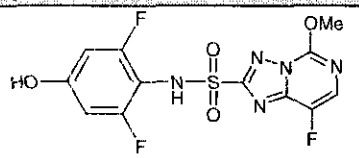
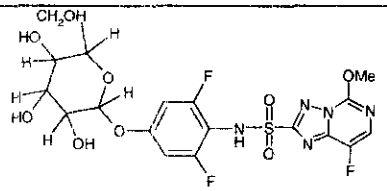
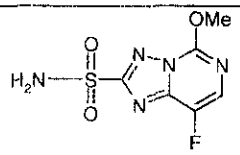
Chemical Name	Structure
4-hydroxy florasulam	
Glucose conjugate of 4-hydroxy florasulam	
2-sulfonamide	

TABLE A.2. Physicochemical Properties		
Parameter	**Value**	**Reference**
Physical State	Solid	PMRA Lab Services
Melting point/range	193.5-230.5°C	
Specific gravity	1.53 at 22°C	
Water solubility	Medium / Solubility (g/L) water 0.121 pH 5 0.084 pH 7 6.36 pH 9 94.2	
Solvent solubility	Solvent / Solubility (g/L) acetone 123 acetonitrile 72.1 ethyl acetate 15.9 methanol 9.81 dichloromethane 3.75 xylene 0.227 n-octanol 0.184 n-heptane 0.000019	
Vapor pressure	1×10^{-5} Pa at 25°C	
Dissociation constant (pK_a)	4.54	
Octanol/water partition coefficient (K_{ow}) at 22°C	pH / Log K_{ow} 4 1.00 7 -1.22 10 -2.06	
UV/visible absorption spectrum	Form / λmax (nm) Acidic 259.8 203.8 Basic 262.4 209.7 Methanolic 204.1 No absorbance above 300 nm.	

860.1200 Directions for Use

Table 1. Summary of Proposed End-Use Products.

Trade Name	Reg. No.	a.i. (% of formulation)	Formulation Type	Target Crops	Target Pests	Label Date
EF-1343	62719-LAN	4.84%	Emulsifiable Concentrate (EC)	Wheat, Barley, Oats, Rye, Triticale	Annual broadleaf weeds	Under Review
EF-1383	62719-LLI	0.58%	Emulsifiable Concentrate (EC)	Wheat, Barley, Rye, Triticale	Annual broadleaf weeds	Under Review
GF-184	62719-LAG	0.25%	Emulsifiable Concentrate (EC)	Wheat, Barley, Oats, Rye, Triticale	Annual broadleaf weeds	Under Review
GF-1727	62719-LAE	0.39%	Emulsifiable Concentrate (EC)	Wheat, Barley, Oats, Rye, Triticale	Annual broadleaf weeds	Under Review

Table 2. Summary of Directions for Use of Florasulam.

Applic. Timing, Type [Equipment].	Formulation	Applic. Rate (lb a.i./A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb a.i./A)	PHI (days)*	Use Directions and Limitations
Wheat, Barley, Oats, Rye, Triticale						
Broadcast foliar (from 3-leaf stage up to flag leaf emergence Zadoks scale 39) [Ground or aerial]	0.25% EC	0.0044	1	0.0044	60	Livestock may be grazed on treated crops 7 days following application. Application through any type of irrigation equipment is prohibited.
Broadcast foliar (from 3-leaf stage up to joint stage Zadoks scale 31) [Ground or aerial]	0.39% EC	0.0044	1	0.0044	60	Livestock may be grazed on treated crops 7 days following application. Application through any type of irrigation equipment is prohibited. Do not apply after boot stage.
Broadcast foliar (from 3-leaf stage up to joint stage Zadoks scale 31) [Ground or aerial]	0.58% EC	0.0045	1	0.0045	60	Livestock may be grazed on treated crops 7 days following application. Application through any type of irrigation equipment is prohibited. Do not apply after boot stage.
Broadcast foliar (from 3-leaf stage up to flag leaf emergence Zadoks scale 39) [Ground or aerial]	4.84% EC	0.0045	1	0.0045	60	Livestock may be grazed on treated crops 7 days following application. Application through any type of irrigation equipment is prohibited.

*PHI of 60 days prior to harvest was listed on the label. This would be correct for grain and straw. HED has concluded the growth stage at which the application is conducted is a more appropriate indicator instead of a numerical PHI.

A plant-back interval of 3 months is listed on the label for field corn, pop corn, seed corn, sweet corn, and sorghum. A plant-back interval of 9 months is listed for alfalfa, canola, chickpea, soybean, dry bean, field pea, flax, lentil, potato, safflower, sugar beet, and sunflower. A 12-month plant-back interval is listed for other crops.

Conclusion: The submitted product labels for EF-1343, EF-1383, GF-1727, and GF-184 are adequate to allow evaluation of the residue data relative to the proposed use on wheat, barley, oats, rye, and triticale.

860.1300 Nature of the Residue - Plants
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In the metabolism study, [^{14}C]-DE-570 (>98%) formulated with EF 1343 blank formulation, radiolabeled as [^{14}C]-phenyl-XDE-570 and [^{14}C]-TP-XDE-570 was applied to winter wheat at crop growth stages of BBCH30 (stem elongation-early application) and BBCH49 (postflag leaf emergence/first awns visible-late application) at 50 g a.i./ha. The rate used herein was equivalent to 10X the proposed label rate of 5 g a.i./ha. The formulation used in the metabolism study was identical to that used in the residue studies and that proposed for registration. Winter wheat plants (10 plants/tub) were planted in sandy loam soil contained in tubs. ^{14}C-DE-570 formulations were applied to run-off to wheat plants using a spray gun. All tubs were placed outdoors, for the duration of the in-life phase of the study, in the lysimeter complex. In addition to natural precipitation, the plants were watered at the soil surface as required. Plants were harvested within 18 hours of treatment (day 0), 30 days after treatment, and finally at crop maturity (129 days after BBCH 30 application and 65 days after BBCH 49).

After early application (BBCH 30 crop stage) and sampling of immature whole wheat plant (0 day after application), the parent (71%, 2.9 ppm phenyl- and 63%, 2.0 ppm TP- labeled TRR) and one other major metabolite identified as the glucose conjugate of 4-OH-(phenyl)-DXD-570 (19%, 0.79 ppm phenyl- and 24.6%, 0.027 ppm TP- labeled TRR) Two minor metabolites were also identified: 4-OH-(phenyl)-DXD-570 (0.9%, 0.038 ppm phenyl- and 0.84%, 0.027 ppm TP-labeled TRR) and 2-sulfonamide (1.5%, 0.048 ppm TP-labeled TRR) was also identified. A total of 91% of the phenyl- and TP-labeled TRR was identified. A total of 97% of phenyl- and TP-labeled TRR was extractable. A total of 5.3% (0.22 ppm) phenyl- and 4.9% (0.16 ppm) TP-labeled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam.

After late application (BBCH 49 crop stage) and sampling of immature whole wheat plant (0 day after application), the parent (84%, 0.57 ppm phenyl- and 81%, 0.61 ppm TP- labeled TRR) and one other major metabolite the glucose conjugate of 4-OH-(phenyl)-DXD-570 (8.5%, 0.058 ppm phenyl and 8.5%, 0.064 ppm TP-labeled TRR) were identified. A total of 90% of the TRR was identified. A total of 94% of the phenyl- and TP-labeled TRR was extractable. A total of 1.9% (0.014 ppm) phenyl- labeled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam. Two minor metabolites were also identified: 4-OH-(phenyl)-DXD-570 (1.2%, 0.0087 ppm phenyl- and 0.4%, 0.003 ppm TP-labeled TRR) and 2-sulfonamide (0.7%, 0.005 ppm TP-labeled TRR) were also identified.

After early application (BBCH 30 crop stage) and sampling of immature whole wheat plant (30 days after application), the parent (28%, 0.12 ppm phenyl- and 27%, 0.11 ppm TP-labeled TRR) and one other major metabolite the glucose conjugate of 4-OH-(phenyl)-DXD-570 (21%, 0.083 ppm phenyl- and 12.8%, 0.051 ppm TP-labeled TRR) were identified. Two minor metabolites were also identified: the 4-OH-(phenyl)-DXD-570 (6.8%, 0.027 ppm phenyl- and 15.1%, 0.060 ppm TP-labeled TRR) and 2-sulfonamide (1%, 0.051 ppm TP labeled TRR) was also identified. A total of 56% the phenyl- and TP-labeled TRR were identified. A total of 63% of the phenyl- and 77% of the TP-labeled TRR was extractable. A total of 2.7% (0.011ppm) phenyl-labeled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam.

After late application (BBCH 49 crop stage) and sampling of immature whole wheat plant (30 days after application), the parent (27%, 0.03 ppm phenyl- and 32%, 0.041ppm TP-labeled TRR) and one other major metabolite the glucose conjugate of 4-OH-(phenyl)-DXD-570 (41.5%, 0.051 ppm phenyl- and 19%, 0.024 ppm TP-labeled TRR) were identified. A total of 69% phenyl- and 51% of TP-labeled TRR was identified. A total of 69% of the phenyl- and 78% of TP-labeled TRR was extractable. A total of 26% (0.034 ppm) TP-labeled TRR consisted of several minor components. Each of these components was estimated to be less than 0.01 ppm. No other metabolite was identified.

After early application (BBCH 30 crop stage) and sampling of mature wheat straw (129 days after application), no parent compound was identified. However, some metabolites were identified: the glucose conjugate of 4-OH-(phenyl)-DXD-570 (6.3%, 0.003 ppm phenyl- and 2.5%, 0.0018 ppm TP-labeled TRR,), 4-OH-(phenyl)-DXD-570 (8.4%, 0.0041 ppm phenyl- and 1.6%, 0.0012 ppm TP-labeled TRR) and 2-sulfonamide (4.7%, 0.0034 ppm TP-labeled TRR). A total of 15% of the phenyl- and 8.8% of the TP-labeled TRR were identified. A total of 61.4% of the phenyl- and 78.2% of the TP-labeled TRR were extractable. A total of 45.8% (0.02 ppm) phenyl- and 43% (0.03 ppm) of the TP-labeled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam. Each of these metabolites was estimated to be less than 0.01 ppm.

After late application (BBCH 49 crop stage) and sampling of mature wheat straw (65 days after application), residues were identified as parent (14%, 0.057 ppm phenyl- and 7%, 0.02 ppm TP-labeled TRR), the glucose conjugate of 4-OH-(phenyl)-DXD-570 (21.5%, 0.088 ppm phenyl- and 13%, 0.041 ppm TP-labeled TRR), 4-OH-(phenyl)-DXD-570 (14%, 0.059 ppm phenyl- and 5.5%, 0.017 ppm TP-labeled TRR), and 2-sulfonamide (19%, 0.058 ppm TP-labeled TRR). A total of 50% phenyl- and 44% TP-labeled TRR was identified. A total of 59% of the phenyl- and 79% of the TP-labeled TRR were extractable. A total of 9.4% (0.039 ppm) phenyl- and 5.3% (0.017 ppm) of the TP-labeled TRR consisted of several minor components, more polar than florasulam. Each of these metabolites was estimated to be less than 0.01 ppm.

The total radioactive residue level in grain was determined by combustion/LSC. The ^{14}C-residues were too low to elucidate the nature of the TRRs in mature wheat ears (up to 0.03 ppm) and grain (up to 0.008 ppm); therefore, no further attempts to characterize/identify the ^{14}C-residues were carried out.

The analysis of wheat plant samples was started within 3 days of sampling. In addition, the petitioner reported that the results of analyses of intact plant samples after 6, 8 and 9 months show the chromatographic profiles of the initial and stored samples are very similar. From these comparisons of chromatographic profiles, the petitioner concluded that radioactive residues of XDE-570 in winter wheat are stable under conditions of storage for up to 9 months.

The metabolism of florasulam in wheat proceeded via hydroxylation in the 4-position of the phenyl ring with subsequent glucose conjugation. Additional degradation was followed by tentative cleavage of the sulfonamide bridge. The metabolites detected in wheat matrices were 4-OH-(phenyl)-florasulam, the glucose conjugate of 4-OH-(phenyl)-florasulam, and 2-sulfonamide. The 4-OH-(phenyl)-florasulam and glucose conjugate of 4-OH-(phenyl)-florasulam were both present in rat metabolism. The metabolism study was conducted at 10X the proposed label rate (5 g a.i./ha) and the 2-sulfonamide metabolite was detected only in winter wheat straw (0.059 ppm) and not in the grain.

Based on the low level of residues observed in wheat grain (0.008 ppm) at the exaggerated application rate (10X the proposed application rate) in the wheat metabolism study, the residue of concern (ROC) is defined as the parent compound florasulam. This conclusion if for cereal grains only.

The winter wheat metabolism study is classified as acceptable and it satisfies the guideline requirement for OPPTS 860.1300. If other crop uses are requested in the future, additional nature of the residue studies may be required.

Conclusion: The nature of the residue in wheat is adequately understood. In an acceptable wheat metabolism study using two radiolabels and an application rate reflecting 10X, the parent was identified along with three metabolites. The metabolites were identified as the glucose conjugate of 4-OH phenyl florasulam, 4-OH phenyl florasulam, and 2-sulfonamide (See Figure 1 for chemical structures). The residue of concern in wheat for both tolerance expression and risk assessment is parent florasulam *per se* (D332983, K. Bailey, 5/31/2007).

860.1300 Nature of the Residue - Livestock

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Lactating Goat

In the lactating goat metabolism study, XDE-570, radiolabeled as either [UL-aniline-^{14}C]XDE-570, or [triazolopyrimidine-9- ^{14}C]XDE-570 was administered to two lactating goats (one per treatment) at a dose level of approximately 0.48 mg/kg bw/day. The dose was administered orally once daily in the morning for five consecutive days using a bolus gun and was equivalent to approximately 11 ppm (~100X the XDE-570 dietary burden) at an average feed consumption of 2 kg/day. Samples of milk, urine and feces were collected throughout the study. Approximately 24 hours after the final dose the animals were sacrificed and tissue including liver, kidneys, muscle, fat along with samples of blood, gastrointestinal contents and urine from the bladder were collected.

The results indicated that the total radioactive residues (TRRs) were almost comparable between two labelling positions for urine, feces, muscle and fat. But a slight difference in TRR was noted for

kidney, liver and milk. Recoveries of the administered dose in goat were 89% of for the aniline label (A-label) and 83% for the triazolopyrimidine label (TP-label). Majority of the radioactivity was excreted in the urine and feces, accounting for a total of 99.8% of the recovered radioactivity. Total residues in tissues were very low. These residues in the tissues, milk and blood samples were below 0.1% of the administered dose. The highest concentration of residues in tissues was found in the kidneys, 0.069 ppm and 0.039 ppm from the A-label and TP-label experiments, respectively. Total radioactive residue in liver was 0.033 ppm and 0.023 ppm from the A-label and TP-label experiments, respectively. Total radioactive residue in muscle was 0.0016 ppm and 0.0009 ppm from the A-label and TP-label experiments, respectively. Total radioactive residue in fat was 0.0016 ppm and 0.0017 ppm from the A-label and TP-label experiments, respectively. Total radioactive residue in milk was 0.016 ppm and 0.033 ppm from the A-label and TP-label experiments, respectively. The predominant radioactive component extracted from urine, milk, liver and kidney samples was parent. One minor metabolite representing up to 1.5% of TRR was tentatively identified as 5-OH-florasulam in urine, liver and kidney samples. Total radioactive residues in tissue (muscle, fat, skin and liver), milk and excreta samples were determined by combustion radioanalysis and/or liquid scintillation counter (LSC). Solvent extraction and subsequent fractionation were performed on the A and TP labeled milk, liver, kidney and urine samples. All aqueous and organic phase extractions were analyzed by LSC. These extracts were also analyzed by reverse phase HPLC to identify radioactive residues. The post solvent extracted material from milk, liver and kidney were analyzed by combustion/LSC. Total radioactive residues in liver were low (0.033 ppm). Liver samples were further treated with a proteolytic enzyme to release and characterize bound residues. The proteolytic enzyme liberated 88.5% (0.029 ppm) and 85.1% (0.02 ppm) of the TRR in the A and TP treated liver tissue.

The parent compound, florasulam, is not likely to concentrate in fat, other tissues or milk as a result of feeding of treated feed. This study demonstrated low levels of radioactivity in edible tissues. These observations are supported by the low Log K_{ow} (1.00 at pH 4.0 and -1.22 at pH 7.0) which is an indication of a low potential for partition into organic solvents. The solvent extraction efficiency tests indicated that recovery of fortified radioactivity for various fractions was excellent. The extraction efficiency of ethyl acetate was tested for milk, liver and kidney samples. Ethyl acetate extracted 88-104 % of radioactivity from spiked (0.015-0.38 ppm) samples of milk, liver and kidney.

Laying Hen

In the laying hen metabolism study, XDE-570, radiolabeled as either [UL-aniline-^{14}C]XDE-570 or [triazolopyrimidine-9- ^{14}C]XDE-570, was administered to two groups of 10 laying hens at a dose level of 0.76± 0.01 mg/kg bw/day. The dose was administered orally twice daily for five consecutive days, by opening the beak and inserting a capsule into the esophagus. The dose was equivalent to approximately 11 ppm (~1300X the XDE-570 dietary burden). Samples of eggs and excreta were collected throughout the study. The test hens were sacrificed approximately 24 hours after the final dose. The tissue samples of fat, composite muscle (light and dark), skin and liver were collected for analysis.

The results indicated that the total radioactive residues (TRRs) were comparable between two labelling positions for excreta, muscle, fat, liver, and egg. TRR in muscle, fat and liver were less than the limit of quantification (< LOQ). TRR in skin and eggs were very low (0.013%, < 0.007 ppm). Almost 100% of the recovered radioactivity that was administered to the hen was found in

excreta. The highest concentration of residues in tissues was found in the skin, 0.0066 ppm and 0.005 ppm in A-label and TP-label, respectively. The concentrations of residues in egg were about 0.004 ppm in both A-label and TP-label, respectively. Total radioactive residue in liver was <LOQ at 0.0014 ppm and 0.001 ppm from the A-label and TP-label experiments, respectively. Total radioactive residue in composite muscle was <LOQ at 0.0005 ppm and 0.0008 ppm from the A-label and TP-label experiments, respectively. Total radioactive residue in composite fat was <LOQ at 0.0004 ppm and 0.0006 ppm from the A-label and TP-label experiments, respectively.

Total radioactive residues in tissue (muscle, fat, skin and liver), eggs and excreta samples were determined by combustion and liquid scintillation counting (LSC). Solvent extraction and subsequent fractionation were performed on the A- and TP-labeled samples of eggs, skin and excreta (the only matrices with residue levels > 0.02 ppm). All samples were initially extracted three times with acetonitrile:water [80:20] (Figure 1). This extraction released most of the radioactivity present in these samples. The post-extracted material was lyophilized and the remaining ^{14}C activity was quantified by combustion/LSC. The excreta extracts were concentrated and analyzed by reverse phase HPLC and normal phase TLC.

The parent compound, florasulam, is not likely to bioaccumulate in fat, other tissues and egg yolk as a result of feeding of treated feed. This study demonstrated low levels of radioactivity in edible tissues. These observations are supported by the low log K_{ow} (1.00 at pH 4.0 and -1.22 at pH 7.0) which is an indication of a low potential for partition into organic solvents.

The total radioactivity in liver, fat and muscle samples was very low (< 0.0001% of administered dose); therefore, no further residue characterization was conducted. Solvent extraction and subsequent fractionation were performed on the A- and TP-labeled samples of excreta, egg and skin. All samples were initially extracted with acetonitrile:water (80:20). Further characterization of residues extracted in the acetonitrile:water phase, from egg and skin were achieved with hexane and ethyl acetate. The predominant radioactive component in extracted residues in egg and skin was parent. No other metabolites were identified in skin samples. The extractability of radioactive residues ranged between 84% and 103% of TRR for excreta, eggs and skin. The behaviour of florasulam residues in hen tissues, egg and excreta during extraction, fractionation, and chromatographic analysis demonstrated no significant differences between A and TP labeled hens.

The metabolism of florasulam in the laying hen and lactating goat were similar. In both, the majority of the radioactivity was found in the excreta. Most of the parent compound in goat and hen was eliminated unchanged with minor unknown metabolites at unquantifiable levels. No significant cleavage of the sulfonanilide bridge was observed

Conclusion: The nature of the residue in livestock is adequately understood. The metabolism of florasulam in the laying hen and goat were similar. In both species, the majority of the radioactivity was found in the excreta. Most of the parent compound in goat and hen was eliminated unchanged with minor unknown metabolites at unquantifiable levels. No significant cleavage of the sulfonanilide bridge was observed.

860.1340 Residue Analytical Methods
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Two different methods were used to quantify florasulam in wheat, barley and oat matrices. The petitioner first used a screening method, the immunoassay (IA) method, to determine the total residues of florasulam. This method determines the residues of florasulam and related metabolites (4-hydroxyphenyl florasulam) and its glucose conjugate. In addition to this method, a gas chromatography-mass selective detection method was used that determines only the parent florasulam. This method was used to reanalyze samples when total residues of florasulam and its metabolites were found above 0.005 ppm for grain and above 0.0025 ppm for other matrices.

Immunoassay (Plants) – MRID 46808018

The residue of concern (ROC) was defined from the wheat metabolism study as the parent compound, florasulam. The petitioner is not proposing a common moiety method.

The principle of the immunoassay method is based on an enzyme linked immunosorbent assay (ELISA) for the determination of residues in barley, oat and wheat. The plant matrices were ground and recovery samples were prepared by fortifying untreated control samples of wheat (immature green and dry plant, hay, grain and straw), barley (immature green and dry plant, hay, grain and straw) and oat (immature green and dry plant, hay, grain and straw) to validate the analytical method. Residues of florasulam were extracted from all matrices with an acetic acid/acetone/water extraction solution. An aliquot of the extract is evaporated to dryness and reconstituted with 0.01 N HCl, which is then extracted using liquid/liquid partitioning or applied to a C_{18} coulmn, evaporated, reconstituted in diluent and assayed with the XDE-570 RaPID Assay test kit.

The calculated method limit of detection (LOD) for the ROC, florasulam, ranged from 0.005 to 0.022 ppm for grain and for immature plant, forage, hay and straw. The method limit of quantitation (LOQ) for florasulam was established at 0.010 ppm for grain and 0.05 ppm for all other crop matrices (immature green and dry plant, forage, hay and straw). This method was found to give good recoveries within an acceptable average range of 93 ± 16 - 116 ± 5% for the analysis of wheat (immature green and dry plant, hay, grain and straw), barley (immature green and dry plant, hay, grain and straw) and oat (immature green and dry plant, hay, grain and straw). The standard deviations measured with respect to recoveries following spiking at the LOQ appear to be indicative of the method having satisfactory repeatability. A good linearity correlation coefficient, $r^2 > 0.990$, within the range of 0.01-0.20 ppm for grain and 0.05-1.0 ppm for forage, hay, straw, immature green and immature dry plant was observed for florasulam analysis.

The method of analysis was validated at the Global Environment Chemistry Laboratory, Dow AgroSciences LLC using wheat, barley and oat. No independent laboratory validation (ILV) for florasulam in wheat, barley and oat was conducted; however, this method was used as a screening method.

HED has determined that this method is acceptable as a screening method and conforms with the criteria of the OPPTS Residue Chemistry Guidelines 860.1340.

GCMS (Plants) - MRIDs 46808019, 46808020, and 46808021

The residue of concern (ROC) was defined from the wheat metabolism study as the parent compound, florasulam. The petitioner is not proposing a common moiety method.

Residues of florasulam were extracted from wheat, barley and oat matrix with acidified acetone. An aliquot of the extract was purified by filtration through a graphitized carbon solid-phase extraction (SPE) column. The extract was concentrated to remove acetone, diluted with 0.01 N hydrochloric acid, and partitioned onto an octadecyl (C_{18}) SPE column. The florasulam was eluted with a 30% acetonitrile in 0.01 N hydrochloride acid. Florasulam is partitioned, after salting, into methyl *t*-butyl ether (MTBE). The MTBE was concentrated to dryness. Residues of florasulam were dissolved in acetone and derivatized at room temperature with iodomethane and triethylamine. The acetone solution was concentrated to dryness and *N*-methyl florasulam residues were dissolved in a 5% sodium thiosulfate solution and partitioned into toluene containing the internal standard *N*-propyl florasulam. Residues of florasulam as the N-methyl florasulam derivative were determined by capillary gas chromatography with mass selective detection (GC/MSD). This is a specific method that identifies/quantifies, florasulam, the parent compound only.

The limit of detection (LOD) was calculated as three times the standard deviation (3s) which was 0.0012 ppm in grain, 0.005 ppm in forage and immature green plant, 0.0036 ppm in hay and immature dried plant and 0.0074 ppm in straw. The limit of quantitation LOQ for florasulam was established at 0.01 ppm for grain over the concentration range of 0.01-0.10 ppm, and at 0.05 ppm for forage, hay, straw, immature green plant and immature dried plant over the concentration range of 0.05-0.50 ppm.

This method was found to give good recoveries within an acceptable average range (74 ± 9% - 89 ± 8%) for the analysis of wheat (immature green and dry plant, hay, grain and straw), barley (immature green and dry plant, hay, grain and straw) and oat (immature green and dry plant, hay, grain and straw). The standard deviations measured with respect to recoveries following spiking at the LOQ appear to be indicative of the method having satisfactory repeatability. A good linearity correlation coefficient, $r^2 > 0.995$, within the range of 0.01-0.20 ppm was observed for florasulam analysis. The method employed *N*-propyl florasulam as an internal standard. Representative chromatograms of control matrices of wheat, barley and oat showed no interferences from crop components or from reagents, solvents and glassware. The chromatographic peaks were sharp and free of interferences in the retention areas of internal standard or *N*-methyl florasulam derivative.

The method of analysis was independently validated at the Enviro-Bio-Tech. Ltd. Bernville, PA using wheat grain, forage, hay and straw. This ILV study successfully validated the Dow AgroSciences method GRM 98.01 for the residues of florasulam in wheat matrices, indicating good reproducibility.

HED has determined that the GC/MSD method (GRM 98.01) is acceptable as a data collection method and conforms with the criteria of the OPPTS Residue Chemistry Guidelines 860.1340.

Conclusion: Residues of florasulam as the N-methyl florasulam derivative were determined by capillary gas chromatography with mass selective detection (GC/MSD). This is a specific method that identifies/quantifies florasulam, the parent compound only. The limit of quantitation LOQ for florasulam was established at 0.01 ppm for grain and at 0.05 ppm for forage, hay, and straw. Radiovalidation of enforcement method was not conducted due to low radioactivity. The enforcement method will be submitted to BEAD/ACL for a petition method validation (PMV).

Methods for Residue Analysis of Food of Livestock Origin - none submitted.

The results of the livestock metabolism studies in connection with very low residues detected in the crop residue studies indicated that residues will not likely be present in food of livestock origin.

However, if additional uses are added which increase the dietary burden for livestock, a livestock analytical method may be required.

860.1360 Multiresidue Methods
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Florasulam was adequately evaluated for recovery through FDA multiresidue methods. The results of the study indicate that the FDA MRM guidelines in PAM, Vol. I are not applicable to florasulam. Florasulam was not found to be naturally fluorescent; therefore, further testing under Protocol A was not required. Florasulam is not an acid or phenol; therefore, further testing under Protocol B was not required. Florasulam was not recovered using Protocol D (with no cleanup) or using Florisil cleanup under Protocols E and F. Florasulam is not a substituted urea; therefore, further testing under Protocol G was not required. The submitted data will be forwarded to the U.S. FDA for further evaluation.

860.1380 Storage Stability
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In the freezer storage stability study, the ground wheat samples of forage, grain, straw and hay spiked with florasulam at a level of 0.5 ppm were stored at -20 °C for a maximum duration of 524, 410, 313 and 459 days, respectively. A set of 0-day samples and other fortified samples were removed at various time intervals and analyzed to study the stability of florasulam. The analytical methods employed to detect residues were GRM 97.01 (Immunoassay) and GRM 98.01, the gas chromatography method with mass selective detection (GC/MSD). These methods were the same as that outlined in the analytical methodology and were used in the crop residue studies. Both methods were validated at a level of 0.05 ppm for the wheat forage, straw and hay and at a level of 0.01 ppm for wheat grain.

Conclusion: The data presented indicate residues of florasulam were relatively stable at -20 °C for 524, 410, 313 and 459 days in spiked forage, grain, straw and hay, respectively.

The freezer storage stability study is classified acceptable and satisfies the guideline requirement for OPPTS 860.1380.

860.1400 Water, Fish, and Irrigated Crops

There are no proposed uses that are relevant to this guideline topic.

860.1460 Food Handling

There are no proposed uses that are relevant to this guideline topic.

860.1480 Meat, Milk, Poultry, and Eggs

The results of the livestock metabolism studies in connection with very low residues detected in the crop residue studies indicated that residues will not likely be present in food of livestock origin. There is no reasonable expectation of finding finite florasulam residues in livestock commodities resulting from the feeding of florasulam treated crops to livestock [40 CFR 180.6(a)(3)].

However, if additional uses are added which increase the dietary burden for livestock, a livestock feeding study may be required.

Dietary Burden for Beef Cattle

Feed stuff	Tolerance	% DM	% Diet	Burden
Wheat forage	0.05	25	55	0.110
Wheat grain	0.01	89	35	0.003
Soybean meal	0	89	15	0
			100	0.113 ppm

Dietary Burden for Dairy Cattle

Feed stuff	Tolerance	% DM	% Diet	Burden
Wheat forage	0.05	25	45	0.090
Wheat grain	0.01	89	45	0.005
Soybean meal	0	89	10	0
			100	0.095 ppm

Dietary Burden for Poultry

Feed stuff	Tolerance	% Diet	Burden
Wheat grain	0.01	80	0.008
Soybean meal	0	20	0
		100	0.008 ppm

Dietary Burden for Swine

Feed stuff	Tolerance	% Diet	Burden
Wheat milled byproducts	0.01	50	0.005
Barley grain	0.01	20	0.002
Sorghum grain	0	10	0
Soybean meal	0	20	0
		100	0.007 ppm

860.1500 Crop Field Trials

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Residue Data Summary from Supervised Field Trials - Wheat Grain (MRID 46808128)

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analyzed	PHI (days)	Residues florasulam equivalent (ppm) *
			Rate (g a.i./ha)	No.	Total Rate (g a.i./ha)	% gap			
Dagmar, MT, **MT** Sheridan County, USA / 1997	Durum - Rugby	EF-1343 + 0.2% Agral 90	10.14	1	10.14	200	Grain	57	< 0.005, <0.005
Velve, ND, **ND1** McHenry County, USA / 1997	Hard red - 2375	EF-1343 + 0.2% Agral 90	10.07	1	10.07	200	Grain	58	< 0.005, <0.005
Velva, ND, **ND2** Ward County, USA / 1997	Hard red - Grandin	EF-1343 + 0.2% Agral 90	9.92	1	9.92	200	Grain	57	< 0.005, <0.005
Barnard, SD, **SD** Brown County, USA / 1997	Soft white - Penewawa	EF-1343 + 0.2% Agral 90	10.04	1	10.04	200	Grain	48	< 0.005, <0.005
Barnwell, AB, **AB1** Taber County, Canada / 1997	Hard red - Makwa	EF-1343 + 0.2% Agral 90	10.2	1	10.2	200	Grain	60	< 0.005, <0.005
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	Hard red - Teal	EF-1343 + 0.2% Agral 90	9.93	1	9.93	200	Grain	58	< 0.005, <0.005
Red Deer, AB **AB3** Red Deer County, Canada /1997	Can. Prairie soft - Oslow	EF-1343 + 0.2% Agral 90	11.1	1	11.1	200	Grain	57	< 0.005, <0.005
Minto, MB **MB1** Whitewater County, Canada / 1997	Can. Prairie soft - Taber	EF-1343 + 0.2% Agral 90	10.26	1	10.26	200	Grain	55	< 0.005, <0.005
Boissevain, MB **MB2** Morton County, Canada / 1997	Can. Prairie soft - Taber	EF-1343 + 0.2% Agral 90	10.28	1	10.28	200	Grain	57	< 0.005, <0.005
Souris, MB **MB3** Glenwood County, Canada/ 1997	Durum -Sceptre	EF-1343 + 0.2% Agral 90	10.15	1	10.15	200	Grain	57	< 0.005, <0.005
Saskatoon, SK **SK1** Corman Park, Canada / 1997	Durum - Kyle	EF-1343 + 0.2% Agral 90	10.01	1	10.01	200	Grain	55	< 0.005, <0.005
Outlook, SK **SK2** Fertile Valley, Canada / 1997	Hard red - Teal	EF-1343 + 0.2% Agral 90	9.52	1	9.52	200	Grain	41	< 0.005, <0.005
Duck Lake, SK **SK3** Duck Lake, Canada / 1997	Durum - Kyle	EF-1343 + 0.2% Agral 90	10.41	1	10.41	200	Grain	54	< 0.005, <0.005

*Residues of florasulam equivalent (parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analyzed by immunoassay method.

Residue Data Summary from Supervised Field Trials - Barley Grain (MRID 46808128)

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analyzed	PHI (days)	Residues florasulam equivalent* (ppm)
			Rate (g a.i./ha)	No.	Total Rate (g a.i./ha)	% gap			
Dagmar, MT. **MT** Sheridan County, USA / 1997	Stark, 2-row	EF-1343 + 0.2% Agral 90	9.98	1	9.98	200	Grain	57	< 0.005, <0.005
Velve, ND, **ND1** McHenry County, USA / 1997	Foster, 6-row	EF-1343 + 0.2% Agral 90	10.03	1	10.03	200	Grain	52	< 0.005, <0.005
Velva, ND, **ND2** Ward County, USA / 1997	Robust, 6-row	EF-1343 + 0.2% Agral 90	10.02	1	10.02	200	Grain	57	< 0.005, <0.005
Barnwell, AB. **AB1** Taber County, Canada / 1997	B1215, 2-row	EF-1343 + 0.2% Agral 90	9.86	1	9.86	200	Grain	60	< 0.005, <0.005
Lacombe, AB. **AB2** Lacombe County, Canada / 1997	AC Lacombe, 6-row	EF-1343 + 0.2% Agral 90	10.05	1	10.05	200	Grain	47	< 0.005, <0.005
Minto, MB **MB1** Whitewater County, Canada / 1997	Excel, 6-row	EF-1343 + 0.2% Agral 90	10.19	1	10.19	200	Grain	56	< 0.005, <0.005
Boissevain, MB **MB2** Morton County, Canada / 1997	Bedford, 2-row	EF-1343 + 0.2% Agral 90	10.24	1	10.24	200	Grain	45	< 0.005, <0.005
Saskatoon, SK **SK1** Corman Park, Canada / 1997	Manely, 2-row	EF-1343 + 0.2% Agral 90	10.09	1	10.09	200	Grain	55	< 0.005, <0.005
Duck Lake, SK **SK2** Duck Lake, Canada / 1997	Stander, 6-row	EF-1343 + 0.2% Agral 90	10.34	1	10.34	200	Grain	54	< 0.005, <0.005

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analyzed by immunoassay method.

Residue Data Summary from Supervised Field Trials - Oat Grain (MRID 46808128)

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analyzed	PHI (days)	Residues florasulam equivalent (ppm) *
			Rate (g a.i./ha)	No.	Total Rate (g a.i./ha)	% gap			
Dagmar, MT, **MT** Sheridan County, USA 1997	Dumont	EF-1343 + 0.2% Agral 90	10.09	1	10.09	200	Grain	57	< 0.005, <0.005
Velve, ND, **ND** McHenry County, USA / 1997	Valley	EF-1343 + 0.2% Agral 90	10.07	1	10.07	200	Grain	58	< 0.005, <0.005
Barnard, SD, **SD** Brown County, USA / 1997	Hytest	EF-1343 + 0.2% Agral 90	10.04	1	10.04	200	Grain	51	< 0.005, <0.005
Barnwell, AB, **AB1** Taber County, Canada / 1997	Mustang	EF-1343 + 0.2% Agral 90	10.73	1	10.73	200	Grain	54	< 0.005, <0.005
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	Cascade	EF-1343 + 0.2% Agral 90	9.94	1	9.94	200	Grain	58	< 0.005, <0.005
Minto, MB **MB1** Whitewater County, Canada / 1997	Robert	EF-1343 + 0.2% Agral 90	9.9	1	9.9	200	Grain	57	< 0.005, <0.005
Boissevain, MB **MB2** Morton County, Canada / 1997	Robert	EF-1343 + 0.2% Agral 90	10.13	1	10.13	200	Grain	57	< 0.005, <0.005
Saskatoon, SK **SK1** Corman Park, Canada / 1997	Derby	EF-1343 + 0.2% Agral 90	10.18	1	10.18	200	Grain	55	< 0.005, <0.005
Duck Lake, SK **SK2** Duck Lake, Canada / 1997	Derby	EF-1343 + 0.2% Agral 90	10.31	1	10.31	200	Grain	54	< 0.005, <0.005

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analyzed by immunoassay method.

Summary of Residue Decline Data on Wheat (forage, straw, and hay) (MRID 46808128)

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analyzed	PHI (days)	Residues of florasulam equivalent (ppm) *	Residues of florasulam equivalent (ppm) **
			Rate (g a.i./ha)	No.	Total Rate (g a.i./ha)	% gap				
Dagmar, MT, MT1 Sheridan County, USA / 1997	Durum - Rugby	EF-1343 + 0.2% Agral 90	10.14	1	10.14	200	Straw	57	< 0.025, <0.025	Not analyzed
							Forage	0	1.87, 1.69	0.691, 0.587 0.519, 0.619
							Forage	7	0.115, 0.030	< 0.025, <0.025
							Forage	15	< 0.025, <0.025	Not analyzed
							Forage	20	< 0.025, <0.025	Not analyzed
							Forage	30	< 0.025, <0.025	Not analyzed
							Forage	40	< 0.025, <0.025	Not analyzed
Velve, ND, ND1 McHenry County, USA / 1997	Hard red - 2375	EF-1343 + 0.2% Agral 90	10.07	1	10.07	200	Straw	58	< 0.025, <0.025	Not analyzed
							Forage	0	1.21, 1.26	0.413, 0.434
							Forage	7	0.112, 0.141	< 0.025, <0.025
							Forage	15	< 0.025, <0.025	Not analyzed
							Forage	20	< 0.025, <0.025	Not analyzed
							Forage	30	< 0.025, <0.025	Not analyzed
							Forage	40	< 0.025, <0.025	Not analyzed
Velva, ND, ND2 Ward County, USA / 1997	Hard red - Grandin	EF-1343 + 0.2% Agral 90	9.92	1	9.92	200	Straw	57	< 0.025, <0.025	Not analyzed
							Hay	7	0.162, 0.249	< 0.025, 0.027
							Hay	15	0.131, 0.097	< 0.025, <0.025
							Hay	30	< 0.025, <0.025	Not analyzed
							Forage	7	0.155, 0.155	< 0.025, <0.025
							Forage	15	< 0.025, 0.028	<0.025
							Forage	30	< 0.025, <0.025	Not analyzed
Barnard, SD, SD	Soft white - Penewawa	EF-1343 + 0.2% Agral 90	10.04	1	10.04	200	Straw	48	< 0.025, <0.025	Not analyzed

Brown County, USA / 1997							Hay	7	0.155, 0.141	< 0.025, <0.025
							Hay	15	< 0.025, 0.026	Not analyzed
							Hay	30	< 0.025, <0.025	Not analyzed
							Forage	7	< 0.025, <0.025	Not analyzed
							Forage	15	< 0.025, <0.025	Not analyzed
							Forage	30	< 0.025, <0.025	Not analyzed
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	Hard red - Teal	EF-1343 + 0.2% Agral 90	9.93	1	9.93	200	Straw	58	< 0.025, <0.025	Not analyzed
Minto, MB **MB1** Whitewater County, Canada / 1997	Can. Prairie soft - Taber	EF-1343 + 0.2% Agral 90	10.26	1	10.26	200	Straw	55	< 0.025, <0.025	Not analyzed
Saskatoon, SK **SK1** Corman Park, Canada / 1997	Durum - Kyle	EF-1343 + 0.2% Agral 90	10.01	1	10.01	200	Straw	55	< 0.025, <0.025	Not analyzed

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analyzed by immunoassay method.
** Residues of florasulam parent only. Samples were analyzed by GC/MSD method.

Summary of Residue Decline Data on Barley (straw and hay) (MRID 46808128)

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analyzed	PHI (days)	Residues of florasulam equivalent (mg/kg) *	Residues of florasulam equivalent (mg/kg) **
			Rate (g a.i./ha)	No.	Total Rate (g a.i./ha)	% gap				
Dagmar, MT, MT Sheridan County, USA / 1997	Stark, 2-row	EF-1343 + 0.2% Agral 90	9.98	1	9.98	200	Straw	57	< 0.025, <0.025	Not analyzed
Velve, ND, **ND1** McHenry County, USA / 1997	Foster, 6-row	EF-1343 + 0.2% Agral 90	10.03	1	10.03	200	Straw	52	< 0.025, <0.025	Not analyzed
Velva, ND, **ND2** Ward County, USA / 1997	Robust, 6-row	EF-1343 + 0.2% Agral 90	10.02	1	10.02	200	Straw	57	< 0.025, <0.025	Not analyzed
							Hay	7	0.187, 0.244	< 0.025, <0.025
							Hay	15	0.083, 0.107	< 0.025, <0.025
							Hay	30	< 0.025, <0.025	Not analyzed
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	AC Lacombe, 6-row	EF-1343 + 0.2% Agral 90	10.05	1	10.05	200	Straw	47	< 0.025, <0.025	Not analyzed
Minto, MB **MB1** Whitewater County, Canada / 1997	Excel, 6-row	EF-1343 + 0.2% Agral 90	10.19	1	10.19	200	Straw	56	< 0.025, <0.025	Not analyzed

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analyzed by immunoassay method.
** Residues of florasulam parent only. Samples were analyzed by GC/MSD method.

Summary of Residue Decline Data on Oat (straw, hay, and forage) (MRID 46808128)

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analyzed	PHI (days)	Residues of florasulam equivalent (mg/kg) *	Residues of florasulam equivalent (mg/kg) **
			Rate (g a.i./ha)	No.	Total Rate (g a.i./ha)	% gap				
Dagmar, MT, **MT** Sheridan County, USA / 1997	Dumont	EF-1343 + 0.2% Agral 90	10.09	1	10.09	200	Straw	57	< 0.025, <0.025	Not analyzed
							Forage	0	1.64, 1.7	0.630, 0.592, 0.514, 0.489
							Forage	7	0.106, 0.112	< 0.025, <0.025
							Forage	15	< 0.025, <0.025	Not analyzed
							Forage	20	< 0.025, 0.028	Not analyzed
							Forage	30	< 0.025, <0.025	Not analyzed
							Forage	40	< 0.025, <0.025	Not analyzed
Velve, ND, **ND** McHenry County, USA / 1997	Valley	EF-1343 + 0.2% Agral 90	10.07	1	10.07	200	Straw	58	< 0.025, <0.025	Not analyzed
							Forage	0	0.905, 0.933	Not analyzed
							Forage	7	0.132, 0.106	< 0.025, <0.025
							Forage	15	< 0.025, <0.025	Not analyzed
							Forage	20	< 0.025, <0.025	Not analyzed
							Forage	30	< 0.025, <0.025	Not analyzed
							Forage	40	< 0.025, <0.025	Not analyzed
Barnard, SD, **SD** Brown County, USA / 1997	Hytest	EF-1343 + 0.2% Agral 90	10.04	1	10.04	200	Straw	51	< 0.025, <0.025	Not analyzed
							Hay	7	0.037, 0.041	< 0.025, <0.025
							Hay	15	< 0.025, <0.025	Not analyzed
							Hay	30	< 0.025, <0.025	Not analyzed
							Forage	7	0.093, 0.096	< 0.025, <0.025
							Forage	15	0.056, 0.048	< 0.025, <0.025
							Forage	30	< 0.025, <0.025	Not analyzed
Lacombe, AB, **AB2**	Cascade	EF-1343 + 0.2% Agral 90	9.94	1	9.94	200	Straw	58	< 0.025, <0.025	Not analyzed

Lacombe County, Canada / 1997										
Minto, MB **MB1** Whitewater County, Canada / 1997	Robert	EF-1343 + 0.2% Agral 90	9.9	1	9.9	200	Straw	57	<0.025, <0.025	Not analyzed
Saskatoon, SK **SK1** Corman Park, Canada / 1997	Derby	EF-1343 + 0.2% Agral 90	10.18	1	10.18	200	Straw	55	<0.043, <0.039	Not analyzed

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analyzed by immunoassay method
** Residues of florasulam parent only. Samples were analyzed by GC/MSD method.

Residue Data from Crop Field Trials with Florasulam (MRIDs 46808129 and 46808031). Not detectable (ND) residues are assumed to be equivalent to LOD of 0.015 ppm.								
Trial ID (City/State/Year)	Reg.	Crop/ Variety	Matrix	Total Rate, g a.i./ha	PHI (days)	Residues [1] (ppm)	Corrected Residues [4] (ppm)	Corrected Residues [2] (ppm)
Pierce/CO/1997 CO1	8	Wheat/Soft White	Hay	9.81	7 15 30	0.039, 0.044, 0.042 0.036, 0.031, 0.035 NA[3]		0.062, 0.071, 0.068*** 0.058, 0.049, 0.055 NA
Brampton/ND/1997 ND1	5	Wheat/Hard Red	Hay	9.88	7 15	0.017 0.015		0.028 0.023
			Forage	9.99	7 15	0, 0 0	ND, ND ND	-
Mooreton/ND/1997 ND2	5	Wheat/Hard Red	Forage	9.97	7 15	0.035, 0.023 0.107[5], 0.029	0.038, 0.025 ND, 0.032	-
Britton/SD/1997 SD1	5	Wheat/Hard Red	Hay	9.77	7	0.033	0.052	-
			Forage	9.89	7	0, 0	ND, ND	-
Theilman/MN/1997 MN1	5	Oat/Ogle	Forage	10.35	7	0, 0	ND, ND	-
			Hay	10.11	7	0	ND	-
Britton/SD/1997 SD2	5	Oat/Jerry	Forage	9.90	7	0, 0	ND, ND	-
			Hay	9.88	7 30	0 0.014	ND	 0.022
Arkansaw/WI/1997 WI1	5A	Oat/Hazel	Forage	10.39	7	0, 0	ND, ND	-
			Hay	10.16	7 15	0.027, 0.034 0	 ND	0.043, 0.054
Brampton/ND/1997 ND5	5	Barley/ Foster	Hay	9.87	7 15 30	0 0 0	ND ND ND	-
Britton/SD/1997 SD4	5	Barley/ Foster	Hay	9.92	7 30	0 0	ND ND	-
Minot/ND/1997 ND4	5	Rye/Dacold	Forage	9.94	0 7 10 15	1.002, 0.972, 0.838 0.073, 0.064 0.046, 0.050 0.029, 0.042	1.101, 1.068, 0.921 0.081, 0.071 0.050, 0.055 0.032, 0.046	-

Method 99.17								
Havelock/New Brunswick/2001	1	Oat/Capital	Grain	9.96	60	0, 0	ND	-
Winchester/Ontario/ 2001	5B	Barley/ Morrison	Grain	9.8	58	0, 0	ND	-
Kemptville/Ontario/ 2001	5B	Barley/ Morrison	Grain	10.2	54	0, 0	ND	-

[1] The screening Immunoassay method GRM 97.01 was used to screen for residues in samples. Detectable residues were confirmed using the GC-MSD method GRM 98.01. Results of confirmatory analyses are reported within this table.
[2] Corrected for daily recovery and storage stability (factor of 0.69).
[3] Not Analyzed. Residues not detected in IA method
[4] Values corrected for daily recovery only.
[5] Peak, not due to DE-570, detected.
*** Residues were greater than proposed tolerance of 0.05 ppm; however, HED concludes proposed tolerance would adequately cover residues of florasulam in forage since field trials were conducted at a 2X exaggerated rate.

The supervised field trials indicated that residues of florasulam in grain, forage, hay, and straw of wheat, barley, rye, and oats were non quantifiable (<0.01 ppm for grain, <0.05 ppm for forage, hay, and straw), following a single foliar application at an exaggerated rate (2 X proposed maximum seasonal application rate). Florasulam residues were greater than the proposed tolerances in one wheat forage field trial. However, HED concludes the proposed tolerance of 0.05 ppm for wheat forage would adequately cover residues in wheat forage since field trials were conducted at a 2X exaggerated rate.

Field trials were not submitted for several of the required EPA regions but additional field trials were submitted for Canadian regions. Since residues were less than the LOQ, HED will allow the reduced dataset.

	REGION														
SUBMITTED	1	2	3	4	5	6	7	8	9	10	11	12	13	14	TOTAL
Crop															
Wheat					3		7	1						6	17
Barley					4		5							4	13
Oats	1				3		6							2	12
Rye					1										1

REQUIRED	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Crop															
Wheat		1		1	5\3	1	5\4	6\4			1				20/15
Barley	1	1			3\2		4\3		1	1	2\1				12/9
Oats	1	1			9\6	1	3\2	1							16/12
Rye		1			2		2								5

Conclusion: Tolerances are being proposed for wheat, oats, rye, barley, and triticale. Canadian and U.S. field trials were submitted for wheat, rye, barley, and oats. Residues of florasulam were below the LOQ for grain (0.01 ppm) and forage, hay, and straw (0.05 ppm). Florasulam residues were greater than the proposed tolerance (LOQ) in one wheat forage field trial. However, HED concludes the proposed tolerance of 0.05 ppm for wheat forage would adequately cover residues in wheat forage since field trials were conducted at a 2X exaggerated rate. Field trials were not submitted for several of the required EPA regions but additional field trials were submitted for Canadian regions. Since residues were less than the LOQ, HED will allow the reduced dataset.

860.1520 Processed Food and Feed

The supervised field trials indicated that residues of florasulam in grain of wheat, barley and oats were not quantifiable (<0.01 ppm) following a single foliar application at an exaggerated rate (2 X the proposed maximum seasonal application rate). In addition, the metabolism studies in wheat treated with ^{14}C-DE-570 at the exaggerated rate of 50 g a.i./ha (10X the proposed maximum season rate) indicated very low radioactive residue levels (maximum of 0.002 ppm).

Conclusion: HED concludes that it is unlikely that residues of florasulam in processed food/feed items will concentrate when treated according to the proposed use pattern (0.0045 lb a.i./acre). The proposed tolerance of 0.01 ppm for the RAC will cover potential residues of florasulam in the processed commodities of wheat, barley and oats.

860.1650 Submittal of Analytical Reference Standards

As of 3/22/2007, no analytical standard for florasulam was available the EPA Analytical Chemistry Lab. The reference standards should be sent to the Analytical Chemistry Lab, which is located at Fort Meade, Maryland. They can be sent to the attention of Terry Cole, Dallas Wright or Frederic Siegelman at the following address:

USEPA
National Pesticide Standards Repository/Analytical Chemistry Branch/OPP
701 Mapes Road
Fort George G. Meade, MD 20755-5350

The full 9 digit zip code is mandatory or the mail will be returned to you.

860.1850 Confined Accumulation in Rotational Crops
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In the confined rotational crop study, XDE-570 (florasulam), > 97% a.i., E-1343 Suspension Concentrate labeled either as the [UL-phenyl-^{14}C]XDE-570 or the [9-triazolopyrimidine-^{14}C]XDE-570, was applied to sandy loam soil at an application rate of 7.5 g a.i./ha (1.5X the maximum proposed postemergent application rate). Spring wheat, sunflower, cabbage and carrots were planted at 30 days after treatment (DAT) of soil.

Spring wheat, sunflowers, cabbage and carrots were harvested at maturity i.e., 168 DAT (spring wheat and sunflowers), 195 DAT (cabbage), and 156 DAT (carrots). Each crop was separated into fractions as spring wheat (ears and straw), sunflower (heads and stems), cabbage (shoots) and carrot (leaves and roots). The samples of crop fractions were subjected to three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash). Each wash was analyzed to determine total ^{14}C-residues (TRRs) using combustion/liquid scintillation counting. None of the fraction from rotational crops had TRRs greater than 0.01 ppm. Therefore, no further attempt was made to profile TRRs.

Because levels of TRRs in the rotational crops were low (≤ 0.01 ppm), no parent or metabolite were identified. Therefore, the confined rotational crop study supports the definition of the residue of

concern (ROC) of parent only as defined in the plant and livestock metabolism studies.

In addition, the soil metabolism study, reviewed by EAD, indicated that the primary transformation product was 5-OH-XDE-570. The sorption of both XDE-570 and 5-OH-XDE-570 increased with time indicating that the remaining XDE-570 in the soil is less bioavailable and less mobile. The concentration of XDE-570 and 5-OH-XDE-570 for potential uptake from soil is very low. At 30 DAT, residues of XDE-570 and 5-OH-XDE-570 in soil was low, ≤ 0.008 ppm. Therefore, it is expected that any residues translocation from the soil to the rotational crops would also be low.

Based on the results of the confined rotational crop study, field rotational crop studies are not required, and a 30-day plant back interval (PBI) can be supported for all crops. The label has a plant back interval greater than of 30 days for barley, canola, forage grasses, oats, peas, rye and wheat.

This confined rotational crop study is classified acceptable and satisfies the guideline requirement for OPPTS 860.1850.

860.1900 Field Accumulation in Rotational Crops

Because levels of TRRs in the confined rotational crop study were low (≤ 0.01 ppm), no field accumulation study is required.

860.1550 Proposed Tolerances

The following tolerances have been proposed for residues of florasulam, *N*-(2,6-difluorophenyl)-8-fluoro-5-methoxy[1,2,4]-triazolo[1,5-*c*]pyrimidine-2-sulfonamide:

Table 3. Tolerance Summary for Florasulam

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (correct commodity definition)
Barley grain	0.01	0.01	Barley, grain
Barley forage	0.05		Not a RAC per Table 1, OPPTS 860 Guidelines.
Barley hay	0.05	0.05	Barley, hay
Barley straw	0.05	0.05	Barley, straw
Oats grain	0.01	0.01	Oat, grain
Oats forage	0.05	0.05	Oat, forage
Oats hay	0.05	0.05	Oat, hay
Oats straw	0.05	0.05	Oat, straw
Rye grain	0.01	0.01	Rye, grain
Rye forage	0.05	0.05	Rye, forage
Rye hay	0.05		Not a RAC per Table 1, OPPTS 860 Guidelines.
Rye straw	0.05	0.05	Rye, straw
Triticale grain	0.01		Triticale is covered by wheat per 40CFR 180.1(g)
Triticale forage	0.05		
Triticale hay	0.05		
Triticale straw	0.05		
Wheat grain	0.01	0.01	Wheat, grain
Wheat forage	0.05	0.05	Wheat, forage
Wheat hay	0.05	0.05	Wheat, hay
Wheat straw	0.05	0.05	Wheat, straw

Maximum residue levels are established in Canada for residues of florasulam in barley, oats, and wheat grain at 0.01 ppm. No harmonization issues exist.

This DER was initially reviewed by Canada's PMRA and has been reviewed by HED. Conclusions herein agree with HED policy. In addition, this DER has been modified to include the submission MRID number.

Thurston Morton **23-May-2007**

Primary Evaluator — Date:
Kimberley Meadows, Evaluation Officer, FREAS, HED, PMRA

Peer Reviewer — Date:
Suzan Mathew, Evaluation Officer, FREAS, HED, PMRA

Date:
Louise G. Croteau, Work Group Lead 2, Senior Evaluation Officer, FREAS, HED, PMRA

Approved by — Date:
Ariff Ally, Section Head, FREAS, HED, PMRA

In the absence of signatures, this document is considered to be a draft with deliberative material for internal use only.

STUDY REPORTS:

46808129 Bargar, E.M., Foster, D.R. March 6, 2000. Magnitude of the Residue of DE-570 in Wheat, Barley, Oats, and Rye. Laboratory Study No. RES97081. Unpublished study prepared by Dow AgroSciences. 128 pages.

46808031 Roberts, D.W., Phillips, A.M. November 7, 2002. Magnitude of the Residue of Florasulam in Canada Oat and Barley Grain. Laboratory Study No. 011164. Unpublished study prepared by Dow AgroSciences. 48 pages.

EXECUTIVE SUMMARY:

Dow AgroSciences has submitted field trial data for florasulam on wheat, oat, rye, and barley. Thirteen trials were conducted as confirmatory trials encompassing Regions 1, 5, 5A, 5B, and 8 during the 1997 and 2001 growing seasons. The number and locations of the confirmatory field trials are in accordance with the request sent to the registrant upon granting temporary registration.

At each test location, florasulam (suspension concentrate) was applied once to the crop from tillering to ligule stage using foliar broadcast or backpack sprayers at a target rate of 10 g a.i./ha/season. An adjuvant, Agral 90 (0.2% v/v) was added to the spray mixture for all applications. Wheat, oat, barley, and rye were harvested at 7, 15, and 30 days after treatment (DAT) for the U.S. trials, while the Canadian trials were harvested at 54, 58, and 60 DAT.

Both the immunoassay screening method (GRM 97.01) and the GC-MSD confirmatory method (GRM 98.01) were deemed acceptable for data gathering and enforcement methods, respectively. The LC-MS/MS method GRM 99.17 used in the Canadian trials was also deemed acceptable as a data gathering method based on method validation. The reported LOQs for method GRM 97.01 were 0.057 ppm (forage), 0.064 ppm (hay), 0.087 ppm (straw), and 0.017 ppm (grain). The reported LOQ for method GRM 98.01 was 0.05 ppm (forage and hay). The reported LOQ for oat and barley grain from method GRM 99.17 was 0.01 ppm.

The maximum storage intervals for wheat, oat, barley, and rye samples from harvest to analysis were 450, 463, 433, and 491 days, respectively. The storage stability data for wheat will be considered adequate to support the storage conditions and intervals of samples from the submitted wheat, barley, oat and rye field trials. Residues in hay samples were corrected for degradation observed during storage (31% in 459 days).

Residues in wheat hay ranged from 0.028 ppm to 0.071 ppm at a 7 day PHI, and from 0.023 ppm to 0.058 ppm at a 15 day PHI. Oat hay residues ranged from 0.015 ppm to 0.054 ppm at a 7 day PHI. Remaining samples of wheat, oat, and barley (hay and forage), as well as oat and barley grain were ≤LOQ at various PHIs. Residue decline data show that residues of florasulam decreased by 96.2% in rye forage with increasing pre-harvest intervals (0 to 15 days).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptobility of this study for regulatory purposes is addressed in the forthcoming Canadian Regulatory Decision Document.

COMPLIANCE:

Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided. Deviations from GLP as follows:

- documentation is incomplete by GLP standards for weather/meteorological data, crop and pesticide history, plot preparation, and pesticide maintenance data
- documentation for the return of all test substance containers is complete, however, the test substance container for the CO1 trial site could not be located in the test substance repository.

These deviations will not impact the validity of this study.

A. BACKGROUND INFORMATION

Florasulam is a member of the triazolopyrimidine family. It is used as a post-emergence herbicide for the control of broadleaf weeds in small cereal grains such as spring wheat (including durum) spring barley and oats (tank mix for oats only). The mode of action is through acetolactate synthesis (ALS) inhibition.

TABLE A.1. Test Compound Nomenclature

Compound	Chemical Structure
Common name	Florasulam
Company experimental name	DE-570 or EF-1343
IUPAC name	2', 6', 8-trifluoro-5-methoxy-*s*-triazolo [1,5-c]pyrimidine-2-sulfonanilide
CAS name	*N*-(2,6-diflurophenyl)-8-fluoro-5-methoxy(1, 2, 4)triazolo(1, 5-c)pyrimidine-2-sulphonamide
CAS #	145701-23-1
End-use product/EP	Florasulam Suspension Concentrate
Molecular Formula	$C_{12}H_8O_3N_5F_3S$
Molecular Mass	359.3

TABLE A.2. Physicochemical Properties		
Parameter	**Value**	**Reference**
Physical State	Solid	PMRA Lab Services
Melting point/range	193.5-230.5°C	
Specific gravity	1.53 at 22°C	
Water solubility	Medium / Solubility (g/L) water 0.121 pH 5 0.084 pH 7 6.36 pH 9 94.2	
Solvent solubility	Solvent / Solubility (g/L) acetone 123 acetonitrile 72.1 ethyl acetate 15.9 methanol 9.81 dichloromethane 3.75 xylene 0.227 n-octanol 0.184 n-heptane0.000019	
Vapour pressure	1×10^{-5} Pa at 25°C	
Dissociation constant (pK_a)	4.54	
Octanol/water partition coefficient (K_{ow}) at 22°C	pH / Log K_{ow} 4 1.00 7 -1.22 10 -2.06	
UV/visible absorption spectrum	Form / λmax Acidic 259.8 203.8 Basic 262.4 209.7 Methanolic 204.1 No absorbence above 300 nm.	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

TABLE B.1.1 Trial Site Conditions

Trial Identification (City, State/Year)	Soil characteristics				Meteorological data		
	Type	%OM*	pH*	CEC* meq/g	Overall monthly rainfall range	Overall T °C range	
						min	max
Pierce/CO/1997	Loam	2.1	7.7	21.8	1.6-5.5 in	40.8-54.8	71.7-84.7
Brampton/ND/1997	Silt Loam	3.5	8.0	33.3	0.84-4.3 in	41.3-60.7	67.1-81.7
Mooreton/ND/1997	Silt Loam	3.2	8.0	22.9	0.74-4.16 in	41.7-60.5	68.3-82.9
Britton/SD/1997	Loam	2.9	8.1	35.7	0.84-4.3 in	41.3-60.7	67.1-81.7
Theilman/MN/1997	Loam	2.9	8.1	35.7	0.13-6.84 in	34.4-60.2	65.9-84.1
Britton/SD/1997	Silt Loam	2.0	6.1	9.0	1.34-3.22 in	41.3-60.7	67.1-81.7
Arkansaw/WI/1997	Loamy Sand	1.7	5.8	9.2	0.5-6.8 in	34.1-61.1	48.4-82.1
Brampton/ND/1997	Loam	7.4	7.7	30.4	0.84-4.3 in	41.3-60.7	67.1-81.7
Britton/SD/1997	Loam	3.9	7.8	35.8	0.84-4.3nm in	41.3-60.7	67.1-81.7
Minot/ND/1997	Loamy sand	7.4	7.7	30.4	0.28-3.11 in	40-58	67-93
Havelock/New Brunswick/2001	Sandy Loam	-	-	-	6.4-37.7 mm	9.26-14.22	23.78-27
Winchester/Ontario/ 2001	Clay Loam	-	-	-	0-27 mm	10.14-13	25.72-28.53
Kemptville/Ontario/ 2001	Sandy Loam	-	-	-	2-64.8 mm	11.05-13.69	25.85-28.36

*These parameters are optional except in cases where their value affects the use pattern for the chemical.

Temperature conditions in the U.S. sites varied around the average historical temperatures. However, the amount of precipitation at all of the sites was significantly lower (average 2" lower) than normal in the early summer months. The registrant stated that one site for rye reported poor crop stand due to the dry weather. Irrigation was used at the Pierce, CO site during June and July (2"). Graphical representation of the weather data of U.S. sites submitted can be found in Appendix 1.

Temperatures is Canada during the trials were slightly above the historical averages. Rainfall was once again significantly less than normal. No information regarding irrigation was provided.

TABLE B.1.2. Study Use Pattern.

Location (County, State/Year)	EP	Application					Tank Mix Adjuvants
		Method/Timing	Vol, L/ha	Rate, g a.i./ha	RTI, days	Total Rate, g a.i./ha	
Pierce/CO/1997	EF-1343	1. Foliar broadcast/flag leaf (8)	0.1868	9.8	N/A	9.8	Agral 90 (0.2%,v/v)
		2. Foliar broadcast/tillering (3)	0.18524				
Brampton/ND/1997	EF-1343	1. Foliar broadcast/flag leaf (9)	0.1869	9.88	N/A	9.88	Agral 90 (0.2%,v/v)
		2. Foliar broadcast/tillering (3)	0.18868	9.98		9.98	
		3. Foliar broadcast/flag leaf (9)	0.47336	25.04		25.04	
Mooreton/ND/1997	EF-1343	1. Foliar broadcast/flag leaf (9)	0.18772	9.93	N/A	9.93	Agral 90 (0.2%,v/v)
		2. Foliar broadcast/tillering (4-5)	0.18848	9.97		9.97	
Britton/SD/1997	EF-1343	1. Foliar broadcast/flag leaf (9)	0.1846	9.77	N/A	9.77	Agral 90 (0.2%,v/v)
		2. Foliar broadcast/tillering (3)	0.18696	9.89		9.89	
Theilman/MN/1997	EF-1343	1. Foliar broadcast/flag leaf (8)	0.1912	10.11	N/A	10.11	Agral 90 (0.2%,v/v)
		2. Foliar broadcast/tillering (3)	0.19492	10.31		10.31	
Britton/SD/1997	EF-1343	1. Foliar broadcast/flag leaf (9)	0.18696	9.89	N/A	9.89	Agral 90 (0.2%,v/v)
		2. Foliar broadcast/tillering (3)	0.18708	9.9		9.9	
Arkansaw/WI/1997	EF-1343	1. Foliar broadcast/flag leaf (8-9)	0.19201	10.16	N/A	10.16	Agral 90 (0.2%,v/v)
		2. Foliar broadcast/tillering (3)	0.19555	10.34		10.34	
Brampton/ND/1997	EF-1343	1. Foliar broadcast/flag leaf (8-9)	0.18656	9.87	N/A	9.87	Agral 90 (0.2%,v/v)
Britton/SD/1997	EF-1343	1. Foliar broadcast/flag leaf (8-9)	0.18756	9.92	N/A	9.92	Agral 90 (0.2%,v/v)
Minot/ND/1997	EF-1343	1. Foliar broadcast/flag leaf (8-9)	0.18819	9.96	N/A	9.96	Agral 90 (0.2%,v/v)
		2. Foliar broadcast/tillering (3)	0.1879	9.94		9.94	
Havelock/New Brunswick/2001	EF-1343	Backpack sprayer/ligule stage	0.1980	9.96	N/A	9.96	Agral 90 (0.2%,v/v)
Winchester/Ontario/2001	EF-1343	Backpack sprayer/last leaf appearance to ligule stage	0.1947	9.8	N/A	9.8	Agral 90 (0.2%,v/v)
Kemptville/Ontario/2001	EF-1343	Backpack sprayer/last leaf appearance to ligule stage	0.2023	10.2	N/A	10.2	Agral 90 (0.2%,v/v)

TABLE B.1.3. Trial Numbers and Geographical Locations

NAFTA Growing Region	Wheat			Oat			Barley		
	Submitted	Requested*		Submitted	Requested		Submitted	Requested	
		Canada	US		Canada	US		Canada	US
1				1	1				
1A									
2									
3									
4									
5	3	2		2	1		2	1	
5A				1	1				
5B							2	1	
6									
7	6	7(5)		5	2		4	2	
7A	1	1		1			1		
8	1								
9									
10									
11									
12									
13									
14	6	10(7)		3	10(7)		4	12(9)	
15									
16									
17									
18									
19									
20									
21									
Total	17	20		13	15		13	16	

*Science Review (2001) requested supplemental confirmatory data (at a reduced # of trials) to support a full registration of Florasulam Suspension Concentrate in order to confirm the lack residues in various cereal crops. Wheat and rye commodities were not requested but were included in the study and have been reviewed.
Numbers in brackets represent the number of trials required for a crop group MRL.

B.2. Sample Handling and Preparation

Using a manual or mechanical harvest method, a single composite sample was taken from the control plot, and duplicate composite samples were taken from plots treated with a single foliar broadcast application of florasulam at a target rate of 10 g a.i./ha/season.

Samples of wheat (forage and hay), oat (forage and hay), barley (hay), and rye (forage and hay) were collected at 7, 15, and 30 days after treatment (DAT). Both grain and straw samples were collected at 60 DAT. A residue decline study was also conducted on rye in which samples were collected at 0, 10, and 40 DAT. After samples were collected, they were placed into polyethylene bags, labelled, and placed on dry ice or frozen within 4 hours of collection.

Samples were treated with liquid nitrogen, ground, and homogenized. Sub-samples were taken and placed in high-density polyethylene freezer containers and stored at -20°C. Wheat forage, hay, and grain were stored for 450, 446, and 248 days, respectively. Barley hay, straw, and grain were stored for 433, 242, and 239 days, respectively. Oat forage, hay, straw, and grain were stored for 463, 449, 260, and 259 days, respectively. Rye forage, straw, and grain were stored for 491, 216, and 256 days, respectively.

B.3. Analytical Methodology

Analytical method GRM 97.01 (Immunoassay kits) developed by Strategic Diagnostics Inc. and Dow AgroSciences was used to determine residues of florasulam in wheat, barely, oats, and rye. This method was previously reviewed by PMRA for the registration of florasulam on wheat, barley, and oats and was deemed acceptable for data gathering purposes based on method validation.

Residues of florasulam were extracted from matrices using an acidified acetone solution, followed by clean-up on C_{18} SPE columns. Forage and the first hay samples were excluded from the C_{18} SPE clean-up columns. These samples were instead partitioned in a dilute acid/hexane solution followed by the addition of a NaOH buffer and dilution. All samples were analyzed using SDI XDE-570 IA kits. An aliquot of diluted extract was transferred to a test tube with enzyme conjugated florasulam and magnetic particles coated with antibodies specific to florasulam. During incubation the florasulam in the extract competes with the enzyme conjugate for antibody sites on the magnetic particles. The bound material was held in place by a magnetic field while the unbound was decanted from the test tube. An enzyme substrate (hydrogen peroxide) and a chromogen were added to the remaining bound material in order to detect the presence of florasulam. The reaction was stopped by adding an acid. The amount of florasulam present was determined by the colour intensity of the final material. A low concentration of florasulam in the sample will yield a sample with a more intense colour (vice versa).

A RPA-1 RaPID Photometric Analyzer was used to measure the absorbence of the sample at 450 nm. The concentration of florasulam in samples was calculated from the regression equation using the preprogrammed software in the Photometric Analyzer.

Since the immunoassay kits have a high affinity for 4-OH-florasulam and the 4-OH-florasulam glucose conjugate metabolites, the residue results are higher than results from a GC-MSD method. Therefore, any results from the IA screening method greater than LOQ were also analyzed by method GRM 98.01, a GC-MSD method specific for florasulam. Method GRM 98.01 was also previously evaluated by PMRA and was deemed acceptable as an enforcement method.

Method GRM 98.01 involved the residues being extracted with an acetone/water/acetic acid (80/20/1) solution. An aliquot of the extract was then filtered on a graphitized carbon solid phase extraction column. The sample is then diluted, after acetone has evaporated, with 0.01N HCl and cleaned up using C_{18} SPE columns. The resulting eluent is then extracted with methyl-tert-butyl ether and evaporated to dryness. Derivitization of the sample was done with iodomethane to form the *N*-methyl derivative. The sample was evaporated to dryness and reconstituted in a 5% sodium thiosulfate solution, then partitioned into toluene (containing *N*-propyl-florasulam as an internal standard) prior to being analyzed by GC-MSD.

The Canadian trials used the LC-MS/MS method GRM 99.17 for analysis (which was not previously evaluated by PMRA). Residues were extracted from the homogenized grain sample using acetone/water/acetic acid solution. An aliquot of the extract was acidified and extracted again into methyl tertiary butyl ether (MTBE), which was evaporated to dryness and reconstituted in ethyl acetate, then finally purified with a Strong Anion Exchange (PE-AX) SPE column. Residues were eluted with 1% formic acid in water/methanol solution containing *N*-methyl florasulam as an internal standard. The quantitation of residues was performed by LC-MS/MS with a different mobile phase (solvent A: 1:1 ACN/methanol with 0.1% acetic acid, Solvent B: water with 0.1% acetic acid). Analysis was performed using a YM AM-302-3 column installed in a PE/Sciex API 2000 LC, with a PE/Sciex MSD operating in the positive ion ESI mode.

The LOD and LOQ for grain in this study were reported as 0.003 ppm and 0.01 ppm, respectively. Recoveries of florasulam in forage, hay, straw, and grain spiked at LOQ were between 70-120% (±20% SDEV), indicating acceptable repeatability and precision.

C. RESULTS AND DISCUSSION

Both analytical methods GRM 97.01 (IA) and GRM 98.01 (GC-MSD) have been previously reviewed by PMRA and have been deemed acceptable data gathering and enforcement methods. The LOQ for method GRM 97.01 reported for forage, hay, straw, and grain was 0.057 ppm, 0.064 ppm, 0.087 ppm, and 0.017 ppm, respectively. The LOD for grain was 0.005 ppm and, 0.025 ppm for all other commodities. Recoveries of florasulam in forage, hay, straw, and grain (TABLE C.1) were between 70-120% (± 20% SDEV), indicating acceptable repeatability and precision.

The LOQ from method GRM 98.01 reported for forage and hay was 0.05 ppm, and the LOD was reported as 0.015 ppm. Most recoveries of florasulam in forage, hay, straw, and grain (TABLE C.1) spiked at LOQ were between 70-120% (±20% SDEV), indicating acceptable repeatability and precision. Samples of straw and grain were not analyzed by GC-MSD since no residues were detected in the IA method.

Although the enforcement method was GC-MSD (GRM 98.01), the LC-MS/MS method GRM 99.17 has a similar extraction process (extraction with acetone/water/acetic acid solution, SPE clean up, a second extraction with methyl tertiary butyl ether (MTBE)), internal standards differed as GRM 98.01 used *N*-propyl-florasulam and GRM 99.17 used *N*-methyl florasulam. Procedural recoveries (TABLE C.1) with LC-MS/MS were within guideline requirements (70-120%) and indicate that the method is adequate for quantifying residues in wheat, oat, barley, and rye. The chromatograms are free from interferences. Detector response was linear ($r^2 = 0.9972$) in the range of 0.0002 to 0.05 µg/mL.

Wheat was used as a representative crop to demonstrate the storage stability of cereal crops (TABLE C.2). The storage stability of oat, barley, and rye is being extended from wheat on the basis of crop group. The actual length of storage is consistent with the demonstrated storage stability for the various matrices. Residues in hay samples were corrected for both method recovery and storage stability, due to a 31% degradation over the storage period. The remaining residues were corrected for method recovery only.

As a result of a Science Review in 2001, the Agency requested a reduced number of supplementary trials to confirm the lack of residues of florasulam in various cereal crops for the support of a full registration. The number of trials submitted corresponds to the request made by the Agency upon granting the temporary registration.

Temperature conditions (TABLE B.1.1) were consistent with the normal historical averages, however the amount of rain was significantly lower in the beginning of the season than was recorded historically. The amount of rain would unlikely affect the outcome of the trial since the date of application was during more normal seasonal precipitation levels. Graphical representation of weather data for the U.S. trials can be found in Appendix 1. Soil characteristics for the Canadian trials were not including in the study report.

TABLE B.1.2 summarizes the study use patterns. A single foliar application was made (to wheat, oat, barley, and rye) at two-fold the proposed label rate of 5 g a.i./ha/season, for total seasonal rate of 9.77 to 10.34 g a.i./ha. Agral 90 (0.2%, v/v) was added prior to application to account for any synergistic effects, since it appears on the proposed label. The proposed label lists the PHI for treated crops as 60 days and the grazing interval as 7 days.

The summary residue data from the crop field trials treated with florasulam (TABLE C.4) reports the highest average residues as 0.067 ppm and 0.058 ppm (corrected for method recovery and freezer storage stability) in wheat hay at a 7 and 15 day PHI, respectively. All residues beyond the 15 day PHI were below LOQ. Treated rye forage was collected at 0, 7, 10, 15 days for a residue decline study. Residues of florasulam decreased by 96.2% with an increasing PHI.

TABLE C.1. Summary of Concurrent Recoveries of Florasulam from Forage, Hay, Straw, and Grain of Rye, Wheat, Oat, and Barley.

Matrix	Spike level (mg/kg)	Sample size (n)	Analysis Day	Recoveries (%)	Mean ± std dev
EF-1343					
Method GRM 97.01					
Rye, oat, and barley forage	0.025	4	Jul 3-Aug 20/97	N/A	-
		1	Apr 16/98	N/A	-
Rye forage	0.05	2	Jul 3-Aug 20/97	108, 102	105
Oat forage	0.05	2	Jul 3-Aug 20/97	90, 72,	81
Wheat forage	0.05	4	Jul 3-Aug 20/97	102, 96, 78, 72	87 ±14.28
Rye forage	0.05	3	Apr 16/98	90, 84, 87	87 ± 3
Wheat forage	0.05	3	Apr 16/98	84, 102, 93	93 ± 9
Rye forage	0.1	1	Jul 3-Aug 20/97	126	-
Oat forage	0.1	1	Jul 3-Aug 20/97	108	-
Wheat forage	0.1	2	Jul 3-Aug 20/97	111, 99	105
Rye forage	0.1	1	Apr 16/98	77	-
Rye forage	0.3	1	Apr 16/98	94	-
Wheat forage	0.3	1	Apr 16/98	98	-
Rye forage	0.5	1	Jul 3-Aug 20/97	121	-
Wheat forage	0.5	2	Jul 3-Aug 20/97	112, 107	109.5
Oat forage	1	1	Jul 16/97	100	-
Wheat hay	0.025	1	Jul 24/97	N/A	-
Wheat hay	0.05	2	Jul 24/97	102, 78	90
Wheat hay	5	5	Apr 23-May 4/98	96, 93, 90, 63, 82	84.8 ± 13.3
Barley hay	1	1	Apr 23-May 4/98	99	-
Wheat hay	0.1	1	Jul 24/97	117	-
Wheat hay	0.1	2	Apr 27-May 4/98	72, 87	79.5
Barley hay	0.1	1	Apr 27-May 4/98	95	-
Wheat hay	0.3	3	Apr 23-May 4/98	108, 96, 91	98.3 ± 8.74
Barley hay	0.3	1	Apr 23-May 4/98	99	-
Wheat hay	0.5	1	Jul 24/97	117	-
Oat Straw	0.025	1	Apr 20/98	N/A	-
	0.05	6	Mar 6-Apr 20/98	129, 129, 114, 99, 90, 96	109.5 ± 17.04
	0.1	2	Mar 6-Apr 20/98	110, 81	95.5
	0.3	2	Mar 6-Apr 20/98	98, 98	98
	0.005	1	Apr 14/98	N/A	-

Wheat Grain	0.01	6	Apr 14/98	80, 84, 80, 84, 104, 120	92 ± 16.4
	0.05	2	Apr 14/98	75, 86	80.5
	0.2	2	Apr 14/98	80, 98	89

TABLE C.1. Summary of Concurrent Recoveries of Florasulam from Forage, Hay, Straw, and Grain of Various Cereals.

Matrix	Spike level (mg/kg)	Sample size (n)	Analysis Day	Recoveries (%)	Mean ± std dev
EF-1343					
Method GRM 98.01					
Wheat Forage	0.015	1	Sept 12/98	N/A	-
	0.05	6	Sept 12/98	106, 96, 105, 98, 98, 114	102.8 ± 6.8
	0.25	1	Sept 12/98	69	-
	0.5	1	Sept 12/98	78	-
	1	1	Sept 12/98	71	-
	2	1	Sept 12/98	74	-
Oat Hay	0.015	1	Sept 11/98	N/A	-
	0.05	6	Sept 11/98	93, 98, 89, 98, 91, 92	93.5 ± 3.7
	0.25	1	Sept 11/98	83	-
	0.5	1	Sept 11/98	78	-
Method GRM 97.01 (Procedural Recoveries)					
Oat grain	0.01	3	Oct 17/01	108, 102, 107	105.67 ±3.21
	0.05	1	Oct 17/01	95	-
	0.1	1	Oct 17/01	98	-
Barley grain	0.01	3	Oct 17/01	106, 108, 103	105.67 ±2.52
	0.05	1	Oct 17/01	98	-
	0.1	1	Oct 17/01	98	-

shaded areas = spiking at LOQ
N/A = not applicable

TABLE C.2. Summary of Storage Conditions of DE-570
Wheat was used as a representative crop to demonstrate the storage stability of cereal crops. Storage stability of oat, barley, and rye are being extended from wheat.

Matrix (RAC or Extract)	Storage Temp. (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability (days)
Wheat Hay	-20	446	459 (31% degradation)
Wheat Forage	-20	450	524
Wheat Straw	-20	251	313
Wheat Grain	-20	248	410
Oat Forage	-20	463	-
Oat Hay	-20	449	-
Oat Straw (U.S. trials)	-20	260	-
Oat Grain (U.S. trials)	-20	259	-
Barley Hay	-20	433	-
Barley Forage	-20	-	-
Barley Straw	-20	242	-
Barley Grain	-20	239	-
Rye Forage	-20	491	-
Rye Hay	-20	-	-
Rye Straw	-20	216	-
Rye Grain	-20	256	-
Oat Grain (Cnd. Trials)	-20	37	-
Barley Grain (Cnd. Trials)	-20	37	-

TABLE C.3. Residue Data from Crop Field Trials with Florasulam. Not detectable (ND) residues are assumed to be equivalent to LOD of 0.015 ppm.

Trial ID (City/State/Year)	Reg.	Crop/ Variety	Matrix	Total Rate, g a.i./ha	PHI (days)	Residues [1] (ppm)	Corrected Residues [4] (ppm)	Corrected Residues [2] (ppm)
Pierce/CO/1997 CO1	8	Wheat/Soft White	Hay	9.81	7 15 30	0.039, 0.044, 0.042 0.036, 0.031, 0.035 NA[3]		0.062, 0.071, 0.068 0.058, 0.049, 0.055 NA
Brampton/ND/1997 ND1	5	Wheat/Hard Red	Hay	9.88	7 15	0.017 0.015		0.028 0.023
			Forage	9.99	7 15	0, 0 0	ND, ND ND	-
Mooreton/ND/1997 ND2	5	Wheat/Hard Red	Forage	9.97	7 15	0.035, 0.023 0.107[5], 0.029	0.038, 0.025 ND, 0.032	-
Britton/SD/1997 SD1	5	Wheat/Hard Red	Hay	9.77	7	0.033	0.052	-
			Forage	9.89	7	0, 0	ND, ND	-
Theilman/MN/1997 MN1	5	Oat/Ogle	Forage	10.35	7	0, 0	ND, ND	-
			Hay	10.11	7	0	ND	-
Britton/SD/1997 SD2	5	Oat/Jerry	Forage	9.90	7	0, 0	ND, ND	-
			Hay	9.88	7 30	0 0.014	ND	 0.022
Arkansaw/WI/1997 WI1	5A	Oat/Hazel	Forage	10.39	7	0, 0	ND, ND	-
			Hay	10.16	7 15	0.027, 0.034 0	 ND	0.043, 0.054
Brampton/ND/1997 ND5	5	Barley/ Foster	Hay	9.87	7 15 30	0 0 0	ND ND ND	-
Britton/SD/1997 SD4	5	Barley/ Foster	Hay	9.92	7 30	0 0	ND ND	-
Minot/ND/1997 ND4	5	Rye/Dacold	Forage	9.94	0 7 10 15	1.002, 0.972, 0.838 0.073, 0.064 0.046, 0.050 0.029, 0.042	1.101, 1.068, 0.921 0.081, 0.071 0.050, 0.055 0.032, 0.046	-
Method 99.17								
Havelock/New Brunswick/2001	1	Oat/Capital	Grain	9.96	60	0, 0	ND	-
Winchester/Ontario/ 2001	5B	Barley/ Morrison	Grain	9.8	58	0, 0	ND	-
Kemptville/Ontario/ 2001	5B	Barley/ Morrison	Grain	10.2	54	0, 0	ND	-

[1] The screening Immunoassay method GRM 97.01 was used to screen for residues in samples. Detectable residues were confirmed using the GC-MSD method GRM 98.01. Results of confirmatory analyses are reported within this table.
[2] Corrected for daily recovery and storage stability (factor of 0.69).
[3] Not Analysed. Residues not detected in IA method
[4] Values corrected for daily recovery only.
[5] Peak, not due to DE-570, detected.

TABLE C.4. Summary of Residue Data from Crop Field Trials with Florasulam.
Residues reported as ND are assumed to be 0 ppm. Residues have been corrected for daily method recovery and/or freezer storage stability.

Commodity	Total Applic. Rate, g a.i./ha	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT*	Median (STMdR)	Mean (STMR)	Std. Dev.
Specify analyte EF-1343 or DE-570									
Wheat									
Grain	9.77-9.88	50-60	14	0.005	0.005	-	-	-	-
Hay	9.81-9.88	7 15	5 4	0.028 0.023	0.071 0.058	0.067 0.058	0.062 0.052	0.056 0.046	0.0174 0.016
Forage	9.89-9.99	7 15	6 3	0.015 0.015	0.038 0.032	0.032 0.024	0.015 0.015	0.021 0.021	0.0095 0.0098
Straw	9.77-9.93	52-60	13	0.026	0.026	-	-	-	-
Oat									
Grain	9.88-10.16	47-54	9	0.005	0.005	-	-	-	-
Forage	9.90-10.39	7	6	0.015	0.015	-	-	-	-
Hay	9.88-10.16	7 15 30	4 1 1	0.015 0.015 0.022	0.054 0.015 0.022	0.049 - -	0.029 - -	0.032 - -	0.0198 - -
Straw	9.88-10.16	47-54	9	0.026	0.026	-	-	-	-
Barley									
Grain	9.87-9.92	56-58	7	0.005	0.005	-	-	-	-
Hay	9.87-9.92	7 15 30	2 1 2	0.015 0.015 0.015	0.015 0.015 0.015	- - -	- - -	- - -	- - -
Straw	9.87-9.92	56-58	7	0.026	0.026	-	-	-	-
Rye									
Grain	9.96	60	4	0.005	0.005	-	-	-	-
Forage	9.94	0 7 10 15	3 2 2 2	0.921 0.071 0.05 0.032	1.101 0.081 0.055 0.046	- - - -	1.068 0.076 0.0525 0.039	1.03 0.076 0.0525 0.039	0.0958 0.007 0.003 0.0098
Straw	9.96	60	3	0.026	0.026	-	-	-	-
GRM 99.17									
Oat Grain	9.96	60	2	0.003	0.003	-	-	-	-
Barley Grain	9.8-10.2	54-58	4	0.003	0.003	-	-	-	-

* HAFT = Highest Average Field Trial.
Residues from all analytical methods were reported in summary.

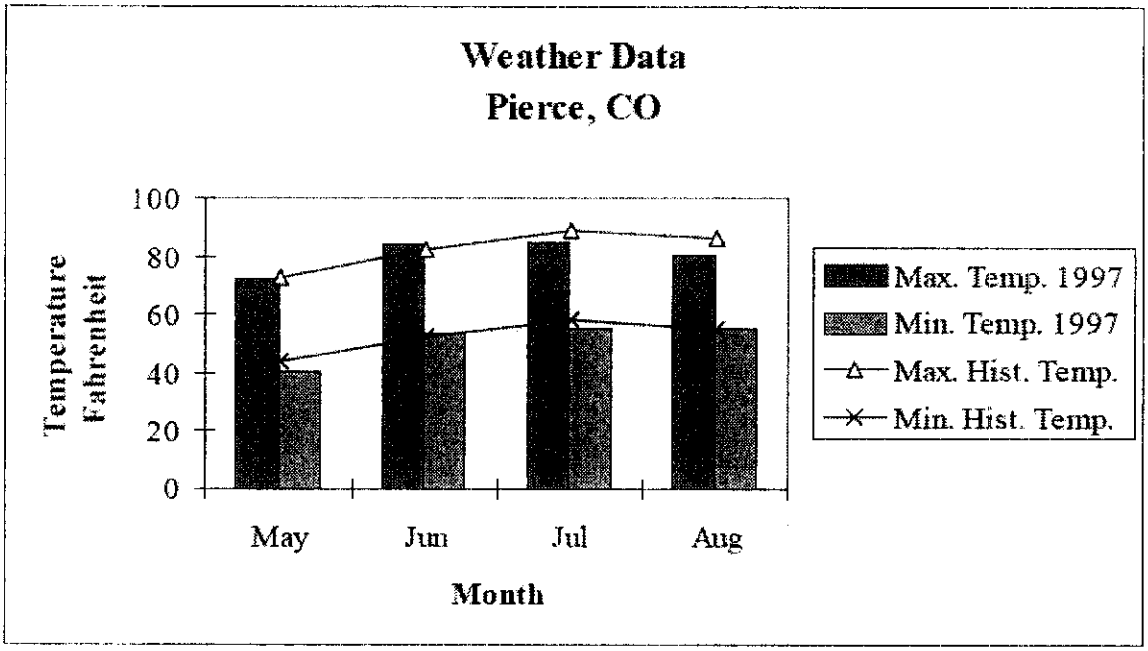
D. CONCLUSION

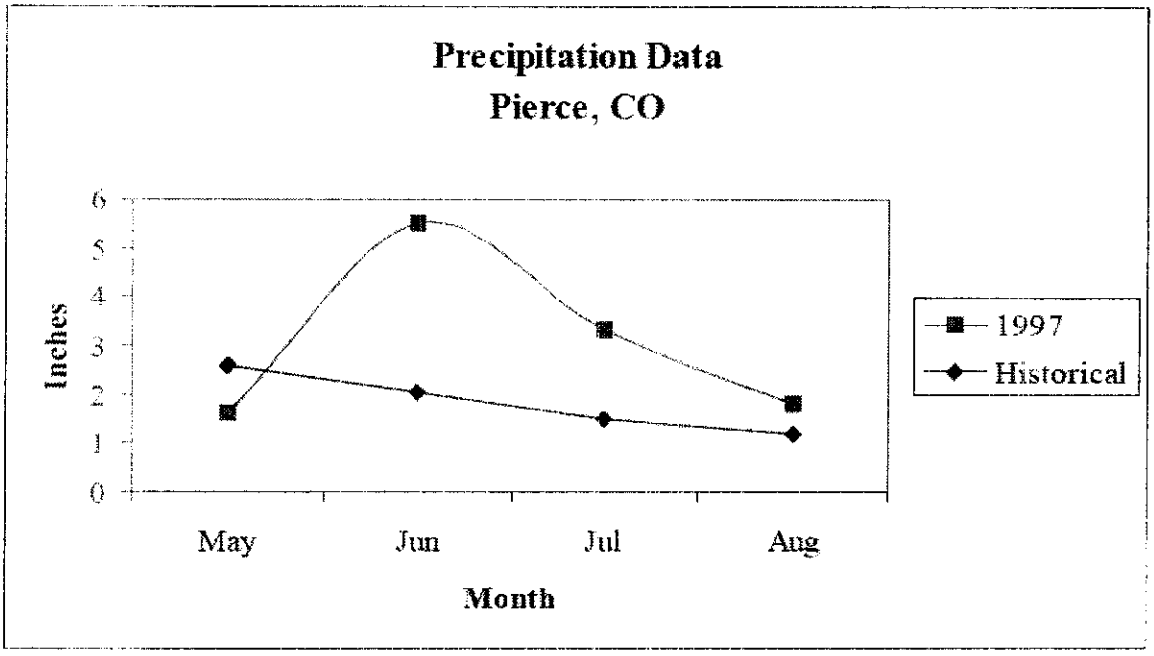
The field trial data on wheat, barley, oat, and rye are acceptable. The data reflect the use of florasulam (suspension concentrate) at the maximum seasonal application of 10 g a.i./ha/season, with a PHI of 60 days, and with the addition of Agral 90 (0.2%, v/v). With this use pattern, residues of florasulam are not expected to exceed 0.005 ppm in wheat, oat, barley, and rye grain.

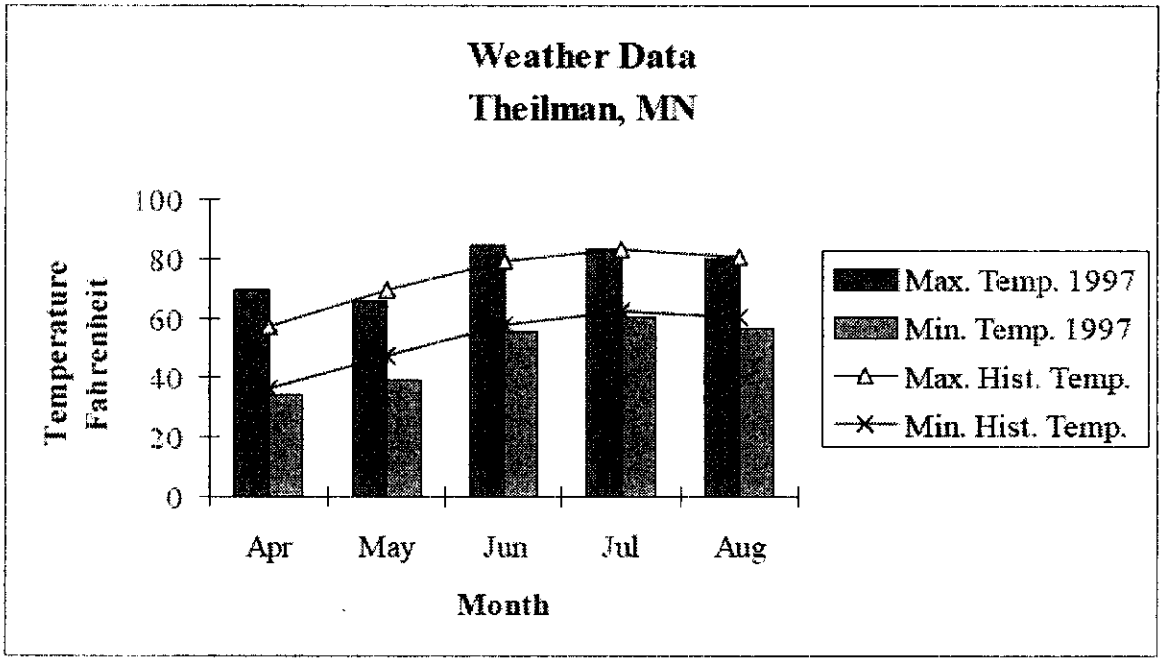
E. REFERENCES

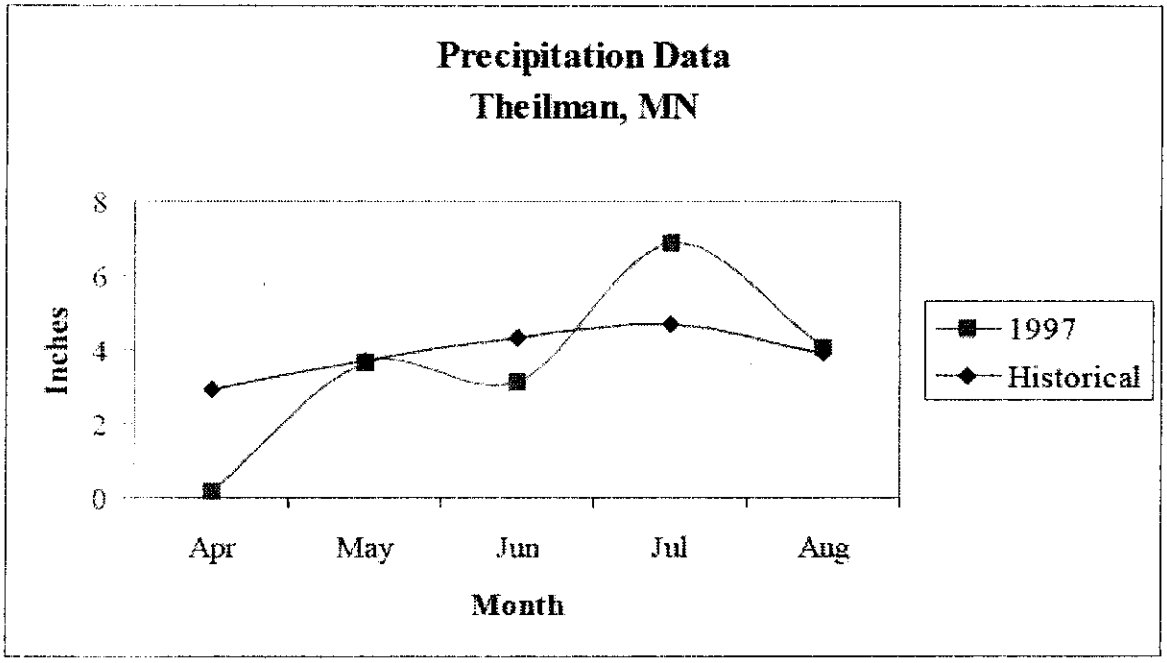
Template Version September 2003

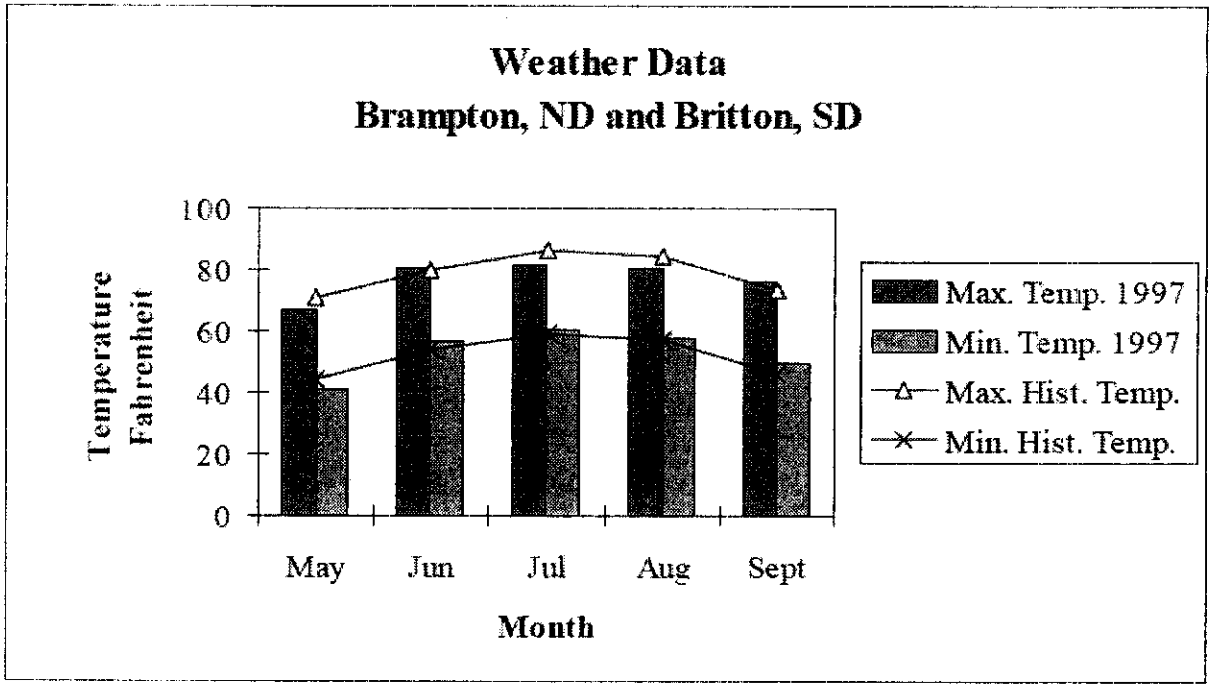
Appendix 1
Weather Data

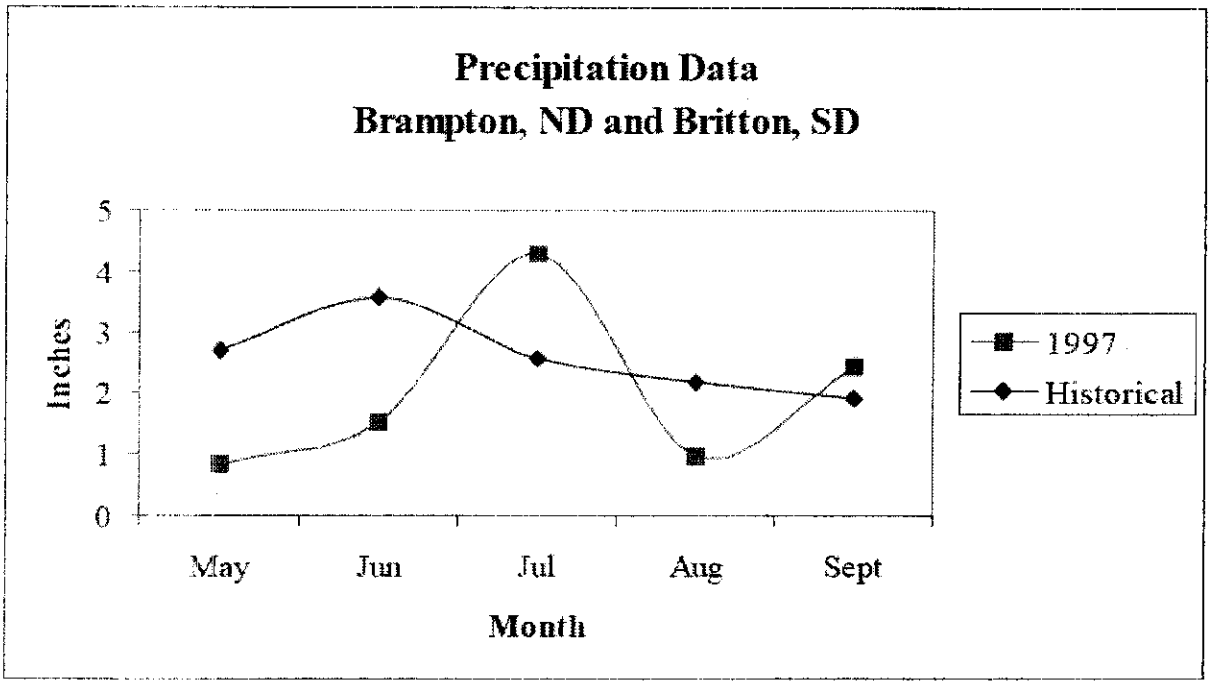


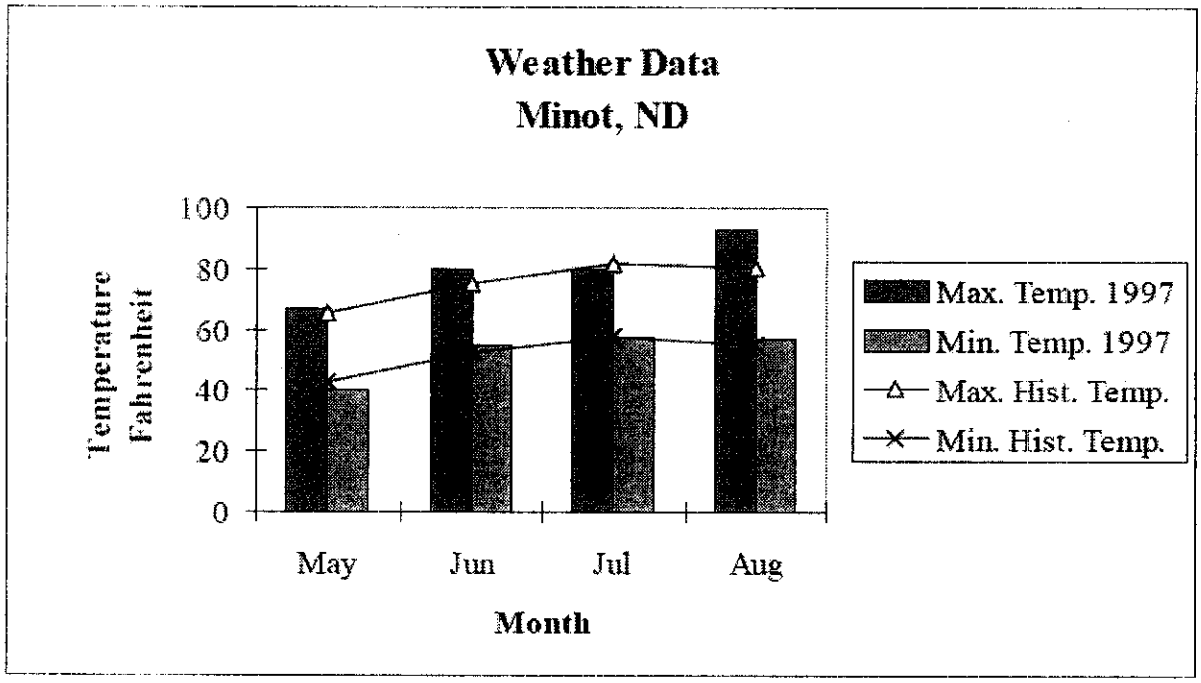


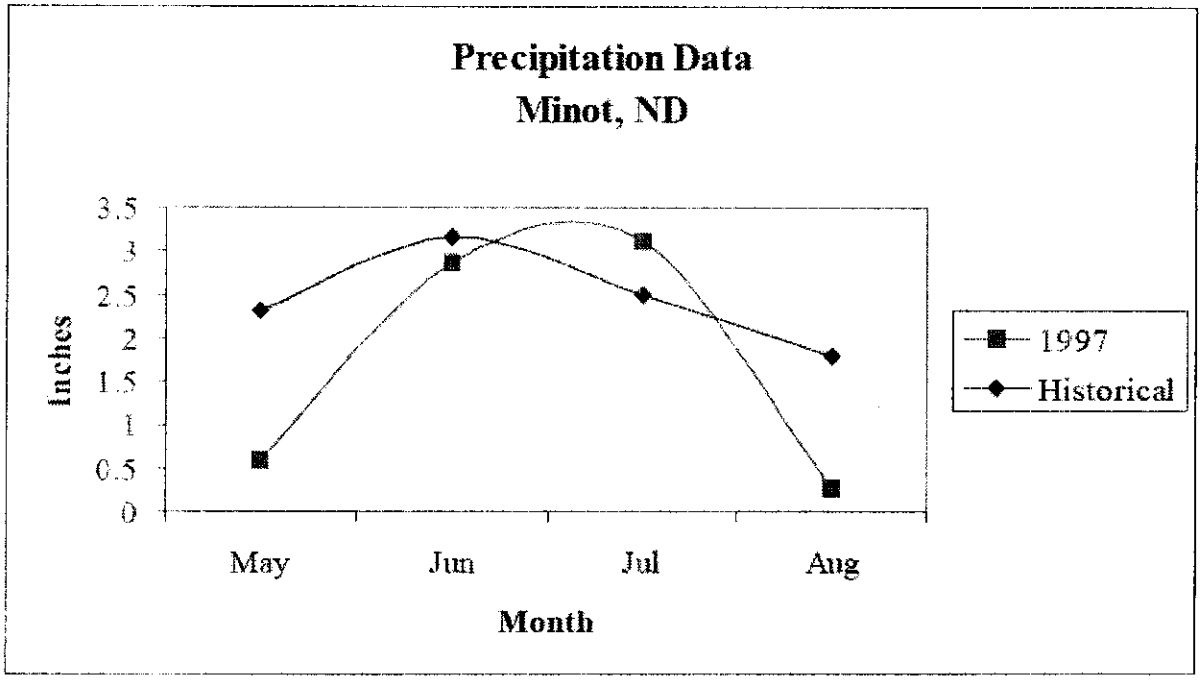


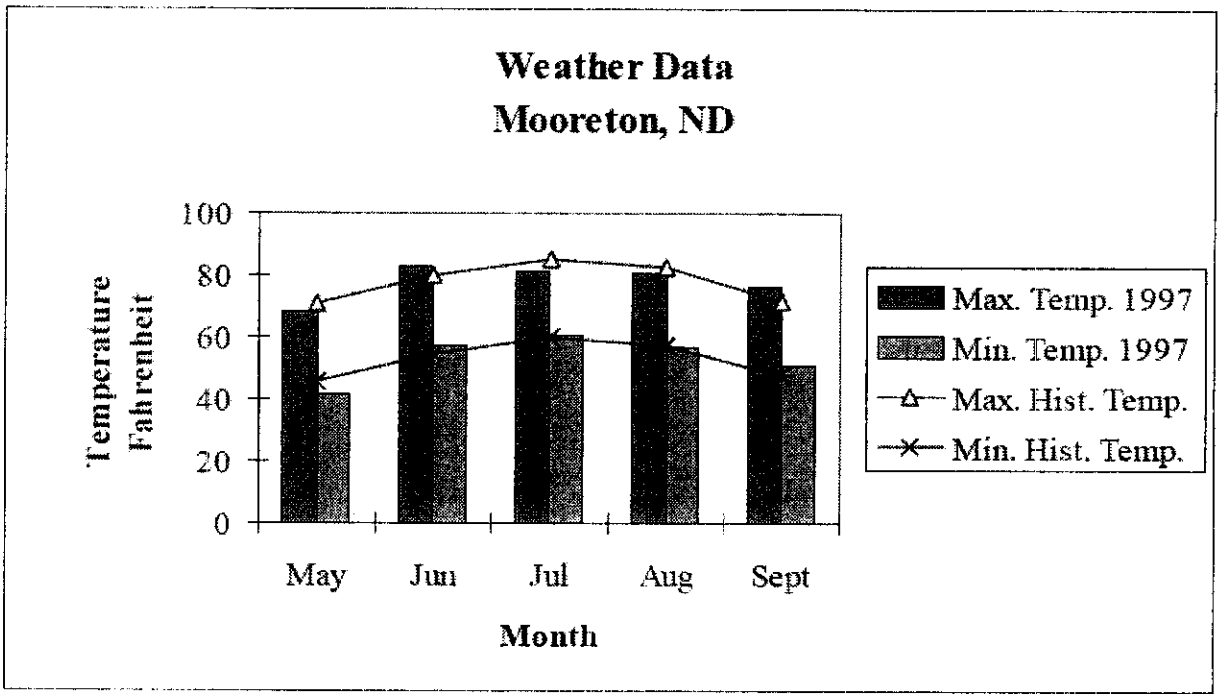


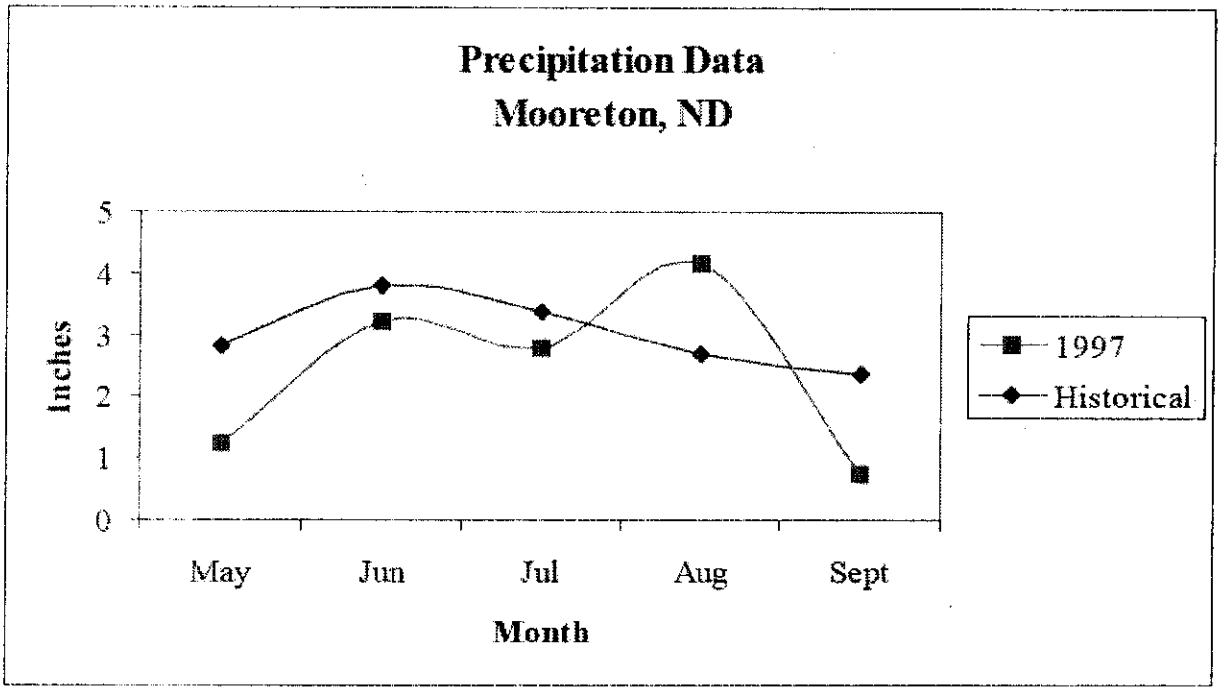


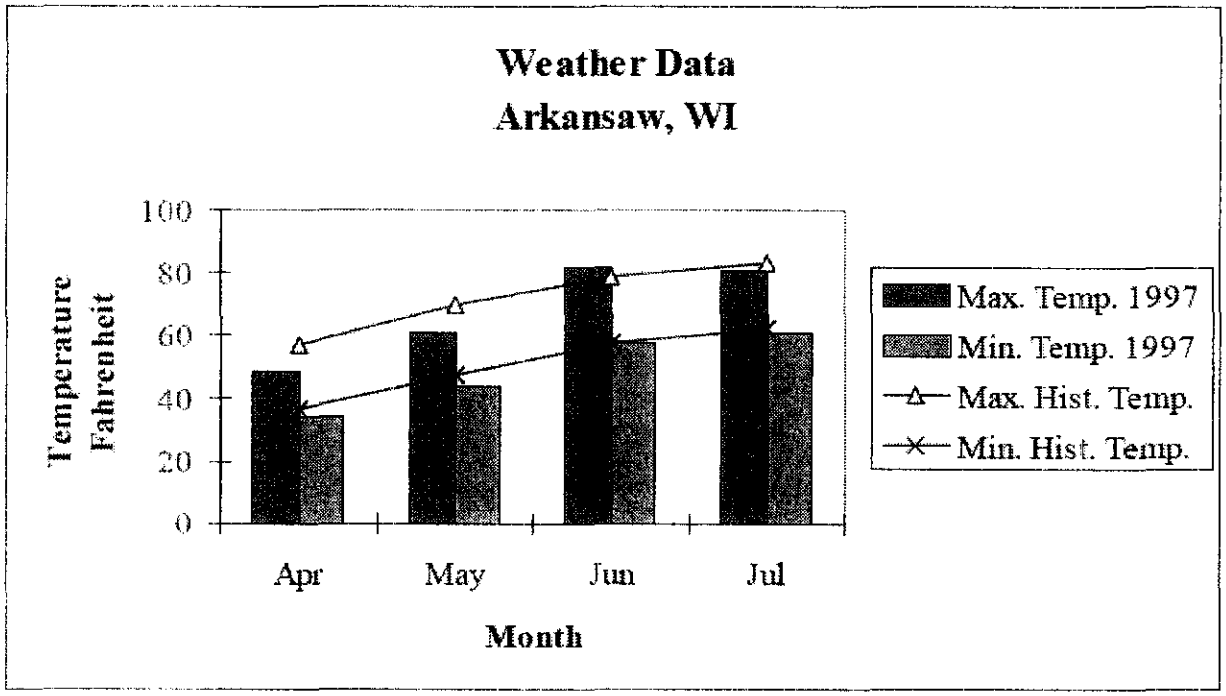


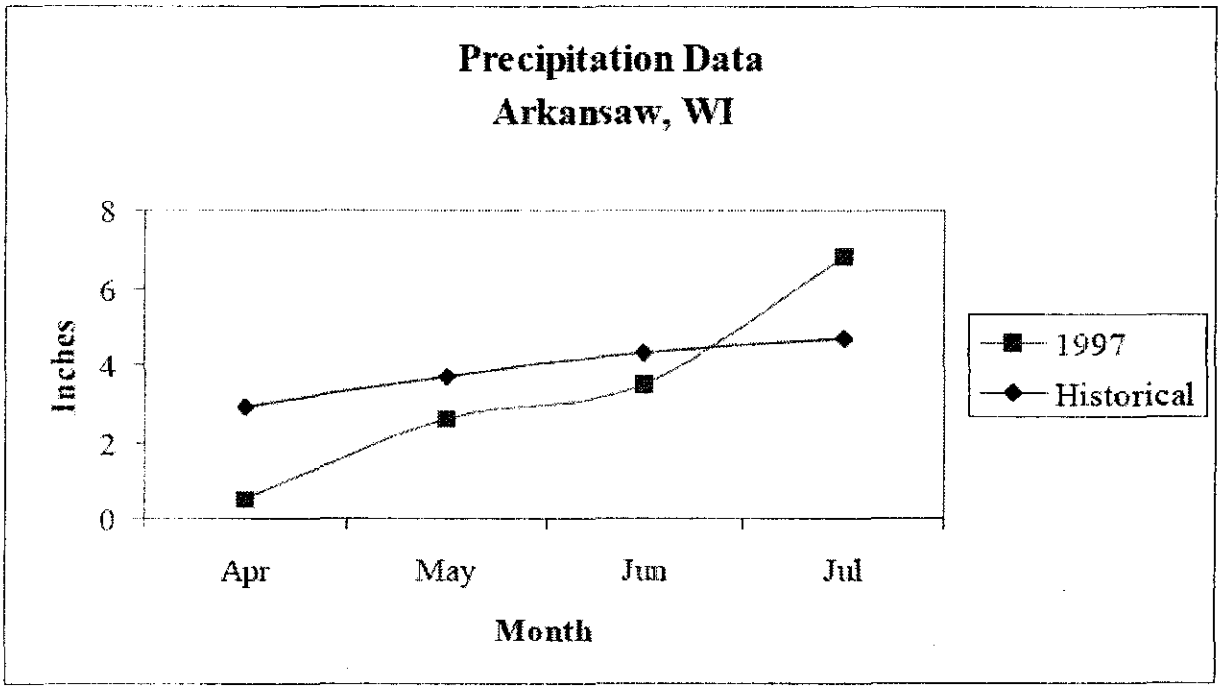




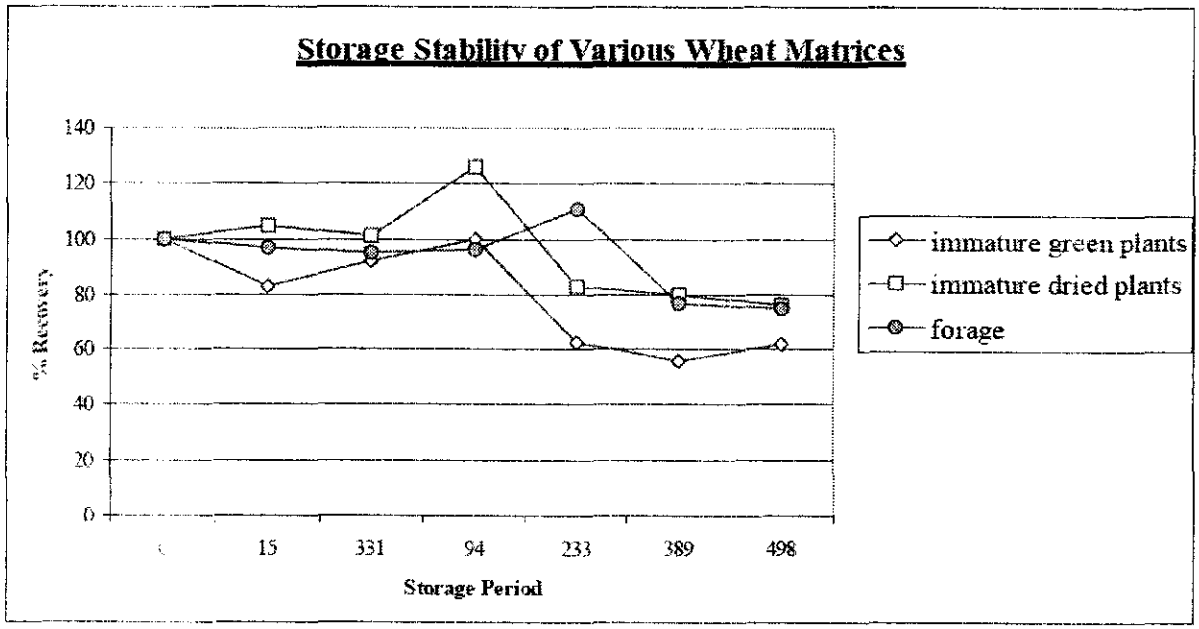


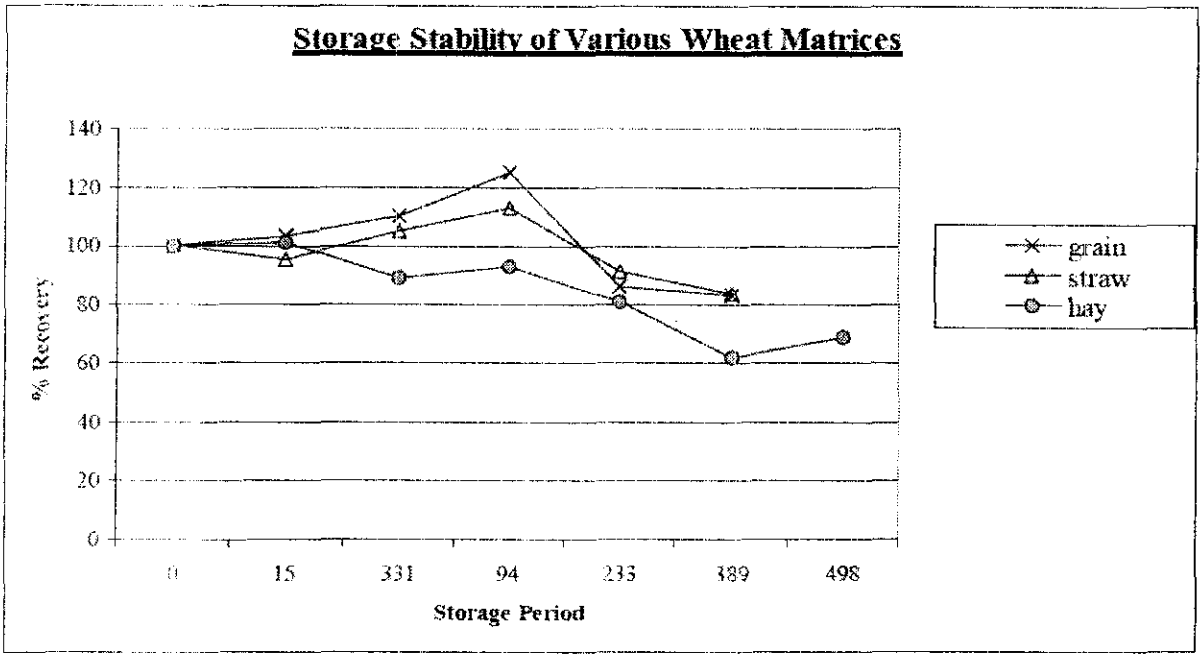






APPENDIX 2
Storage Stability





Florasulam/PC Code 129108/Dow AgroSciences LLC/Company Code 62719
DACO 7.3/OPPTS 860.1380/OECD IIA 6.1.1 and IIIA 8.1.1
Storage Stability - Wheat

Primary Evaluator: Thurston G. Morton, Chemist
HED/RRB4 (7509P) Date: 4/3/07 4/3/07

Approved by: Susan V. Hummel. Branch Senior Scientist
HED/RRB4 (7509P) Susan V. Hummel Date: 4/3/07

In the absence of signatures, this document is considered to be a draft with deliberative material for internal use only.

STUDY REPORTS:

46808025 Blakeslee, B. (2000) Frozen Storage Stability of XDE-570 in Wheat Immature Green Plants, Immature Dried Plants, Forage, Grain, Straw and Hay. Project Number: RES97100/01. Unpublished study prepared by Dow AgroSciences LLC. 80 p.

EXECUTIVE SUMMARY:

In the freezer storage stability study, the ground wheat samples of forage, grain, straw and hay spiked with florasulam (99.7 % ai) at a level of 0.5 ppm were stored at -20° C for a maximum duration of 524, 410, 313 and 459 days, respectively. A set of 0-day samples and other fortified samples were removed at various time intervals and analyzed to study the stability of florasulam. The analytical methods employed to detect residues were GRM 97.01 (Immunoassay) and GRM 98.01, the gas chromatography with mass selective detection (GC/MSD). These methods were the same as that outlined in the analytical methodology and were used in the crop residue studies. Both methods were validated at a level of 0.05 ppm for the wheat forage, straw and hay and at a level of 0.01 ppm for wheat grain.

The data presented indicated that residues of florasulam were relatively stable at -20 °C for durations of 524, 410, 313 and 459 days in the spiked wheat forage, grain, straw and hay samples.

This freezer storage stability study is classified acceptable and satisfy the guideline requirement for a freezer storage stability study (OPPTS 860.1380).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the storage stability data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document DP Barcode D333759 and in Canada's Regulatory Decision Document.

COMPLIANCE:

Signed and dated GLP, Quality Assurance and Data Confidentiality were provided.
No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Florasulam, N-(2,6-diflurophenyl)-8-fluoro-5-methoxy(1, 2, 4)triazolo(1, 5-c)pyrimidine-2-sulphonamide, is a sulphonamide herbicide that is currently registered in Europe and Canada for use in cereal weed control. Florasulam is being developed in the U.S. for control of wild buckwheat, wild mustard, volunteer canola, field pennycress, common chickweed, shepherd's purse, bedstraw, and smartweed, when used in a post-emergent application in wheat, barley, oats, rye, and triticale. The mode of action at the cellular level involves the inhibition of the enzyme, acetolactate synthase (ALS).

TABLE A.1. Test Compound Nomenclature

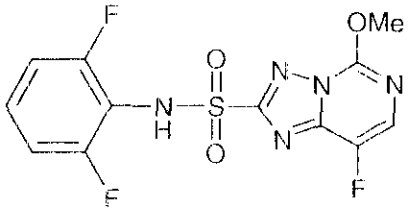
Compound	Chemical Structure
	
Common name	Florasulam
Company experimental name	DE-570 or EF-1343
IUPAC name	**2', 6', 8-trifluoro-5-methoxy-s-triazolo [1,5-c]pyrimidine-2-sulfonanilide**
CAS name	***N*-(2,6-diflurophenyl)-8-fluoro-5-methoxy(1, 2, 4)triazolo(1, 5-c)pyrimidine-2-sulphonamide**
CAS #	**145701-23-1**
End-use product/EP	Florasulam Suspension Concentrate
Molecular Formula	$C_{12}H_8O_3N_6F_3S$
Molecular Mass	359.3

TABLE A.2. Physicochemical Properties		
Parameter	**Value**	**Reference**
Physical State	Solid	PMRA Lab Services
Melting point/range	193.5-230.5°C	
Specific gravity	1.53 at 22°C	
Water solubility	Medium / Solubility (g/L) water 0.121 pH 5 0.084 pH 7 6.36 pH 9 94.2	
Solvent solubility	Solvent / Solubility (g/L) acetone 123 acetonitrile 72.1 ethyl acetate 15.9 methanol 9.81 dichloromethane 3.75 xylene 0.227 n-octanol 0.184 n-heptane0.000019	
Vapour pressure	1×10^{-5} Pa at 25°C	
Dissociation constant (pK_a)	4.54	
Octanol/water partition coefficient (K_{ow}) at 22°C	pH / Log K_{ow} 4 1.00 7 -1.22 10 -2.06	
UV/visible absorption spectrum	Form / λmax Acidic 259.8 203.8 Basic 262.4 209.7 Methanolic 204.1 No absorbence above 300 nm.	

B. EXPERIMENTAL DESIGN

B.1. Sample Handling and Preparation

The ground control samples weighing 10 gram each were placed into 250 ml high density polyethylene (HDPE) bottle which were then fortified with 1.0 ml of a 5.0 ppm solution of XDE-570 resulting in 0.5 ppm in sample. A set of 0-day samples were removed for analysis while the remaining fortified samples and bulk control samples were placed in frozen storage at -20° C. No significant deviation from this temperature was reported. Samples were removed at the specific interval and were analyzed for florasulam residues. The unfortified control samples were weighed on the day of analysis used as recovery and control samples.

B.2. Analytical Methodology

Samples were analyzed for residues of florasulam using Dow AgroSciences analytical methods GRM 97.01 (IA) and GRM 98.01 (GC/MSD) with minor modifications.

GRM 97.01 (Immunoassay):

Residues of florasulam were extracted from crop fractions using a solution of 80% acetone:19 water:1% acetic acid. An aliquot was evaporated to dryness. The remaining residues were reconstituted in 0.01N hydrochloric acid (HCl). The sample was purified on an octadecyl (C_{18}) solid phase extraction (SPE) from which the residue was eluted with 30% acetonitrile in 0.01 N HCl. Sodium chloride was added to eluent from the immature plant, hay and grain and the residues were then partitioned into an organic solvent (for immature plant and hay - 50% ethyl acetate:50% toluene; for grain - tert-butyl methyl ether). The organic solvents were evaporated to dryness and the residues were dissolved in methanol and diluted with Sample Diluent (provided in the immunoassy kit). The eluent from the forage and straw samples was diluted with 0.01 N HCl and an aliquot was neutralized with the addition of 0.01 N sodium hydroxide (NaOH) and diluted with Sample Diluent. Aliquots of the diluted sample solutions were assayed using XDE-570 RaPID Assay kit. This method analysis total residues of florasulam and related metabolites (4-hydroxyphenyl florasulam) and glucose conjugate. It has been validated at a level of 0.05 ppm for the immature plants, forage, straw and hay and 0.01 ppm for grain.

GRM 98.01 (GC/MSD):

Residues of florasulam were extracted from wheat immature plant, forage, grain, straw and hay matrices with acidified acetone (80% acetone:19% water:1% acetic acid). An aliquot of the extract was purified by filtration through a graphitized carbon solid-phase extraction (SPE) column. The extract was concentrated to remove acetone, diluted with the addition of 0.01 N hydrochloric acid and partitioned onto an octadecyl (C_{18}) SPE column. The florasulam was eluted with a 30% acetonitrile in 0.01 N hydrochloride acid solution. Florasulam was partitioned, after addition of salt, into methyl *t*-butyl ether (MTBE). The MTBE was concentrated to dryness. Residues of florasulam were dissolved in acetone and derivatized at room temperature with iodomethane and triethylamine. The acetone solution was concentrated to dryness and *N*-methyl florasulam residues are dissolved in a 5% sodium thiosulfate solution and partitioned into toluene containing the internal standard *N*-propyl florasulam. Residues of florasulam as the N-methyl florasulam derivative in the toluene aliquots were determined by capillary gas chromatography with mass selective detection (GC/MSD).

C. RESULTS AND DISCUSSION

The recovery data indicate that florasulam residues when corrected for concurrent recoveries are stable in wheat grain for 410 days (13.5 months), forage for 524 days (17.2 months), straw for 313 days (10.3 months), and hay for 459 days (15.1 months.

The storage period of samples of wheat, barley and oat raw agricultural commodities (RACs) collected in supervised residue field trials are covered by the freezer storage stability study.

TABLE 1. Stability of Florasulam Residues in Wheat Matrices Following Storage at -20° C

Commodity	Storage Period (days)	Analyte	Residue Level (ppm)	Fresh Spike Recovery [a] (%)	Apparent Recovery in Stored Sample [b] (%)	Recovery in Stored Samples Corrected for Fresh Spike [c] (%)
Wheat grain	0	florasulam	0.5	112	106	95
	14	florasulam	0.5	94	93	99
	39	florasulam	0.5	100	105	105
	123	florasulam	0.5	84	101	120
	264	florasulam	0.5	93	77	83
	410	florasulam	0.5	84	67	80
Wheat forage	0	florasulam	0.5	98	99	101
	14	florasulam	0.5	88	85	97
	41	florasulam	0.5	91	87	96
	92	florasulam	0.5	86	83	96
	183	florasulam	0.5	73	82	112
	378	florasulam	0.5	93	72	77
	524	florasulam	0.5	84	63	75
Wheat straw	0	florasulam	0.5	85	106	125
	14	florasulam	0.5	84	81	96
	25	florasulam	0.5	81	85	105
	90	florasulam	0.5	75	85	113
	194	florasulam	0.5	88	80	91
	313	florasulam	0.5	93	78	84
Wheat hay	0	florasulam	0.5	103	107	104
	14	florasulam	0.5	92	93	103
	25	florasulam	0.5	92	84	91
	90	florasulam	0.5	109	104	95
	94	florasulam	0.5	88	73	83
	350	florasulam	0.5	87	55	63
	459	florasulam	0.5	84	59	70

[a] Average of two samples
[b] Average of three samples
[c] Recovery Corrected for Fresh Spike = Apparent Recovery/ Concurrent Fresh Spike Sample Set Recovery x 100

D. CONCLUSION

In the freezer storage stability study, the ground wheat samples of forage, grain, straw and hay spiked with florasulam (99.7 % ai) at a level of 0.5 ppm were stored at -20° C for a duration of 524, 410, 313 and 459 days. respectively. A set of 0-day samples and other fortified samples were removed at various time intervals and analyzed to study the stability of florasulam. The analytical methods employed to detect residues were GRM 97.01 (Immunoassay) and GRM 98.01, the gas chromatography with mass selective detection (GC/MSD). These methods were the same as that outlined in the analytical methodology and were used in the crop residue studies. Both methods were validated at a level of 0.05 ppm for the wheat immature green and dried plants, forage, straw and hay and at a level of 0.01 ppm for wheat grain.

The data presented indicated that residues of florasulam were relatively stable at -20 °C for durations of 524, 410, 313 and 459 days in the spiked forage, grain, straw and hay, respectively.

The storage period of wheat, barley and oat RACs collected in supervised residue field trials are covered by the freezer storage stability study.

The freezer storage stability study for wheat is used as a surrogate study for barley and oat. The result of this study applies to both barley and oat matrices therefore, no additional studies for barley and oat are required.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: T. Morton (4/3/07); S. Hummel (4/3/07)
Petition Number: 6F7061
DP Barcode(s): D333759
PC Code: 129108

Template Version September 2003

Primary Evaluator	Thurston G. Morton, Chemist HED/RRB4 (7509P)	Date: 4/3/07
Approved by	Susan V. Hummel, Branch Senior Scientist HED/RRB4 (7509P)	Date: 4/3/07

In the absence of signatures, this document is considered to be a draft with deliberative material for internal use only.

STUDY REPORTS:

46808021 Conrath, B.; West, S. (1998) Multi-Residue Methods Testing for DE-570 According to PAM I. Appendix II, as Updated January, 1994. Project Number: 44706, ACFS/44706. Unpublished study prepared by ABC Laboratories, Inc. 44 p.

EXECUTIVE SUMMARY:

Dow AgroSciences has submitted multiresidue method data for florasulam. Aminopyralid was analyzed according to the FDA Multi-Residue Method Test guidelines in PAM Vol. I, 3rd Edition (dated 1/94). Florasulam was not found to be naturally fluorescent, therefore, further testing under Protocol A was not required. Florasulam was not an acid or phenol, therefore, no further testing was required under Protocol B.

We note that the testing laboratory (ABC Labs Inc.) did not address the testing of florasulam using Protocol G; however, testing of this compound using Protocol G is not required because the compound is not a substituted urea. The petitioner and the testing laboratory should note that the most recent version of PAM Vol. I is dated 10/99.

Florasulam was not recovered using Protocol D (with no cleanup), or using Florisil cleanup under Protocols E and F. The results of the study indicate that the FDA MRM guidelines in PAM Vol. I are not applicable to florasulam.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the multiresidue method residue data are classified as scientifically acceptable. These data will be forwarded to the U.S. FDA for further evaluation.

The petitioner and the testing laboratory should note that the most recent version of PAM Vol. I is dated 10/99 and has additional protocols not provided in the 1/94 version.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP Barcode D333759 and in Canada's Regulatory Decision Document.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided.
No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Florasulam, N-(2,6-difluorophenyl)-8-fluoro-5-methoxy(1, 2, 4)triazolo(1, 5-c)pyrimidine-2-sulphonamide, is a sulphonamide herbicide that is currently registered in Europe and Canada for use in cereal weed control. Florasulam is being developed in the U.S. for control of wild buckwheat, wild mustard, volunteer canola, field pennycress, common chickweed, shepherd's purse, bedstraw, and smartweed, when used in a post-emergent application in wheat, barley, oats, rye, and triticale. The mode of action at the cellular level involves the inhibition of the enzyme, acetolactate synthase (ALS).

TABLE A.1. Test Compound Nomenclature

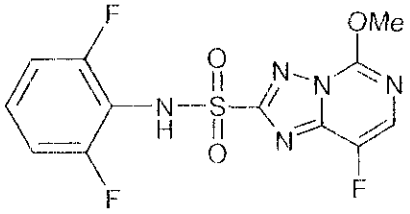
Compound	Chemical Structure
	
Common name	Florasulam
Company experimental name	DE-570 or EF-1343
IUPAC name	2', 6', 8-trifluoro-5-methoxy-*s*-triazolo [1,5-c]pyrimidine-2-sulfonanilide
CAS name	*N*-(2,6-difluorophenyl)-8-fluoro-5-methoxy(1, 2, 4)triazolo(1, 5-c)pyrimidine-2-sulphonamide
CAS #	145701-23-1
End-use product (EP)	Florasulam Suspension Concentrate
Molecular Formula	$C_{12}H_8O_3N_5F_3S$
Molecular Mass	359.3

TABLE A.2. Physicochemical Properties		
Parameter	Value	Reference
Physical State	Solid	PMRA Lab Services
Melting point/range	193.5-230.5°C	
Specific gravity	1.53 at 22°C	
Water solubility	Medium / Solubility (g/L) water 0.121 pH 5 0.084 pH 7 6.36 pH 9 94.2	
Solvent solubility	Solvent / Solubility (g/L) acetone 123 acetonitrile 72.1 ethyl acetate 15.9 methanol 9.81 dichloromethane 3.75 xylene 0.227 n-octanol 0.184 n-heptane0.000019	
Vapour pressure	1×10^{-5} Pa at 25°C	
Dissociation constant (pK_a)	4.54	
Octanol/water partition coefficient (K_{ow}) at 22°C	pH / Log K_{ow} 4 1.00 7 -1.22 10 -2.06	
UV visible absorption spectrum	Form / λmax *Acidic* 259.8 203.8 Basic 262.4 209.7 Methanolic 204.1 No absorbence above 300 nm.	

B. MATERIALS AND METHODS

Florasulam was analyzed according to the FDA Multi-Residue Method Test guidelines in PAM Vol I, Appendix II (1/94). Florasulam was found not to naturally fluoresce, therefore, no further testing under Protocol A was required. Florasulam is not an acid, phenol, or substituted urea, therefore, further testing under Protocols B and G were not required. As a result of Protocol C testing, florasulam was also tested through Protocols D and E. Based on the results of Protocol E testing, testing under Protocol F was not required.

C. RESULTS AND DISCUSSION

TABLE C.1. Results of Multiresidue Methods Testing with Florasulam.

PAM I Protocol	Results	Comments
A	Florasulam was not found to be naturally fluorescent.	Florasulam is not an *N*-methylcarbamate. No further testing needed.
B	Not tested.	Florasulam is not an acid or phenol. No further testing needed.
C	For the column/detector combinations tested under Level I conditions (modules DG1, DG3, DG5, and DG13) a peak for florasulam was detected. For Modules DG18 and DG23, no peak for florasulam was detected. Due to retention times for modules DG1 and DG3, Level II testing at 230 ° C was required (DG10 and DG12). Various concentrations of florasulam were analyzed and resulted in 5.27 ng resulting in 50 % full scale deflection using a electron capture detector, and 98.1 ng resulted in 50 % full scale deflection using a electrolytic conductivity detector .	Further work conducted using Protocols D, E, and F
D	Aliquots of florasulam were tested for recovery from florisil. The average recovery of florasulam from Protocol D 302 C1 cleanup was 0%. Because recovery was <30 % testing through the complete method was not required.	
E	Florasulam was not recovered using Florisil cleanup methods C1 and C2 for Protocol E.	Because florasulam could not be recovered during Florisil column cleanup, no further testing was conducted.
F	Not tested, because florasulam could not be recovered from the Florisil column cleanup.	
G	Not tested.	Florasulam is not a substituted urea. No further testing needed.

D. CONCLUSION

Florasulam was adequately evaluated for recovery through FDA multiresidue methods. The results of the study indicate that the FDA MRM guidelines in PAM Vol. I are not applicable to florasulam. Florasulam was not found to be naturally fluorescent; therefore, further testing under Protocol A was not required. Florasulam is not an acid or phenol, therefore, further testing under Protocol B was not required. Florasulam was not recovered using Protocol D (with no cleanup), or using Florisil cleanup under Protocols E and F. Florasulam is not a substituted urea, therefore, further testing under Protocol G was not required. The submitted data will be forwarded to the U.S. FDA for further evaluation.

E. REFERENCES

None.

F. DOCUMENT TRACKING

RDI: T. Morton (4/3/07); S. Hummel (4/3/07)
Petition Number: 6F7061
DP Barcode(s): D333759
PC Code: 129108
Template Version June 2005

PMRA Reviewer: Ali Ismaily, **Date** October 26, 2000

This DER was initially reviewed by Canada's PMRA and has been reviewed by HED. Conclusions herein agree with HED policy. In addition, this DER has been modified to include the submission MRID number.

Thurston Morton **23-May-2007**

STUDY TYPE: Nature of the Residue in Laying Leghorn Hen (*Gallus domesticus*); OPPTS 860.1300

TEST MATERIAL (PURITY): XDE-570 (99.7%)
[UL-aniline-^{14}C]XDE-570 (> 99%)
[triazolopyrimidine-9- ^{14}C]XDE-570 (> 99%)

SYNONYMS: **XDE-570** (Florasulam)
Common name : Florasulam (ISO-proposed)
IUPAC: 2', 6', 8-Trifluoro-5-methoxy-s-triazolo [1,5-c]pyrimidine-2-sulfonanilide
CAS: N-(2,6-difluorophenyl)-8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide

CAS#: ***145701-23-1***

MRID 46827903 D.E. Barnekow and M.A. Huskin, (1994), Nature of the Residues of [^{14}C]XDE-570 in Laying Hens. North American Environmental chemical laboratory, DowElanco (9330 Zionsville Road, Indianapolis, Indiana 46268-1053) and ABC Laboratories, Inc. (7200E. ABC Lane, Columbia, MO 65202). DowElanco Laboratory Study No. MET94018, ABC Laboratories' Study No. 41556, December 23, 1994. Unpublished.

SPONSOR: DowElanco

EXECUTIVE SUMMARY:

In the laying hen metabolism study, XDE-570, radiolabelled as either [UL-aniline-^{14}C]XDE-570, or [triazolopyrimidine-9- ^{14}C]XDE-570 was administered to two groups of 10 laying hens at a dose level of 0.76± 0.01 mg/kg bw/day. The dose was administered orally twice daily for five consecutive days, by opening the beak and inserting a capsule into the esophagus. The dose was equivalent to10.7 ± 0.2 ppm XDE-570 dietary burden at an average feed consumption of 0.13 kg/day. Samples of eggs, excreta were collected throughout the study. The test hens were sacrificed approximately 24 hours after the final dose. The tissue samples of fat, composite muscle (light and dark), skin and liver were collected for analysis.

The results indicated that the total radioactive residues (TRRs) were comparable between two labelling positions for excreta, muscle, fat, liver, and egg. TRR in muscle, fat and liver were less than limit of quantification (< LOQ). TRR in skin and eggs were very low (0.013%, < 0.007 ppm). Almost 100% of the recovered radioactivity that was administered to hen was found in excreta. These residues in the tissues and egg samples were approximately 0.01% of the applied dose (up to 0.013 ppm). The highest concentration of residues in tissues were found in the skin, 0.0066 ppm and 0.005 ppm in A-label and TP-label, respectively. The concentration of residues in egg were about 0.004 ppm in both A-label and TP-labelled, respectively. Total radioactive residues in tissue (muscle, fat, skin and liver), eggs and excreta samples were determined by

combustion and liquid scintillation counter (LSC). Solvent extraction and subsequent fractionation were performed on the A and TP labelled samples of eggs, skin and excreta (the only matrices with residue levels > 0.02 ppm). All samples were initially extracted three times with acetonitrile:water [80:20] (Figure 1). This extraction released most of the radioactivity present in these samples. The post extracted material was lyophilized and the remaining ^{14}C activity was quantified by combustion/LSC. The excreta extracts were concentrated and analysed by reverse phase HPLC and normal phase TLC.

The parent compound, florasulam, is not likely to bioaccumulate in fat, other tissues and egg yolk as a result of feeding of treated feed. This study demonstrated low levels of radioactivity in edible tissues. These observations are supported by the low Log K_{ow} (1.00 at pH 4.00 and -1.22 at pH 7.0) which is an indication of a low potential for partition into organic solvents.

The total radioactivity in liver, fat and muscle samples very low (< 0.0001% of administered dose), therefore, no further residue characterization was conducted. Solvent extraction and subsequent fractionation were performed on the A and TP labelled samples of excreta, egg and skin. All sample were initially extracted with acetonitrile:water (80:20). Further characterization of residues, extracted in acetonitrile:water phase, from egg and skin were achieved with hexane and ethyl acetate. The predominant radioactive component in extracted residues in egg and skin was parent. No other metabolites were identified in skin samples. The extractability of radioactive residues ranged between 84% and 103% of TRR for excreta, eggs and skin. The behaviour of florasulam residues in hen tissues, egg and excreta during extraction, fractionation, and chromatographic analysis demonstrated no significant differences between A and TP labelled hens.

The Residue of Concern (ROC) based on the laying hen metabolism study may be defined as the parent compound, florasulam. The metabolism of florasulam in the laying hen, goat and rat were similar. Therefore, swine metabolism is not required. In all three species, the majority of the radioactivity was found in the excreta. Most of the parent compound in goat, hen and rat was eliminated unchanged with minor unknown metabolites at unquantifiable levels. No significant cleavage of the sulfonanilide bridge was observed

Based on the ruminant, laying hen and rat metabolism studies, the residue of concern (ROC) may be defined as the parent compound, florasulam. These metabolism studies are classified acceptable and satisfy the guideline requirements for goat metabolism studies (Residue Chemistry Guidelines Dir98-02, Section 2).

COMPLIANCE:

Signed and dated GLP, Quality Assurance and no Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

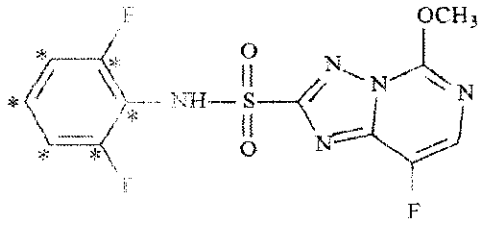
MATERIALS:

1. **Test Compound:**

[UL-aniline-^{14}C]XDE-570 ["A" labelled compound]
Radiochemical purity: 100% [determined by HPLC/LSC]
Specific activity: 152 µCi/mg
4.41 x 10^4 dpm/µg

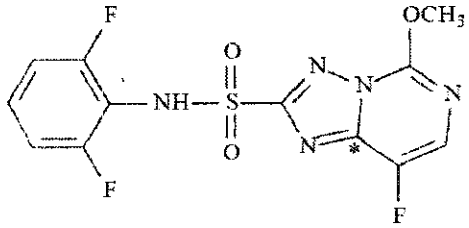
[9-triazolopyrimidine-^{14}C]DXE-570 ["TP" labelled compound]
Radiochemical purity: 100% [determined by HPLC/LSC]
Specific activity: 67.4 µCi/mg
4.36 x 10^4 dpm/µg

Nonradioactive DXE-570
Chemical purity: 99.7% (supplied by sponsor)



[UL-aniline-^{14}C]XDE-570

"A" label



Triazolopyrimidine-9- ^{14}C]XDE-570

"TP" label

2. **Test animals:**

Species:	Laying Leghorn Hen *Gallus domesticus*
Strain/breed:	Hyline Hybrid
Age:	30 weeks of age at dosing
Gender:	female
Weight at study initiation:	control (1.48 kg), "A" label (1.49 kg), "TP" label (1.54 kg)
Health status:	good health
Housing/holding areas:	Hens were kept in individual galvanized cages. The study room was maintained at 22.4 ± 0.6 ^{0}C and 61.6 ± 5.6% relative humidity. Fresh air was supplied to the room at a sufficient rate.
Diet:	Hens were fed once daily for a total of 0.13 kg feed per day.
Water:	Fresh water was provided *ad libitum*.
Acclimation period:	Hens were acclimatised to conditions for at least 7 days. During acclimation, the hens were observed for feed consumption, egg production and general condition and health.
Predosing:	None.

METHODS:

1. **Dosing regime:**

Oral:

Level of administered dose:	1.10 mg/day for aniline label 1.14 mg/day for TP label
Food Consumption:	Average feed consumption of 0.105 kg/day/hen
Residue Intake in Diet:	10.5 ppm and 10.9 ppm
Vehicle:	A capsule were administered by opening the beak and inserting into esophagus until the capsule was swallowed.
Timing:	once daily in the morning between 10:00-10:15 a.m.
Duration:	5 consecutive days.

Dermal:	Not applicable
Formulation:	None
Number of treatments:	None
Application level:	N/A
Type of treatment:	N/A

Water (aquaculture):	Not applicable
Formulation:	None
Number of treatments:	None
Application level:	N/A
Type of treatment:	N/A

2. **Sample collection:**

Eggs: Eggs were collected twice daily before the morning and evening doses. The eggs were weighed at every collection and composited within each group.

Hen	Egg Production Acclimation	Egg Production Dosing
Control	45	48
A label	47	49
TP label	45	48

The average values reported for egg production indicated that egg production was not affected by dosing with XDE-570.

Excreta: Collected twice daily before the morning and evening doses.

Interval from last dose to sacrifice: The hens were sacrificed within 20-22 hours after the last dose by cervical dislocation.

Tissues harvested and analysed: The following tissues were collected: muscle (composite of light and dark), abdominal fat, liver, skin (from underside and back). Muscle, fat, skin and liver samples were analysed.

3. **Quantification of Total Radioactive Residues (TRRs):**

Total radioactive residues in tissue (muscle, fat, skin and liver), eggs and excreta samples were determined by combustion and liquid scintillation counter (LSC). The radiocarbon in the samples was combusted to ^{14}C-carbon dioxide and trapped in an appropriate solvent along with scintillation fluid and quantitated by LSC. The performance of the oxidizer was determined by ^{14}C-benzoic acid standard. Minimum quantifiable limit (MQL) was determined for each set of samples by analysing control samples with each set of samples of tissue, eggs or excreta.

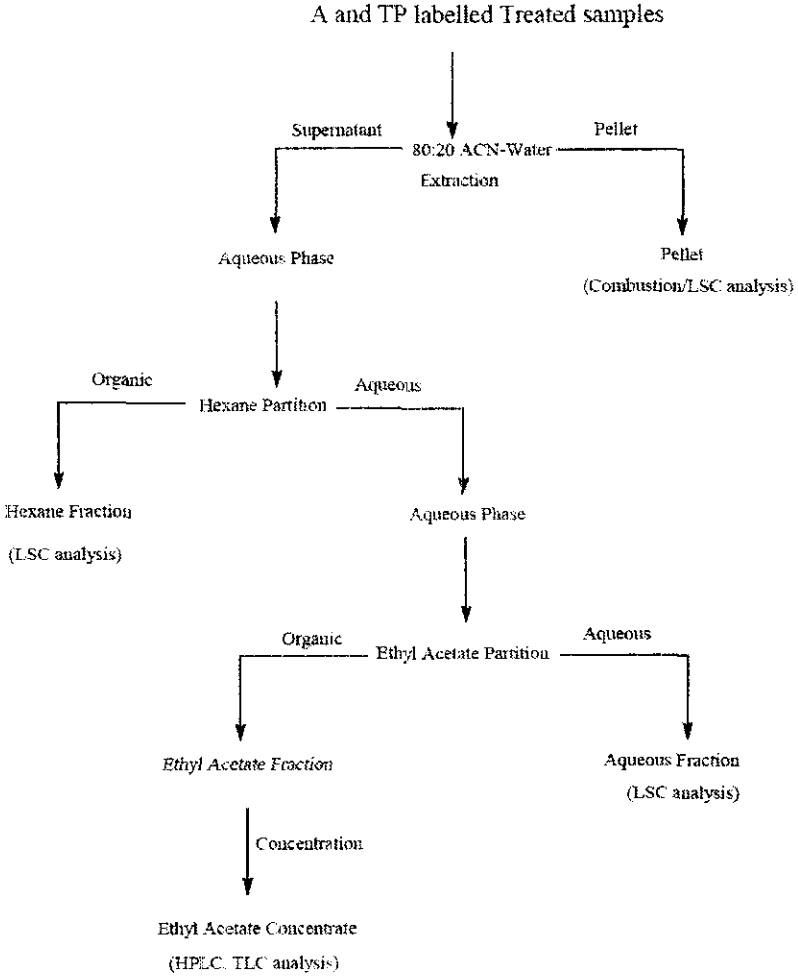
4. Extraction and Hydrolysis of Radioactive Residues (TRRs):

Solvent extraction and subsequent fractionation were performed on the A and TP labelled samples of eggs, skin and excreta (the only matrices with residue levels > 0.02 ppm). All samples were initially extracted three times with acetonitrile:water [80:20] (Figure 1). This extraction released most of the radioactivity present in these samples. The post extracted material was lyophilized and the remaining ^{14}C activity was quantified by combustion/LSC. The excreta extracts were concentrated and analysed by reverse phase HPLC and normal phase TLC. The eggs and skin extracts were concentrated, defatted using hexane, then acidified and extracted/partitioned with ethyl acetate resulting in organosoluble and aqueous fractions. The ^{14}C activity in hexane and aqueous fractions was quantified by LSC. Each of ethyl acetate organic fraction of the A and TP labelled eggs and skin was concentrated to dryness and the residue resolubilized in acetonitrile with 1% acetic acid. Radioactive residues in ethyl acetate organic fraction were analyzed by reverse phase HPLC and normal phase TLC. The extraction efficiency and stability of the parent compound was evaluated by using fortified control samples.

5. Characterization and Identification of Radioactive Residues (TRRS):

All aqueous and organic phase extractions except ethyl acetate organic fraction were analysed by LSC. The post extracted material from eggs, skin and excreta were analysed by combustion/LSC. The ethyl acetate organic fractions of eggs and skin and acetonitrile/water extract of excreta were the only extracts that had residues levels > 0.02 ppm. These extracts were initially analysed by reverse phase HPLC to identify radioactive residues. HPLC analysis were performed using C_{18} analytical column and an ultraviolet detector (UV). The effluent was monitor with UV detector and timed fractions were collected. The radioactivity in each fraction was determined by LSC. The fortified control and treated extracts were analysed by HPLC. The data was processed to produce a histogram representing the radioactivity in each fraction of the HPLC eluent as a function of time. Reference standards were used to compare the retention times with samples. The identity of compounds was confirmed by TLC analysis of the radioactive residues compared with the standards. TLC analysis were performed under normal conditions using silica gel plates developed in lined chambers with hexane-acetone (50:50). TLC plates bearing ^{14}C-compounds were scanned with an Imaging System to determine the location of the ^{14}C-compounds.

Figure 1.Extraction Scheme for the A and TP label samples of eggs, skin



II. RESULTS

1. **Total Radioactive Residues (TRRs):**

Radiochemical analysis indicated that amount of TRRs in tissues was very low. The recovery of the radioactivity was approximately 91% and 97% for the phenyl label and TP label respectively. Total radioactive residues (TRRs) recovered as XDE-570 equivalents are shown in Table 1 below.

TABLE 1. Total Radioactive Residues (TRRs) of ^{14}C phenyl and ^{14}C TP labelled XDE-570 in Tissue, Eggs and Excreta

Matrix	^{14}C phenyl- XDE-570		^{14}C TP-XDE-570	
	ppm	% administered Dose	ppm	% administered Dose
Composite muscle	0.0005*	< 0.0001	0.0008*	< 0.0001
Composite fat	0.0004*	< 0.0001	0.0006*	< 0.0001
Liver	0.0014*	< 0.0001	0.001*	< 0.0001
Skin	0.0066	0.002	0.005	0.002
Eggs	0.0038	0.013	0.004	0.013
Total Tissue		0.015		0.015
Excreta	10.0	91.3	11.5	96.9
Total Recovery		91.3		96.9

* Tissue residue levels below the experimental quantifiable amount (QA).

Comments:

The results indicated that the total radioactive residues (TRRs) were comparable between two labelling positions for excreta, muscle, fat, liver, and egg. Total residues in muscle, fat and liver were less than limit of quantification (< LOQ). Total residues in skin and eggs were very low (< 0.007 ppm). Almost 100% of the recovered radioactivty that was administered to hen was found in excreta. These residues in the tissues and egg samples were approximately 0.01% of the applied dose. The highest concentration of residues in tissues were found in the skin, 0.0066 ppm and 0.005 ppm in A-label and TP-label, respectively. The concentration of residues in egg were about 0.004 ppm in both A-label and TP-labelled, respectively.

The parent compound, florasulam, is not likely to bioaccumulate in fat, other tissues and egg yolk as a result of feeding of treated feed. This study demonstrated low levels of radioactivity in edible tissues. These observations are supported by the low Log K_{ow} (1.00 at pH 4.00 and -1.22 at pH 7.0) wich is an indication of a low potential for bioaccumulation.

2. **Quantitative Distribution of Radioactive Residues:**

TABLE 2. Quatitative Distribution of ^{14}C-Residues in Urine, Milk, Liver and Milk when Dosed with ^{14}C phenyl and ^{14}C TP labelled XDE-570

Tissues	Excreta		Eggs		Skin	
Labelling group	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP
Total Radioactive Residues (TRRs)						
Total Radioactive Residues *	100 % TRR (10 ppm)	100 % TRR (11.5 ppm)	100 % TRR (0.0038 ppm)	100 % TRR (0.0043 ppm)	100 % TRR (0.0066 ppm)	100 % TRR (0.005 ppm)
Total Extractable Radioactive Residues - % TRR (ppm)						
Acetonitrile/water phase	103 (10.4)	84.7 (9.8)	98.2 (0.0038)	102 (0.0044)	95.4 (0.0063)	96.4 (0.0048)
Fractionation of Extracted Radioactive Residues - % TRR (ppm)						
Hexane phase	Not performed		< MDA (0.00006)	< MQA (<0.0002)	< MDA (< 0.0001)	< MQA (0.0004)
EtoAc partition phase**			95.6 (0.0037)	96.2 0.0042	89.7 (0.0059)	89.9 (0.0045)
Aqueous soluble phase			<MQA (< 0.0002)	< MQA (< 0.0002)	< MQA (< 0.0003)	< MQA (< 0.0003)
Unextracted	1.2 (0.13)	2.1 (0.24)	< MQA (<0.0007)	< MQA (<0.0002)	< MDA (< 0.004)	< MDA (< 0.004)
Identification of Radioactive Residues - % TRR (ppm)						
Parent Compound (XDE-570)	95.1 (9.6)	79.7 (9.2)	95.1 (0.0037)	95.2 (0.0042)	85.9 (0.00570	80.7 (0.004)
Unidentified Metabolite	< 1 (<0.11)	4.5 (0.5)	<1.7 (<0.00007)	<1.7 (<0.00007)	<1.7 (<0.0001)	<2.9 (<0.0001)
Unidentified Metabolite	6.8 (0.7)	-	-	<1.7 (<0.00007)	<1.7 (<0.0001)	<2.9 (<0.0001)
Unidentified Metabolite	-	-	-	-	<1.7 (<0.0001)	4.8 0.0002
Unidentified Metabolite	-	-	-	-	<1.7 (<0.0001)	-
Distribution of Radioactive Residues - %TRR						
Total Extactable	103	84.7	98.2	102	95.4	96.4
Total Identified	95	79.7	95.1	95.2	85.9	80.7
Total Charecterized	103	84.2	97	98	94	92
Total Unextractable	1.2	2.1				
TOTAL	104.2	84.7	98.2	102	95.4	96.4

* Analysed by combustion/LSC
** Fraction used for TLC and HPLC analysis
Acetonitrile/water fraction was used in the case of excreta)
\- Not radiodetected
MDA Minimum detectable amount for each sample
MQLMinimum quantifiable limit for each sample

Comments:

The total radioactivity in liver, fat and muscle samples very low (0.015% TRR of administered dose), therefore, no further residue characterization was conducted. Solvent extraction and subsequent fractionation were performed on the A and TP labelled samples of excreta, egg and skin. All sample were initially extracted with acetonitrile:water (80:20). Further characterization of residues, extracted in acetonitrile:water phase, from egg and skin were achieved with hexane and ethyl acetate.

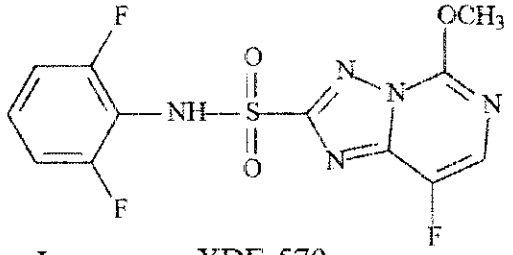
The acetonitrile:water extracted 103% (10.4 ppm) and 84.7% (9.8 ppm) of the TRR in A and TP label treated excreta samples. The predominant radioactive component in excreta , representing 92.3% and 94.1% TRR in A and TP treated extracted residues was identified as parent, florasulam. In the HPLC analysis, one other minor metabolite was eluted in the retention region of 5-OH-XDE-570 metabolite. However, it was not seen in TLC analysis and was not positively identified as 5-OH-XDE-570.

Egg sample were initially extracted with acetonitrile:water (80:20). The acetonitrile:water extracted 98.2% (0.0038 ppm) and 102% (0.0044 ppm) of the TRR in A and TP treated egg samples, respectively. The hexane extract of the aqueous phase contain less than MQA (<0.0002 ppm) of TRR for both A and TP treated egg. The aqueous fraction after ethyl acetate fractionation also represented less than MQA (<0.0002 ppm) of TRR for both A and TP treated egg. The ethyl acetate fractions represented 95.6% (0.0037 ppm) and 96.2% (0.0042 ppm) of the TRR for A and TP treated egg. The predominant radioactive component, representing 95% TRR in both label extracted residues in egg was parent. No other metabolites were identified in egg samples.

Skin sample were initially extracted with acetonitrile:water (80:20). The acetonitrile:water extracted 95.4% (0.006 ppm) and 96.4% (0.0048 ppm) of the TRR in A and TP treated skin samples, respectively. The hexane extract of the aqueous phase contain less than < MQA (<0.0004 ppm) of TRR for both A and TP treated skin. The aqueous fraction after ethyl acetate fractionation represented less than < MQA (<0.0003 ppm) of TRR for both A and TP treated skin. The ethyl acetate fractions represented 89.7% (0.0059 ppm) and 89.9% (0.0045 ppm) of the TRR for A and TP treated skin. The predominant radioactive component, representing 85.9% and 80.7% TRR in extracted residues in skin was parent. No other metabolites were identified in skin samples.

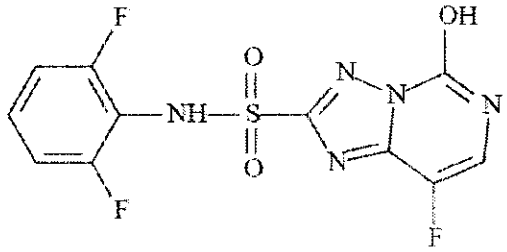
The extractability of radioactive residues ranged between 84% and 103% of TRR for excreta, eggs and skin. The behaviour of florasulam residues in hen tissues, egg and excreta during extraction, fractionation , and chromatographic analysis demonstrated no significant differences between A and TP labelled hens. Therefore, no significant sulfonilide bridge cleavage occurred during metabolism of florasulam in hen.

Figure 2. Proposed Metabolic Profile of XDE-570 in Laying Hen



I XDE-570

Minor metabolites



II 5-OH-XDE-570

Identification of Metabolites

Roman Numeral Identification	Common Name/Code	Chemical Name
I	XDE-570	N-(2,6-diflurophenyl)-8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide
II	5-OH-XDE-570	N-(2,6-diflurophenyl)-8-fluoro-5-hydroxyl(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide

Comments:

Based on the data submitted XDE-570 does not undergo a significant metabolism on laying hens. The parent compound is eliminated unchanged with minor unknown metabolites postulated to be 5-OH-XDE-570. However, the observed levels were below the limit of quantification.

III. STORAGE STABILITY

All samples and extracts were stored frozen at approximately -20 ^{0}C during the study. All tissue, egg and excreta samples were prepared and characterized within 28 days after sacrifice. Therefore, no storage stability tests were necessary for samples analysed in hen metabolism study.

V. CONCLUSIONS

Florasulam is rapidly excreted in excreta. Almost 100% of the recovered radioactivty that was administered to hen was found in excreta. Residue in tissues and egg samples was low with only a small portion of the recovered radioactivity (< 0.02% TRR, up to 0.004 ppm) found in all tissue and egg. The highest concentration of residue was found in skin at 0.0068 ppm (0.002% TRR) of the applied dose. The major metabolite in egg and skin was parent. In egg, the parent accounting for 95% of the isolated radioactivity from both phenyl and TP label florasulam. The available methods clearly identified presence of parent compound in samples. The remainder unidentified residues accounted for less than 3%. The very low residues in egg and other tissues with a major excretion of the parent compound indicted that florasulm only slightly metabolised in laying hen and no significant cleavage of the sulfonanilide bridge occurred (Figure 2). Based on the data reviewed, the Residue of concern (ROC) in hen is defined as parent compound, florasulam.

VI. DEFINITION OF THE RESIDUE OF CONCERN (ROC)

The Residue of Concern based on the laying hen metabolism study is defined as parent only.

IV. FINAL SUMMARY

In the laying hen metabolism study, XDE-570, radiolabelled as either [UL-aniline-^{14}C]XDE-570, or [triazolopyrimidine-9-^{14}C]XDE-570 was administered to two groups of 10 laying hens at a dose level of 0.76± 0.01 mg/kg bw/day. The dose was administered orally twice daily for five consecutive days, by opening the beak and inserting a capsule into the esophagus. The dose was equivalent to10.7 ± 0.2 ppm XDE-570 dietary burden at an average feed consumption of 0.13 kg/day. Samples of eggs, excreta were collected throughout the study. The test hens were sacrificed approximately 24 hours after the final dose. The tissue samples of fat, composite muscle (light and dark), skin and liver were collected for analysis.

The results indicated that the total radioactive residues (TRRs) were comparable between two labelling positions for excreta, muscle, fat, liver, and egg. Total residues in muscle, fat and liver were less than limit of quantification (< LOQ). Total residues in skin and eggs were very low (< 0.007 ppm). Almost 100% of the recovered radioactivty that was administered to hen was found in excreta. These residues in the tissues and egg samples were approximately 0.01% of the applied dose. The highest concentration of residues in tissues were found in the skin, 0.0066 ppm and 0.005 ppm in A-label and TP-label, respectively. The concentration of residues in egg were about 0.004 in both A-label and TP-labelled, respectively.

Total radioactive residues in tissue (muscle, fat, skin and liver), eggs and excreta samples were determined by combustion and liquid scintillation counter (LSC). Solvent extraction and subsequent fractionation were performed on the A and TP labelled samples of eggs, skin and excreta (the only matrices with residue levels > 0.02 ppm). All samples were initially extracted three times with acetonitrile:water [80:20] (Figure 1). This extraction released most of the radioactivity present in these samples. The post extracted material was lyophilized and the remaining ^{14}C activity was quantified by combustion/LSC. The excreta extracts were concentrated and analysed by reverse phase HPLC and normal phase TLC.

The total radioactivity in liver, fat and muscle samples very low, therefore, no further residue characterization was conducted. Solvent extraction and subsequent fractionation were performed on the A and TP labelled samples of excreta, egg and skin. All sample were initially extracted with acetonitrile:water (80:20). Further characterization of residues, extracted in acetonitrile:water phase, from egg and skin were achieved with hexane and ethyl acetate. The predominant radioactive component in extracted residues in egg and skin was parent. No other metabolites were identified in skin samples. The extractability of radioactive residues ranged between 84% and 103% of TRR for excreta, eggs and skin. The behaviour of florasulam residues in hen tissues, egg and excreta during extraction, fractionation, and chromatographic analysis demonstrated no significant differences between A and TP labelled hens.

The Residue of Concern (ROC) based on the laying hen metabolism study may be defined as the parent compound, florasulam. The metabolism of florasulam in the laying hen, goat and rat were similar. In all three species, the majority of the radioactivity was found in the excreta. Most of the parent compound in goat, hen and rat was eliminated unchanged with minor unknown metabolites at unquantifiable levels. No significant cleavage of the sulfonanilide bridge occurred in their metabolism. Swine metabolism is not required.

Based on the ruminant, laying hen and rat metabolism studies, the residue of concern (ROC) may be defined as the parent compound, florasulam.

VII. STUDY DEFICIENCIES

No deficiencies were identified.

Signatures:

Reviewed by:

Ali Ismaily
Evaluation Officer
FREAS

Date

Peer Reviewed by:

Henri Bietlot, Ph. D.
Evaluation Officer
FREAS

Date

Approved by:

Ariff Ally, Ph. D.
Section Head
FREAS

Date

Reviewer: Ali Ismaily , **Date** February 20 , 2001

This DER was initially reviewed by Canada's PMRA and has been reviewed by HED. Conclusions herein agree with HED policy. In addition, this DER has been modified to include the submission MRID number.

Thurston Morton **23-May-2007**

STUDY TYPE: Crop Field Trials (Canada/US) - Spring wheat, Barley and Oat OPPTS 860.1500

TEST MATERIAL: N-(2,6-difluorophenyl)-8-fluoro-5-methoxy-(1,5 c)-pyrimidine-2-sulfonanilide

FORMULATION AND TYPE: EF-1343 SC (52 g ai/ha) with Agral 90 adjuvant, 0.2% v/v.

SYNONYMS: **XDE-570** (Florasulam)

MRID 46808128 E. M. Bargar and D. R. Foster, (1998), "Magnitude of Residues of DE-570 in Spring Wheat, Barley, and Oat" Global Environmental Chemistry Laboratory - Indianapolis Lab, Dow AgroSciences LLC, Laboratory Study ID: RES97041, October 12, 1998. Unpublished

R. F. Elsharaiha, D. S. Lindsay, A. D. Thomas, B. A. Blakeslee, D. O. Duebelbeis, and D. R. Foster, "Summary of the Residues of DE-570 in Wheat, Barley, and Oat Samples Collected in Association with Protocol RES97041" Global Environmental Chemistry Laboratory - Indianapolis Lab, Dow AgroSciences LLC, Appendix B of Laboratory Study ID: RES97041, September14, 1998. Unpublished

SPONSOR: Dow AgroSciences (DWE)

EXECUTIVE SUMMARY:

The limited supervised crop field trials study in wheat, barley and oat conducted in zones 7, 7A and 14 in Canada/USA have shown that residues in wheat grain, barley grain and oat grain collected at 41-60 days following a single foliar broadcast ground application of EF-1343 SC formulation (52 g ai/L), 10 g ai/ha of florasulam (with Agral 90 Adjuvant, 0.2% v/v), when plants were at BBCH 37-55 stage, equivalent to 2X the proposed Canadian maximum season rate, were less than limit of quantification (<0.01 ppm). However, the residue trials conducted for these crop were insufficient and did not represent all the major growing zones for wheat, barley and oat in Canada. The residue trials were not classified acceptable and did not satisfy the guideline requirement for residue trials (Residue Chemistry Guidelines Dir98-02, Section 9).

The petitioner has submitted residue field trials conducted over one growing season in zones common to both the USA and Canada. As the residue trials requirements were not met for a geographically restricted registration or a national registration, the petitioner must submit the results from additional residue trials. However, since residue of florasulam in wheat, barley and oat was < LOQ, a 25% reduction in residue trials is allowed. Results of these additional residue trials must be consistent with the data previously reviewed (i.e., <LOQ of 0.01 ppm). In the mean time, FREAS can recommend the promulgation of MRLs for wheat (0.01 ppm), barley (0.01 ppm) and oat (0.01 ppm) to cover residues of florasulam in these crops. The MRL on the RAC will cover potential residues in processed commodities.

The results from the residue decline studies for wheat, barley and oat (green and dried immature plant, straw and hay) conducted in zones 7, 7A and 14 in Canada/USA have shown that residues in these crop fractions collected at 0, 3, 7, 10, 15, 30 and 40 days following a single foliar broadcast ground application of EF-1343 SC formulation (52 g ai/L), approximately 10 g ai/ha of florasulam (with Agral 90 Adjuvant, 0.2% v/v), when plants were at BBCH 37-55 stage, equivalent to 2X the proposed Canadian maximum season rate, indicated rapid decline of florasulam residues. No residues were detected in any whole plant sample collected at/after 7 days after application. Therefore, grazing on wheat, barley and oat crop can be supported 7 days after application of EF-13443 SC.

COMPLIANCE:

Signed and dated GLP, Quality Assurance and Data Confidentiality were provided.

I. MATERIALS AND METHODS

All residue samples were analysed by immunoassay (IA), as the screening method for residues of florasulam and related florasulam metabolites (4-hdroxyphenyl florasulam and its glucose conjugate), using Dow AgroSciences IA method GRM 97.01 with a limit of quantification (LOQ) of 0.01 for grain and 0.050-0.068 ppm for straw, green and dried immature whole plants. This method is based on the use of a magnetic particle-based immunoassay test kit co-developed by Strategic Diagnostics Inc. and Dow AgroSciences. Samples found to contain residues above LOQ were reanalysed by a specific method, capillary gas chromatography with mass selective detection (GC/MSD), using Dow AgroSciences GC/MSD method, GRM 98.01 with a limit of quantification (LOQ) of 0.01 ppm for grain and 0.05 ppm for straw, green and dried immature whole plants. The quantification of florasulam residues by GC/MSD was based on the peak ratio of *m/z* 138 (N-methyl derivative of DE-570) to *m/z* 170 (internal standard).

1. Test Compound

Chemical name:

IUPAC: **2', 6', 8-Trifluoro-5-methoxy-s-triazolo [1,5-c]pyrimidine-2-sulfonanilide**

CAS name: **N-(2,6-diflurophenyl)-8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide**

CAS #: **145701-23-1**

Common name (ANSI, BSI or ISO): **Florasulam (ISO-proposed)**

Company developmental/experimental name: XDE-570

2. Trial Numbers and Locations

NUMBER OF FIELD TRIALS BY CANADIAN/US GROWING REGION									
Crop	Residue Trials	Canadian/Canadian Equivalent US Growing Regions							Total Trials
		1	5	5A	5B	7	0	14	
Wheat	Submitted					6	1	6	13
	Requested		2			7 (5)	1	10 (7)	20 (15)
	Deficient		**2**					**1**	**3**
Barley	Submitted					4	1	4	9
	Requested		1		1	2		12 (9)	16 (13)
	Deficient		**1**		**1**			**5**	**7**
Oat	Submitted					5	1	3	9
	Requested	1	1	1	1	2		10 (7)	16 (13)
	Deficient	**1**	**1**	**1**	**1**			**4**	**8**

(#) Number of residue trials reduced by 25% (Residues from all trials were < 0.025 ppm , i.e., less than LOD).

Comments:

Supervised residue trials were conducted in Canada and USA, applying EF-1343 Suspension Concentrate at 10 g a.i./ha (twice the Canadian proposed rate) with 0.2 % (v/v) Agral 90 Adjuvant, on wheat, barley and oat. It did not meet the established requirements both in terms of the number and the geographical representation for wheat, barley and oat as per the Residue Chemistry Guideline (Residue Chemistry Guidelines Dir98-02, Section 9). However, since residue of florasulam in wheat, barley and oat was < LOQ, a 25% reduction in residue trials is allowed.

European residue data on wheat and barley were also submitted. However, soil characteristics and climatic conditions in the European growing zones cannot be compared with Canadian/US growing zones. Therefore, data form European source cannot be used as surrogate data.

3. Proposed Canadian Use Pattern

Crop	Formulation Type	Application				
		Method/Timing	Rate (g ai/ha)	Number/ season	Maximum Rate (g ai/ha)	PHI (days)
wheat (spring, durum), barley (spring), oat	EF-1343 Suspension concentrate (50 g/L)	postemergent 2-leaf crop up to and including the flag leaf extended stage	5	1	5	60

Comments/Label Restrictions:

I. Addition of a surfactant Agral 90, at a rate of 0.2% v/v is used with this herbicide.
II. Do not apply by air.
III. Fields previously treated with EF-1343 herbicide can be seeded the following year to barley, canola, forage grasses, oats, peas, rye or wheat or fields can be summerfallowed.
IV. Livestock may be grazed on treated crops 7 days following application.
V. Do not harvest the treated crop within 60 days after application.

Tankmixes:

Crop	Tankmix		Rate of Tankmix Partner (g ai/ha)	Timing of Application of Tankmix Partner	Rate of Surfactant (% v/v)
	Common Name (active ingredient)	Trade Name (formulated product)			
wheat (spring and durum) barley (spring) oats	MCPA ester (500 g ai/L)	MCPA LV 500	420	postemergent	No surfactant should be added.
wheat (spring and durum) barley (spring) oats	clopyralid (50 g ae/L)	Curtail M	75	postemergent	No surfactant should be added.
	MCPA ester (280 g ae/L)		420		
wheat (spring and durum) barley (spring)	MCPA ester (500 g ai/L)	MCPA LV 500	420	postemergent	Acidulate at 0.25% w/w
	imazamethabenz (300 g ai/L)	Assert 300 SC	480		
wheat (spring and durum) barley (spring)	MCPA ester (500 g ai/L)	MCPA LV 500	420	postemergent	Not recommended
	fenoxaprop-p-ethyl (92 g/L)	Puma Super *	92		
wheat (spring and durum) barley (spring)	clopyralid (50 g ae/L)	Curtail M	75	postemergent	Acidulate at 0.25% w/w
	MCPA ester (280 g ae/L)		420		
	imazamethabenz (300 g ai/L)	Assert 300 SC	480		
wheat (spring and durum) barley (spring)	clopyralid (50 g ae/L)	Curtail M	75	postemergent	Not recommended
	MCPA ester (280 g ae/L)		420		
	fenoxaprop-p-ethyl (92 g/L)	Puma Super *	92		
wheat (spring and durum)	MCPA ester (500 g ai/L)	MCPA LV 500	420	postemergent	Score at 0.8% v/v or Score at 1.0% v/v
	clodinafop-propargyl (240 g/L)	Horizon	55.2 or 70		
wheat (spring and durum)	clopyralid (50 g ae/L)	Curtail M	75	postemergent	Score at 0.8% v/v or Score at 1.0% v/v
	MCPA ester (280 g ae/L)		420		
	clodinafop-propargyl (240 g/L)	Horizon	55.2 or 70		

Comments/Label Restrictions:

1. Do not cut the treated crop for hay or graze treated crop within 7 days after application.
2. Do not harvest the treated crop within 60 days after application.
3. Follow all precautions, directions for use, and limitations on the tankmix partner labels.

Puma Super label indicated a PHI of 65 days. The PHI of 65 days must be respected for the tankmix with Puma Super. All other tankmix partners do not recommend a PHI on their labels. The PHI of 60 days applies to these tankmixes.

Comments:

The proposed use pattern supported the single application rate of 5 g ai/ha per season with and without tankmix partners and PHI of 60 days for all crops as confirmed by Efficacy and Sustainability Evaluation Division (ESAD).

All the corresponding tankmix partners are registered for application on wheat, barley and oats. The active ingredients (MCPA ester, clopyralid, imazamethabenz, fenoxaprop-p-ethyl, clodinafop-propargyl) in the proposed tankmixes are registered on their respective crops in Canada. The proposed tankmix label rates are at or below the rate for each active ingredient. The residues of MCPA ester, imazamethabenz, fenoxaprop-p-ethyl, clodinafop-propargyl are covered under subsection B.15.002(1) of the Food and Drugs Act & Regulations, i.e. ≤ 0.1 ppm and the residues of clopyralid on wheat, barley and oat are covered under MRL of 2 ppm.

The addition of an adjuvant is required for postemergent application with tank mixing of Assert and Horizon. This requirement is listed on the Assert and Horizon labels. The PHI of 65 days is indicated on Puma Super label. The Puma Super label restricts grazing of livestock. The PHI of 65 days must be respected and no grazing of livestock must be allowed for the tankmix with Puma Super.

4. <u>Analytical Method Validation</u> (Concurrent)

The samples were analysed either by IA method or GC/MSD method. While the GC/MSD method is specific for DE-570, the IA method is not, as it can also detect certain metabolites that exhibit a competitive binding site of DE-570 (e.g., 4-hydroxy phenyl DE-570 metabolite and its glucose conjugate). Thus, residues obtained by the IA method were generally higher than those generated by the GC/MSD method because of the presence of 4-hydroxy phenyl DE-570 metabolite and its glucose conjugate. The IA method served as a screening tool to determine DE-570 and other DE-570 related metabolites in the samples.

a. <u>Immunoassay method</u>:

Crop matrix	Spiking Level (ppm)	Recoveries obtained	Range (%)	Mean recovery (SD)
Wheat Grain	0.010 0.050 0.200	108, 116, 116, 88 103, 87 100, 94	88-116 87-103 94-100	107 ± 13 95 ± 11 97 ± 4
Barley Grain	0.010 0.050 0.200	112, 92, 96 111, 95 94, 94	92-112 95-111 NA	100 ± 11 103 ± 11 NA
Oat Grain	0.010 0.050 0.200	92, 96 91 82	92-96 NA NA	94 ± 3 NA NA
Wheat Forage	0.050 0.100 0.500	66, 72, 102, 102, 78, 84, 108, 84, 78 102, 111, 102, 120, 135 105, 103, 115, 112	66-108 102-135 105-115	86 ± 15 114 ± 14 109 ± 6
Oat Forage	0.050 0.100 0.500 2.000	114, 96, 84, 78, 102, 102 117, 99, 123 110, 103, 104 111, 117, 111	78-114 99-123 103-110 111-117	96 ± 13 113 ± 12 106 ± 4 113 ± 3

Crop matrix	Spiking Level (ppm)	Recoveries obtained	Range (%)	Mean recovery (SD)
Wheat Hay	0.050 0.100 0.300	99, 90 101 99	90-99 NA NA	95 ± 6 NA NA
Barley Hay	0.050 0.100	108, 99, 96 102	96-108 NA	103 ± 6 NA
Wheat Straw	0.050 0.100 0.300	132, 123 126 102	123-132 NA NA	128 ± 6 NA NA
Barley Straw	0.050 0.300	126, 120 110	120-126 NA	123 ± 4 NA
Oat Straw	0.050 0.100	108, 114 101	108-114 NA	111± 4 NA
Wheat Immature Green Plant	0.050 0.100	105, 93, 114 128, 122	93-114 122-128	104 ± 11 125 ± 4
Barley Immature Green Plant	0.050 0.100 0.300 0.500 1.00	105, 99, 108, 120, 96, 96 96, 105, 102, 113 101, 97 123, 113 104	96-120 96-113 97-101 113-123 NA	104 ± 9 104 ± 7 99 ± 3 118 ± 7 NA
Oat Immature Green Plant	0.050 0.100 0.200 0.300	114, 111 102, 99, 107, 116 89 145	111-114 99-116 NA NA	113 ± 2 106 ± 7 NA NA
Wheat Immature Dried Green Plant	0.050 0.100 0.300	88, 102 99 91	88-102 NA NA	95 ± 10 NA NA
Barley Immature Dried Green Plant	0.050 0.100 0.300 0.500	111, 99, 114, 120, 102, 120, 102 117, 116, 116, 110, 114 108, 103 112, 122	99-120 110-117 103-108 112-122	110 ± 9 115 ± 3 106 ± 4 117 ± 7
Oat Immature Dried Green Plant	0.050 0.100 0.300	123, 78, 102 119, 115 104	78-123 115-119 NA	101 ± 32 117 ± 3 NA

NA not applicable

b. GC/MSD method:

Crop matrix	Spiking Level (ppm)	Recoveries obtained	Range (%)	Mean recovery (SD)
Oat Forage	0.050	79, 78, 83, 82, 82, 93, 82	78-93	83 ± 5
	0.100	84	NA	NA
	0.250	83, 75, 88	75-88	82 ± 7
	2.000	73, 128	73-128	101 ± 39
Wheat Hay	0.100	106	NA	NA
	0.250	90	NA	NA
Barley Hay	0.050	90, 89, 92, 97, 121, 87, 103	87-121	97 ± 12
	0.100	101	NA	NA
	0.250	95	NA	NA
Oat Straw	0.050	108	NA	NA
	0.100	113	NA	NA
Barley Immature Green Plant	0.050	95, 98, 105, 107, 107, 102, 82	82-107	99 ± 9
	0.100	95	NA	NA
	0.250	79, 77	77-79	78 ± 1
	1.000	75	NA	NA
Barley Immature Dried Green Plant	0.050	75, 79, 88, 84, 86, 91, 113	75-113	88 ± 12
	0.100	104	NA	NA
	0.250	72, 99	72-99	86 ± 19
	1.000	134	NA	NA

NA not applicable.

Comment:

The results from the control samples spiked with florasulam and analysed concurrently to the samples from supervised crop field trials shown adequate recoveries of florasulam residues.

5. Storage Stability Conditions

Freezer Storage From Freezer Storage Stability Tests

Commodity	Storage Temperature (°C) (approximately)	Duration (days)
Wheat grain	-20	264
Wheat forage	-20	378
Wheat straw	-20	313
Wheat hay	-20	194
Wheat immature green plant	-20	194
Wheat immature dried plant	-20	389

Freezer Storage From the Supervised Trials

Commodity	Storage Temperature (°C) (averaged approximately)	Duration (days)
Wheat grain	-20	216
Wheat forage	-20	363
Wheat straw	-20	248
Wheat hay	-20	343
Wheat immature green plant	-20	264
Wheat immature dried plant	-20	348

Comments:

Storage Stability of florasulam (XDE-570) has been demonstrated for approximately 264 days for wheat grain, 313 days for wheat straw, 378 days for forage, 194 days for hay, 94 days for immature green plant and 389 days for immature dried plant. Residue samples from supervised residue trials were stored under similar conditions reported in the storage stability studies for wheat. The storage intervals for the residue samples were shorter than the storage stability demonstrated in the freezer test. Since the residues of florasulam were stable in wheat grain, the freezer storage stability study will have no impact on the magnitude of the residue of concern (ROC) in grain. Hence, no correction for the magnitude of residue in grain is required to the proposed MRLs in wheat, barley and oat grain.

6-1. Application and RAC Information - Wheat

EF-1343/Suspension Concentrate/ 10 g ai/ha (with Agral 90 adjuvant, 0.2% v/v)

LOCATION (city, province/state)/ YEAR	# TRIALS/ LOCATION	ZONE #	CROP/ VARIETY	GROWTH STAGE/ APPLICATION	METHOD OF APPLICATION *	TANK MIXES/ ADJUVANTS	GROWTH STAGE/ HARVEST	HARVESTED RAC	CROP GROUP	HARVEST PROCEDURES	
										Method/equipment (mechanical/hand from the plant/ground/ flotation)	# & wt of samples/ replicate; replicates/ treatment **
Dagmar, MT, Sheridan County, USA / 1997 **MT**	1	7	Durum - Rugby	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	Immature and mature crop	grain straw forage immature plant	15 16 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Velve, ND, McHenry County, USA / 1997 **ND1**	1	7	Hard red - 2375	flag leaf (8)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	Immature and mature crop	grain straw forage immature plant	15 16 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Velva, ND, Ward County, USA / 1997 **ND2**	1	7	Hard red - Grandin	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	Immature and mature crop	grain straw hay forage	15 16 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Barnard, SD, Brown County, USA / 1997 **SD**	1	7	Soft white - Penewawa	flag leaf (8-9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	Immature and mature crop	grain straw hay forage	15 16 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Barnwell, AB, Taber County, Canada / 1997 **AB1**	1	7A	Hard red - Makwa	flag leaf (8)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Lacombe, AB, Lacombe County, Canada / 1997 **AB2**	1	14	Hard red - Teal	flag leaf (8-9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	Immature and mature crop	grain straw immature plant	15 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Red Deer, AB Red Deer County, Canada /1997 **AB3**	1	14	Can. Prairie soft - Oslow	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg

Wheat Continued ..

EF-1343/Suspension Concentrate/ 10 g ai/ha (with Agral 90 adjuvant, 0.2% v/v)

LOCATION (city, province/state)/ YEAR	# TRIALS/ LOCATION	ZONE #	CROP/ VARIETY	GROWTH STAGE/ APPLICATION	METHOD OF APPLICATION *	TANK MIXES/ ADJUVANTS	GROWTH STAGE/ HARVEST	HARVESTED RAC	CROP GROUP	HARVEST PROCEDURES	
										Method/equipment (mechanical/hand from the plant/ground/ flotation)	# & wt of samples/ replicate; replicates/ treatment **
Minto, MB **MB1** Whitewater County, Canada / 1997	1	14	Can. Prairie soft - Taber	flag leaf (8-9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain straw	15 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Boissevain, MB **MB2** Morton County, Canada / 1997	1	14	Can. Prairie soft - Taber	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain.: 1-2 kg straw: 0.5-2 kg
Souris, MB **MB3** Glenwood County, Canada/ 1997	1	14	Durum - Sceptre	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Saskatoon, SK **SK1** Corman Park, Canada / 1997	1	7	Durum - Kyle	flag leaf (8)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain straw	15 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Outlook, SK **SK2** Fertile Valley Canada / 1997	1	7	Hard red - Teal	boot (10)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Duck Lake, SK **SK3** Duke Lake Canada / 1997	1	14	Durum - Kyle	flag leaf (8)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg

* Foliar broadcast ground spray application using a tractor mounted 12-nozzle boom air pressurized sprayer with T-jet nozzles or flat fan nozzles
** Each sample was collected from 12 randomly selected areas over the entire plot

6-2. Application and RAC Information - Barley

EF-1343/Suspension Concentrate/ 10 g ai/ha (with Agral 90 adjuvant, 0.2% v/v)

LOCATION (city, province/state)/ YEAR	# TRIALS/ LOCATION	ZONE #	CROP/ VARIETY	GROWTH STAGE/ APPLICATION	METHOD OF APPLICATION *	TANK MIXES/ ADJUVANTS	GROWTH STAGE/ HARVEST	HARVESTED RAC	CROP GROUP	HARVEST PROCEDURES	
										Method/equipment (mechanical/hand from the plant/ground/ flotation)	# & wt of samples/ replicate; replicates/ treatment **
Dagmar, MT, MT Sheridan County, USA / 1997	1	7	Stark, 2-row	flag leaf (8-9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	immature and mature crop	grain straw immature plant	15 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Velve, ND, ND1 McHenry County, USA / 1997	1	7	Foster, 6-row	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	immature and mature crop	grain straw immature plant	15 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Velva, ND, ND2 Ward County, USA / 1997	1	7	Robust, 6-row	flag leaf (8)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	immature and mature crop	grain straw	15 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Barnwell, AB, AB1 Taber County, Canada / 1997	1	7A	B1215, 2-row	flag leaf (8)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Lacombe, AB, AB2 Lacombe County, Canada / 1997	1	14	AC Lacombe, 6-row	boot (9-10)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	immature and mature crop	grain straw immature plant	15 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Minto, MB MB1 Whitewater County, Canada / 1997	1	14	Excel, 6-row	flag leaf (8)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain straw	15 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Boissevain, MB MB2 Morton County, Canada / 1997	1	14	Bedford, 2-row	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg

Barley Continued ..

EF-1343/Suspension Concentrate/ 10 g ai/ha (with Agral 90 adjuvant, 0.2% v/v)

LOCATION (city, province/state)/ YEAR	# TRIALS/ LOCATION	ZONE #	CROP/ VARIETY	GROWTH STAGE/ APPLICATION	METHOD OF APPLICATION *	TANK MIXES/ ADJUVANTS	GROWTH STAGE/ HARVEST	HARVESTED RAC	CROP GROUP	HARVEST PROCEDURES	
										Method/equipment (mechanical/hand from the plant/ground/ flotation)	# & wt of samples/ replicate; replicates/ treatment **
Saskatoon, SK SK1 Corman Park, Canada / 1997	1	7	Manely, 2-row	flag leaf (8-9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Duck Lake, SK SK2 Duke Lake Canada / 1997	1	14	Stander, 6-row	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg

* Foliar broadcast ground spray application using a tractor mounted 12-nozzle boom air pressurized sprayer with T-jet nozzles or flat fan nozzles
** Each sample was collected from 12 randomly selected areas over the entire plot

6-3. Application and RAC Information - Oat

EF-1343/Suspension Concentrate/ 10 g ai/ha (with Agral 90 adjuvant, 0.2% v/v)

LOCATION (city, province/state)/ YEAR	# TRIALS/ LOCATION	ZONE#	CROP/ VARIETY	GROWTH STAGE/ APPLICATION	METHOD OF APPLICATION *	TANK MIXES/ ADJUVANTS	GROWTH STAGE/ HARVEST	HARVESTED RAC	CROP GROUP	HARVEST PROCEDURES	
										Method/equipment (mechanical/hand from the plant/ground/ flotation)	# & wt of samples/ replicate; replicates/ treatment **
Dagmar, MT, **MT** Sheridan County, USA / 1997	1	7	Dumont	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	immature and mature crop	grain straw forage immature plant	15 16 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Velve, ND, **ND** McHenry County, USA / 1997	1	7	Valley	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	immature and mature crop	grain straw forage immature plant	15 16 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Barnard, SD, **SD** Brown County, USA / 1997	1	7	Hytest	flag leaf (8-9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	immature and mature crop	grain straw hay forage	15 16 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Barnwell, AB, **AB1** Taber County, Canada / 1997	1	7A	Mustang	flag leaf (8-9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	1	14	Cascade	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	Immature and mature crop	grain straw immature plant	15 16 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Minto, MB **MB1** Whitewater County, Canada / 1997	1	14	Robert	flag leaf (8)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain straw	15 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Boissevain, MB **MB2** Morton County, Canada / 1997	1	14	Robert	flag leaf (8)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg

Oat Continued ..

EF-1343/Suspension Concentrate/ 10 g ai/ha (with Agral 90 adjuvant, 0.2% v/v)

LOCATION (city, province/state)/ YEAR	# TRIALS/ LOCATION	ZONE#	CROP/ VARIETY	GROWTH STAGE/ APPLICATION	METHOD OF APPLICATION *	TANK MIXES/ ADJUVANTS	GROWTH STAGE/ HARVEST	HARVESTED RAC	CROP GROUP	HARVEST PROCEDURES	
										Method/equipment (mechanical/hand from the plant/ground/ flotation)	# & wt of samples/ replicate; replicates/ treatment **
Saskatoon, SK **SK1** Corman Park, Canada / 1997	1	7	Derby	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain straw	15 16	mechanical and/or manual harvest	control: single treated: duplicate grain:: 1-2 kg straw: 0.5-2 kg
Outlook, SK **SK2** Fertile Valley Canada / 1997	1	7	Derby	flag leaf (9)	foliar broadcast spray using 12- nozzle boom	no tankmix / Agral 90 (0.2% v/v)	mature crop	grain	15	mechanical and/or manual harvest	control: single treated: single grain:: 0.27-0.43 kg straw: 0.5-2 kg

* Foliar broadcast ground spray application using a tractor mounted 12-nozzle boom air pressurized sprayer with T-jet nozzles or flat fan nozzles
** Each sample was collected from 12 randomly selected areas over the entire plot

7-1. Site Specific Information - Wheat

LOCATION (city, province/state)/ YEAR	FARMING PRACTICES			SOIL CHARACTERISTICS				
	CULTIVATION/ IRRIGATION*	FERTILIZER	MAINTENANCE CHEMICALS/RATE/TIMING ***	TYPE	% Organic Matter (OM)	pH	Cation Exchange Capacity (CEC)	WEATHER DATA** (Appendix I)
Dagmar, MT, Sheridan County, USA / 1997 **MT**	Irrigation (50.8 mm)	46-0-0 (urea)	BRONNATE (bromoxynil + MCPA)	Loam	3.5	7.8	32.6	dry weather conditions compare to the historical data
Velve, ND, McHenry County, USA / 1997 **ND1**	No irrigation	18-46-0 (DAP) 46-0-0 (urea)	TILLER (fenoxaprop-p-ethyl + MCPA ester + 2, 4-D), Buctril (bromoxynil)	Loam	5.9	5.2	24.8	within historical data
Velva, ND, Ward County, USA / 1997 **ND2**	Irrigation (2.5 mm)	NH_3, 82-0-0	BRONATE (bromoxynil + MCPA)	Loam	3.0	6.9	26.7	dry weather conditions compare to the historical data
Barnard, SD, Brown County, USA / 1997 **SD**	No irrigation	18-46-0 (DAP) 46-0-0 (urea)	BRONNATE (bromoxynil + MCPA) + Rhonax (MCPA)	Loam	3.6	6.3	19.5	dry weather conditions compare to the historical data
Barnwell, AB, Taber County, Canada / 1997 **AB1**	Irrigation (236 mm)	51-0-0	Tralkoxydim, Bromoxynil, MCPA, Diquat	Loam	2.5	7.9	33.1	within historical data
Lacombe, AB, Lacombe County, Canada / 1997 **AB2**	No irrigation	none	Tralkoxydim, 2, 4-D, Glyphosate	Loam	6.7	6.3	27.1	within historical data
Red Deer, AB Red Deer County, Canada /1997 **AB3**	No irrigation	none	ACHIEVE (Tralkoxydim) 2, 4-D, ROUNDUP (glyphosate)	Loam	9.4	7.1	40.3	within historical data
Minto, MB Whitewater County, Canada / 1997 **MB1**	No irrigation	N, P, K	Tralkoxydim, Dichlorprop, 2, 4-D	Clay loam	6.3	7.6	25.6	within historical data
Boissevain, MB Morton County, Canada / 1997 **MB2**	No irrigation	N, P	FORTRESS (Triallate, trifluralin), Tralkoxydim, MCPA	Loam	5.2	8.1	36.7	within historical data
Souris, MB Glenwood County, Canada/ 1997 **MB3**	No irrigation	N, P	Triallate, Trifluralin, Glyphosate	Silt loam	7.5	7.4	25.3	within historical data
Saskatoon, SK Corman Park, Canada / 1997 **SK1**	No irrigation	none	Tralkoxydim, 2, 4-D	Loam	3.0	7.5	36.7	within historical data

Wheat Continued ..

LOCATION (city, province/state)/ YEAR	FARMING PRACTICES			SOIL CHARACTERISTICS				
	CULTIVATION/ IRRIGATION*	FERTILIZER	MAINTENANCE CHEMICALS/RATE/TIMING ***	TYPE	% Organic Matter (OM)	pH	Cation Exchange Capacity (CEC)	WEATHER DATA** (Appendix I)
Outlook, SK Fertile Valley Canada / 1997	No irrigation	none	Tralkoxydim, 2, 4-D	Clay loam	2.9	7.4	30.9	within historical data
Duck Lake, SK Duke Lake Canada / 1997	No irrigation	none	Tralkoxydim, 2, 4-D	Loam	3.8	6.2	19.7	within historical data

* Most sites experienced drier conditions than normal during early summer. One U.S. site (MT) reported poor crop stand due to the dry weather. Otherwise, temperatures for May-August were within historical range.

** Precipitation for growing crop period May-August was within historical data, except in MT and SD (about 50% less) and AB2 (about 45% more). Irrigation was provided for these three sites (Dagmar, MT, Velva, ND and Barnard, SD).

*** Plants were maintained using fertilizers and approved pesticide for each crop.

7-2. Site Specific Information - Barley

LOCATION (city, province/state) YEAR	FARMING PRACTICES			SOIL CHARACTERISTICS				
	CULTIVATION/ IRRIGATION*	FERTILIZER	MAINTENANCE CHEMICALS/RATE/TIMING ***	TYPE	% Organic Matter (OM)	pH	Cation Exchange Capacity (CEC)	WEATHER DATA** (Appendix I)
Dagmar, MT, **MT** Sheridan County, USA / 1997	Irrigation (50.8 mm)	46-0-0 (urea)	BRONNATE (bromoxynil + MCPA)	Loam	3.4	7.8	31.5	Dry weather conditions compare to the historical data
Velve, ND, **ND1** McHenry County, USA / 1997	No irrigation	18-46-0 (DAP) 46-0-0 (urea)	TILLER (fenoxaprop-p-ethyl + MCPA ester + 2, 4-D)	Loam	5.7	5.2	25.4	within historical data
Velva, ND, **ND2** Ward County, USA / 1997	Irrigation (2.5 mm)	NH_3, 82-0-0	BRONATE (bromoxynil + MCPA)	Loam	3.3	6	25.4	Dry weather conditions compare to the historical data
Barnwell, AB, **AB1** Taber County, Canada / 1997	Irrigation (236 mm)	51-0-0	Tralkoxydim, Bromoxynil, MCPA, Diquat	Clay loam	3	8	32.9	within historical data
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	No irrigation	none	2, 4-D	Loam	3.7	7.5	21.7	within historical data
Minto, MB **MB1** Whitewater County, Canada / 1997	No irrigation	N, P, K	TILLER (fenoxaprop-p-ethyl + MCPA ester + 2, 4-D) Trifluralin, Tralkoxydim, MCPA	Silt loam	6	7.8	27.9	within historical data
Boissevain, MB **MB2** Morton County, Canada / 1997	No irrigation	N, P	TILLER (fenoxaprop-p-ethyl + MCPA ester + 2, 4-D) Trifluralin, Tralkoxydim, MCPA	Silt loam	4.5	8.3	36.7	within historical data
Saskatoon, SK **SK1** Corman Park, Canada / 1997	No irrigation	none	Tralkoxydim, 2, 4-D	Loam	3.1	7.3	28.7	within historical data
Outlook, SK **SK2** Fertile Valley Canada / 1997	No irrigation	none	Tralkoxydim, 2, 4-D	Loam	3.8	6.1	19.9	within historical data

* Most sites experienced drier conditions than normal during early summer. One U.S. site (MT) reported poor crop stand due to the dry weather. Otherwise, temperatures for May-August were within historical range.

** Precipitation for growing crop period May-August was within historical data, except in MT and SD (about 50% less) and AB2 (about 45% more).

*** Plants were maintained using fertilizers and approved pesticide for each crop.

7-23 Site Specific Information - Oats

LOCATION (city, province/state)/ YEAR	FARMING PRACTICES			SOIL CHARACTERISTICS				
	CULTIVATION/ IRRIGATION*	FERTILIZER	MAINTENANCE CHEMICALS/RATE/TIMING ***	TYPE	% Organic Matter (OM)	pH	Cation Exchange Capacity (CEC)	WEATHER DATA** (Appendix I)
Dagmar, MT, **MT** Sheridan County, USA / 1997	Irrigation (50.8 mm)	46-0-0 (urea)	BRONNATE (bromoxynil + MCPA)	Loam	3.5	7.8	30.7	Dry weather conditions compare to the historical data
Velve, ND, **ND1** McHenry County, USA / 1997	No irrigation	18-46-0 (DAP) 46-0-0 (urea)	TILLER (fenoxaprop-p-ethyl + MCPA ester + 2, 4-D) Buctril (bromoxynil)	Loam	5.4	5.2	25.8	within historical data
Barnard, SD, **SD** Brown County, USA / 1997	No irrigation	18-46-0 (DAP) 46-0-0 (urea)	TILLER (fenoxaprop-p-ethyl + MCPA ester + 2, 4-D) + Rhonax (MCPA)	Loam	4	6	20.1	Dry weather conditions compare to the historical data
Barnwell, AB, **AB1** Taber County, Canada / 1997	Irrigation (236 mm)	51-0-0	Tralkoxydim, Bromoxynil, MCPA, Diquat	Clay loam	2.5	8	33.9	within historical data
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	No irrigation	none	Tralkoxydim, 2, 4-D, Glyphosate	Loam	9.8	7.5	48.6	within historical data
Minto, MB **MB1** Whitewater County, Canada / 1997	No irrigation	N, P, K	Tralkoxydim, Dichlorprop, 2, 4-D	Silt loam	5.3	7.8	25.8	within historical data
Boissevain, MB **MB2** Morton County, Canada / 1997	No irrigation	N, P	FORTRESS (Triallate, trifluralin), Tralkoxydim, MCPA	Silt loam	4.7	8.2	37.2	within historical data
Saskatoon, SK **SK1** Corman Park, Canada / 1997	No irrigation	none	Tralkoxydim, 2, 4-D	Loam	4.1	6.4	21.7	within historical data
Outlook, SK **SK2** Fertile Valley Canada / 1997	No irrigation	none	Tralkoxydim, 2, 4-D	Loam	3.9	6.2	20.5	within historical data

* Most sites experienced drier conditions than normal during early summer. One U.S. site (MT) reported poor crop stand due to the dry weather. Otherwise, temperatures for May-August were within historical range.

** Precipitation for growing crop period May-August was within historical data, except in MT and SD (about 50% less) and AB2 (about 45% more).

*** Plants were maintained using fertilizers and approved pesticide for each crop.

II. RESULTS

TABLE 1. Residue Data Summary from Supervised Field Trials - Wheat Grain

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analysed	PHI (days)	Residues florasulam equivalent (ppm) *
			Rate (g ai/ha)	No.	Total Rate (g ai/ha)	% gap			
Dagmar, MT, **MT** Sheridan County, USA / 1997	Durum - Rugby	EF-1343 + 0.2% Agral 90	10.14	1	10.14	200	Grain	57	< 0.005, <0.005
Velve, ND, **ND1** McHenry County, USA / 1997	Hard red - 2375	EF-1343 + 0.2% Agral 90	10.07	1	10.07	200	Grain	58	< 0.005, <0.005
Velva, ND, **ND2** Ward County, USA / 1997	Hard red - Grandin	EF-1343 + 0.2% Agral 90	9.92	1	9.92	200	Grain	57	< 0.005, <0.005
Barnard, SD, **SD** Brown County, USA / 1997	Soft white - Penewawa	EF-1343 + 0.2% Agral 90	10.04	1	10.04	200	Grain	48	< 0.005, <0.005
Barnwell, AB, **AB1** *Taber County, Canada* / 1997	Hard red - Makwa	EF-1343 + 0.2% Agral 90	10.2	1	10.2	200	Grain	60	< 0.005, <0.005
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	Hard red - Teal	EF-1343 + 0.2% Agral 90	9.93	1	9.93	200	Grain	58	< 0.005, <0.005
Red Deer, AB **AB3** Red Deer County, Canada /1997	Can. Prairie soft - Oslow	EF-1343 + 0.2% Agral 90	11.1	1	11.1	200	Grain	57	< 0.005, <0.005
Minto, MB **MB1** Whitewater County, Canada / 1997	Can. Prairie soft - Taber	EF-1343 + 0.2% Agral 90	10.26	1	10.26	200	Grain	55	< 0.005, <0.005
Boissevain, MB **MB2** Morton County, Canada / 1997	Can. Prairie soft - Taber	EF-1343 + 0.2% Agral 90	10.28	1	10.28	200	Grain	57	< 0.005, <0.005
Souris, MB **MB3** Glenwood County, Canada/ 1997	Durum -Sceptre	EF-1343 + 0.2% Agral 90	10.15	1	10.15	200	Grain	57	< 0.005, <0.005
Saskatoon, SK **SK1** Corman Park, Canada / 1997	Durum - Kyle	EF-1343 + 0.2% Agral 90	10.01	1	10.01	200	Grain	55	< 0.005, <0.005
Outlook, SK **SK2** Fertile Valley, Canada / 1997	Hard red - Teal	EF-1343 + 0.2% Agral 90	9.52	1	9.52	200	Grain	41	< 0.005, <0.005
Duck Lake, SK **SK3** Duck Lake, Canada / 1997	Durum - Kyle	EF-1343 + 0.2% Agral 90	10.41	1	10.41	200	Grain	54	< 0.005, <0.005

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analysed by immunoassay method.

TABLE 2. Residue Data Summary from Supervised Field Trials - Barley Grain

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analysed	PHI (days)	Residues florasulam equivalent (ppm)*
			Rate (g ai/ha)	No.	Total Rate (g ai/ha)	% gap			
Dagmar, MT, **MT** Sheridan County, USA / 1997	Stark, 2-row	EF-1343 + 0.2% Agral 90	9.98	1	9.98	200	Grain	57	< 0.005, <0.005
Velve, ND, **ND1** McHenry County, USA / 1997	Foster, 6-row	EF-1343 + 0.2% Agral 90	10.03	1	10.03	200	Grain	52	< 0.005, <0.005
Velva, ND, **ND2** Ward County, USA / 1997	Robust, 6-row	EF-1343 + 0.2% Agral 90	10.02	1	10.02	200	Grain	57	< 0.005, <0.005
Barnwell, AB, **AB1** Taber County, Canada / 1997	B1215, 2-row	EF-1343 + 0.2% Agral 90	9.86	1	9.86	200	Grain	60	< 0.005, <0.005
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	AC Lacombe, 6-row	EF-1343 + 0.2% Agral 90	10.05	1	10.05	200	Grain	47	< 0.005, <0.005
Minto, MB **MB1** Whitewater County, Canada / 1997	Excel, 6-row	EF-1343 + 0.2% Agral 90	10.19	1	10.19	200	Grain	56	< 0.005, <0.005
Boissevain, MB **MB2** Morton County, Canada / 1997	Bedford, 2-row	EF-1343 + 0.2% Agral 90	10.24	1	10.24	200	Grain	45	< 0.005, <0.005
Saskatoon, SK **SK1** Corman Park, Canada / 1997	Manely, 2-row	EF-1343 + 0.2% Agral 90	10.09	1	10.09	200	Grain	55	< 0.005, <0.005
Duck Lake, SK **SK2** Duck Lake, Canada / 1997	Stander, 6-row	EF-1343 + 0.2% Agral 90	10.34	1	10.34	200	Grain	54	< 0.005, <0.005

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analysed by immunoassay method.

TABLE 3. Residue Data Summary from Supervised Field Trials - Oat Grain

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analysed	PHI (days)	Residues florasulam equivalent * (ppm)
			Rate (g ai/ha)	No.	Total Rate (g ai/ha)	% gap			
Dagmar, MT, **MT** Sheridan County, USA / 1997	Dumont	EF-1343 + 0.2% Agral 90	10.09	1	10.09	200	Grain	57	< 0.005, <0.005
Velve, ND, **ND** McHenry County, USA / 1997	Valley	EF-1343 + 0.2% Agral 90	10.07	1	10.07	200	Grain	58	< 0.005, <0.005
Barnard, SD, **SD** Brown County, USA / 1997	Hytest	EF-1343 + 0.2% Agral 90	10.04	1	10.04	200	Grain	51	< 0.005, <0.005
Barnwell, AB, **AB1** Taber County, Canada / 1997	Mustang	EF-1343 + 0.2% Agral 90	10.73	1	10.73	200	Grain	54	< 0.005, <0.005
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	Cascade	EF-1343 + 0.2% Agral 90	9.94	1	9.94	200	Grain	58	< 0.005, <0.005
Minto, MB **MB1** Whitewater County, Canada / 1997	Robert	EF-1343 + 0.2% Agral 90	9.9	1	9.9	200	Grain	57	< 0.005, <0.005
Boissevain, MB **MB2** Morton County, Canada / 1997	Robert	EF-1343 + 0.2% Agral 90	10.13	1	10.13	200	Grain	57	< 0.005, <0.005
Saskatoon, SK **SK1** Corman Park, Canada / 1997	Derby	EF-1343 + 0.2% Agral 90	10.18	1	10.18	200	Grain	55	< 0.005, <0.005
Duck Lake, SK **SK2** Duck Lake, Canada / 1997	Derby	EF-1343 + 0.2% Agral 90	10.31	1	10.31	200	Grain	54	< 0.005, <0.005

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analysed by immunoassay method.

TABLE 4. Summary of Residue Decline Data on Wheat (forage, straw, hay, green immature plant and immature dry plant)

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analysed	PHI (days)	Residues of florasulam equivalent (ppm) *	Residues of florasulam equivalent (ppm) **
			Rate (g ai/ha)	No.	Total Rate (g ai/ha)	% gap				
Dagmar, MT, **MT** Sheridan County, USA / 1997	Durum - Rugby	EF-1343 + 0.2% Agral 90	10.14	1	10.14	200	Straw	57	< 0.025, <0.025	Not analysed
							Green Immature	7	0.073, 0.079	< 0.025, <0.025
							Green Immature	15	0.027, 0.032	Not analysed
							Dried Immature	7	0.189, 0.292	0.31, < 0.025
							Dried Immature	15	0.104, 0.061	< 0.025, <0.025
							Forage	0	1.87, 1.69	0.691, 0.587 0.519, 0.619
							Forage	7	0.115, 0.030	< 0.025, <0.025
							Forage	15	< 0.025, <0.025	Not analysed
							Forage	20	< 0.025, <0.025	Not analysed
							Forage	30	< 0.025, <0.025	Not analysed
							Forage	40	< 0.025, <0.025	Not analysed
Velve, ND, **ND1** McHenry County, USA / 1997	Hard red - 2375	EF-1343 + 0.2% Agral 90	10.07	1	10.07	200	Straw	58	< 0.025, <0.025	Not analysed
							Green Immature	3	0.031, 0.034	Not analysed
							Green Immature	7	< 0.025, <0.025	Not analysed
							Green Immature	10	< 0.025, <0.025	Not analysed
							Green Immature	15	< 0.025, <0.025	Not analysed
							Green Immature	30	< 0.025, <0.025	Not analysed
							Dried Immature	3	0.035, 0.042	Not analysed
							Dried Immature	7	< 0.025, 0.031	Not analysed
							Dried Immature	10	< 0.025, <0.025	Not analysed

							Dried Immature	15	<0.025, <0.025	Not analysed
							Dried Immature	30	< 0.025, <0.025	Not analysed
							Forage	0	1.21, 1.26	0.413, 0.434
							Forage	7	0.112, 0.141	<0.025, <0.025
							Forage	15	< 0.025, <0.025	Not analysed
							Forage	20	< 0.025, <0.025	Not analysed
							Forage	30	< 0.025, <0.025	Not analysed
							Forage	40	< 0.025, <0.025	Not analysed
Velva, ND. **ND2** Ward County, USA / 1997	Hard red - Grandin	EF-1343 + 0.2% Agral 90	9.92	1	9.92	200	Straw	57	< 0.025, <0.025	Not analysed
							Hay	7	0.162, 0.249	< 0.025, 0.027
							Hay	15	0.131, 0.097	<0.025, <0.025
							Hay	30	< 0.025, <0.025	Not analysed
							Forage	7	0.155, 0.155	< 0.025, <0.025
							Forage	15	< 0.025, 0.028	<0.025
							Forage	30	< 0.025, <0.025	Not analysed
Barnard, SD, **SD** Brown County, USA / 1997	Soft white - Penewawa	EF-1343 + 0.2% Agral 90	10.04	1	10.04	200	Straw	48	< 0.025, <0.025	Not analysed
							Hay	7	0.155, 0.141	< 0.025, <0.025
							Hay	15	< 0.025, 0.026	Not analysed
							Hay	30	< 0.025, <0.025	Not analysed
							Forage	7	< 0.025, <0.025	Not analysed
							Forage	15	< 0.025, <0.025	Not analysed
							Forage	30	< 0.025, <0.025	Not analysed
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	Hard red - Teal	EF-1343 + 0.2% Agral 90	9.93	1	9.93	200	Straw	58	< 0.025, <0.025	Not analysed
							Green Immature	3	< 0.025, 0.202	0.066
							Green Immature	7	0.046, 0.069	< 0.025

							Green Immature	10	0.065 , 0.042	< 0.025
							Green Immature	15	0.025, 0.033	Not analysed
							Green Immature	30	< 0.025, <0.025	Not analysed
							Green Immature	40	< 0.025, <0.025	Not analysed
							Dried Immature	3	0.726	0.435
							Dried Immature	7	0.209, 0.327	< 0.025, <0.025
							Dried Immature	10	0.148, 0.262	< 0.025, <0.025
							Dried Immature	15	0.099, 0.147	< 0.025, <0.025
							Dried Immature	30	< 0.025, 0.028	Not analysed
							Dried Immature	40	< 0.025, <0.025	
Minto, MB **MB1** Whitewater County, Canada / 1997	Can Prairie soft - Taber	EF-1343 + 0.2% Agral 90	10.26	1	10.26	200	Straw	55	< 0.025, <0.025	Not analysed
Saskatoon, SK **SK1** Corman Park, Canada / 1997	Durum - Kyle	EF-1343 + 0.2% Agral 90	10.01	1	10.01	200	Straw	55	< 0.025, <0.025	Not analysed

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analysed by immunoassay method.
** Residues of florasulam parent only. Samples were analysed by GC/MSD method.

TABLE 5. Summary of Residue Decline Data on Barley (straw, hay, immature green plant and immature dry plant)

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analysed	PHI (days)	Residues of florasulam *equivalent* (mg/kg) *	Residues of florasulam *equivalent* (mg/kg) **
			Rate (g ai/ha)	No.	Total Rate (g ai/ha)	% gap				
Dagmar, MT, MT Sheridan County, USA / 1997	Stark, 2-row	EF-1343 + 0.2% Agral 90	9.98	1	9.98	200	Straw	57	< 0.025, <0.025	Not analysed
							Green Immature	3	< 0.025, <0.025	Not analysed
							Green Immature	7	0.046, 0.072	< 0.025
							Green Immature	10	0.037, 0.032	Not analysed
							Green Immature	15	< 0.025, <0.025	Not analysed
							Green Immature	30	< 0.025, <0.025	Not analysed
							Green Immature	40	< 0.025, <0.025	Not analysed
							Dried Immature	3	0.181, 0.199	0.032, 0.028
							Dried Immature	7	0.174, 0.150	< 0.025, <0.025
							Dried Immature	10	0.095, 0.113	< 0.025, <0.025
							Dried Immature	15	0.056, 0.075	< 0.025, <0.025
							Dried Immature	30	< 0.025, <0.025	Not analysed
							Dried Immature	40	< 0.025, <0.025	Not analysed
Velve, ND, ND1 McHenry County, USA / 1997	Foster, 6-row	EF-1343 + 0.2% Agral 90	10.03	1	10.03	200	Straw	52	< 0.025, <0.025	Not analysed
							Green Immature	3	< 0.025, <0.025	Not analysed
							Green Immature	7	< 0.025, <0.025	Not analysed
							Green Immature	10	< 0.025, <0.025	Not analysed
							Green Immature	15	< 0.025, <0.025	Not analysed
							Green Immature	30	< 0.025, <0.025	Not analysed
							Dried Immature	3	0.042, 0.057	< 0.025, <0.025
							Dried Immature	7	0.053, 0.051	< 0.025, <0.025

							Dried Immature	10	0.030, 0.028	Not analysed
							Dried Immature	15	0.027, 0.030	Not analysed
							Dried Immature	30	< 0.025, <0.025	Not analysed
Velva, ND, ND2 Ward County, USA / 1997	Robust, 6-row	EF-1343 + 0.2% Agral 90	10.02	1	10.02	200	Straw	57	< 0.025, <0.025	Not analysed
							Hay	7	0.187, 0.244	< 0.025, <0.025
							Hay	15	0.083, 0.107	< 0.025, <0.025
							Hay	30	< 0.025, <0.025	Not analysed
Lacombe, AB, AB2 Lacombe County, Canada / 1997	AC Lacombe, 6-row	EF-1343 + 0.2% Agral 90	10.05	1	10.05	200	Straw	47	< 0.025, <0.025	Not analysed
							Green Immature	3	0.035, 0.038	0.027
							Green Immature	7	< 0.025, 0.040	Not analysed
							Green Immature	10	< 0.025, 0.028	Not analysed
							Green Immature	15	< 0.025, 0.030	Not analysed
							Green Immature	30	0.088, 0.081	< 0.025, <0.025
							Green Immature	40	< 0.025, <0.025	Not analysed
							Dried Immature	3	0.025, 0.154	< 0.025, 0.051
							Dried Immature	7	0.080, 0.069	< 0.025
							Dried Immature	10	0.074, 0.067	<0.025
							Dried Immature	15	0.026, 0.031	Not analysed
							Dried Immature	30	< 0.025, <0.025	Not analysed
							Dried Immature	40	< 0.025, <0.025	Not analysed
Minto, MB MB1 Whitewater County, Canada / 1997	Excel, 6-row	EF-1343 + 0.2% Agral 90	10.19	1	10.19	200	Straw	56	< 0.025, <0.025	Not analysed

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analysed by immunoassay method.
** Residues of florasulam parent only. Samples were analysed by GC/MSD method.

TABLE 6. Summary of Residue Decline Data on Oat (straw, hay, immature green plant and immature dry plant)

Location (city, province/ state)/ Year	Variety	Formulation	Application				Commodity Portion analysed	PHI (days)	Residues of florasulam equivalent (mg/kg) *	Residues of florasulam equivalent (mg/kg) **
			Rate (g ai/ha)	No.	Total Rate (g ai/ha)	% gap				
Dagmar, MT. MT Sheridan County, USA / 1997	Dumont	EF-1343 + 0.2% Agral 90	10.09	1	10.09	200	Straw	57	< 0.025, <0.025	Not analysed
							Green Immature	3	0.106, 0.075	0.039, < 0.025
							Green Immature	7	< 0.025, 0.059	< 0.025, <0.025
							Green Immature	10	< 0.025, <0.025	Not analysed
							Green Immature	15	< 0.025, <0.025	Not analysed
							Green Immature	30	< 0.025, <0.025	Not analysed
							Green Immature	40	< 0.025, <0.025	Not analysed
							Dried Immature	3	0.157, 0.107	not reported
							Dried Immature	7	0.135, 0.143	0.030, 0.033
							Dried Immature	10	0.067, 0.070	< 0.025, <0.025
							Dried Immature	15	< 0.025, 0.031	<0.025
							Dried Immature	30	< 0.025, <0.025	Not analysed
							Dried Immature	40	< 0.025, <0.025	Not analysed
							Forage	0	1.64, 1.7	0.630, 0.592, 0.514, 0.489
							Forage	7	0.106, 0.112	< 0.025, <0.025
							Forage	15	< 0.025, <0.025	Not analysed
							Forage	20	< 0.025, 0.028	Not analysed
							Forage	30	< 0.025, <0.025	Not analysed
							Forage	40	< 0.025, <0.025	Not analysed
Velve, ND, ND McHenry County, USA / 1997	Valley	EF-1343 + 0.2% Agral 90	10.07	1	10.07	200	Straw	58	< 0.025, <0.025	Not analysed
							Green Immature	3	< 0.025, <0.025	Not analysed

							Green Immature	7	< 0.025, <0.025	Not analysed
							Green Immature	10	< 0.025, <0.025	Not analysed
							Green Immature	15	< 0.025, <0.025	Not analysed
							Green Immature	30	< 0.025, <0.025	Not analysed
							Dried Immature	3	< 0.025, <0.025	Not analysed
							Dried Immature	7	< 0.025, <0.025	<0.025
							Dried Immature	10	< 0.025, <0.025	Not analysed
							Dried Immature	15	< 0.025, <0.025	Not analysed
							Dried Immature	30	< 0.025, <0.025	Not analysed
							Forage	0	0.905, 0.933	Not analysed
							Forage	7	0.132, 0.106	< 0.025, <0.025
							Forage	15	< 0.025, <0.025	Not analysed
							Forage	20	< 0.025, <0.025	Not analysed
							Forage	30	< 0.025, <0.025	Not analysed
							Forage	40	< 0.025, <0.025	Not analysed
Barnard, SD, **SD** Brown County, USA / 1997	Hytest	EF-1343 + 0.2% Agral 90	10.04	1	10.04	200	Straw	51	< 0.025, <0.025	Not analysed
							Hay	7	0.037, 0.041	< 0.025, <0.025
							Hay	15	< 0.025, <0.025	Not analysed
							Hay	30	< 0.025, <0.025	Not analysed
							Forage	7	0.093, 0.096	< 0.025, <0.025
							Forage	15	0.056, 0.048	< 0.025, <0.025
							Forage	30	< 0.025, <0.025	Not analysed
Lacombe, AB, **AB2** Lacombe County, Canada / 1997	Cascade	EF-1343 + 0.2% Agral 90	9.94	1	9.94	200	Straw	58	< 0.025, <0.025	Not analysed
							Green Immature	3	< 0.025, <0.025	Not analysed
							Green Immature	7	< 0.025, <0.025	Not analysed

							Green Immature	10	< 0.025, <0.025	Not analysed
							Green Immature	15	< 0.025, <0.025	Not analysed
							Green Immature	30	< 0.025, <0.025	Not analysed
							Green Immature	40	< 0.025, <0.025	Not analysed
							Dried Immature	3	0.147, 0.224	< 0.025, <0.025
							Dried Immature	7	< 0.025, <0.025	Not analysed
							Dried Immature	10	0.135, 0.143	< 0.025, <0.025
							Dried Immature	15	< 0.025, <0.025	Not analysed
							Dried Immature	30	< 0.025, <0.025	Not analysed
							Dried Immature	40	< 0.025, <0.025	Not analysed
Minto, MB MB1 Whitewater County, Canada / 1997	Robert	EF-1343 + 0.2% Agral 90	9.9	1	9.9	200	Straw	57	< 0.025, <0.025	Not analysed
Saskatoon, SK SK1 Corman Park, Canada / 1997	Derby	EF-1343 + 0.2% Agral 90	10.18	1	10.18	200	Straw	55	< 0.043, <0.039	Not analysed

* Residues of florasulam equivalent (florasulam parent, 4-hydroxyphenyl florasulam and its glucose conjugate). Samples were analysed by immunoassay method.
** Residues of florasulam parent only. Samples were analysed by GC/MSD method.

Comments:

EF-1343 SC formulation (52 g ai/L) is proposed for use in Canada on spring wheat, including Durum, spring barley and oats (applied in tank mixture only). The proposed label limits its use geographically to the Prairie Provinces and Peace River Region of British Columbia in Canada. The proposed postemergent application of EF-1343 SC at a rate of 5 g ai/ha is to be applied to spring wheat (including Durum), barley and oat from the 2-leaf stage up to and including the flag leaf extended stage. Addition of an adjuvant is required, specifically Agral 90 at 0.2% v/v. The treated crop is to be harvested after 60 days of application.

The residue field trials conducted for wheat, barley and oat were insufficient and did not represent all the major growing zones for these crops in Canada. The limited supervised crop field trials conducted in zones 7, 7A and 14 in Canada/USA were submitted for wheat, barley and oat. These residue trials indicated that residues in wheat, barley and oat grain collected at 41-60 days following a single foliar broadcast ground application of EF-1343 SC formulation, 10 g ai/ha of florasulam (with Agral 90 Adjuvant, 0.2% v/v), equivalent to 2x the proposed Canadian maximum season rate, at BBCH 37-55 growth stage, were less than limit of quantification (<0.01 ppm). The STMaR and STMdR for wheat, barley and oat grain and immature crop fractions (straw, hay, forage) were <0.005 ppm and <0.025 ppm, respectively.

The results from the residue decline studies for wheat, barley and oat (green and dried immature plant, straw and hay) conducted in zones 7, 7A and 14 in Canada/USA have shown that residues in these crop fractions collected at 0, 3, 7, 10, 15, 30 and 40 days following a single foliar broadcast ground application of EF-1343 SC formulation (52 g ai/L), approximately 10 g ai/ha of florasulam (with Agral 90 Adjuvant, 0.2% v/v), when plants were at BBCH 37-55 stage, equivalent to 2X the proposed Canadian maximum season rate, indicated rapid decline of florasulam residues. No residues were detected in any whole plant sample collected at/after 7 days after application. Therefore, grazing on wheat, barley and oat crop can be supported 7 days after application of EF-13443 SC.

Storage stability of florasulam has been demonstrated in wheat grain for 264 days, forage 378 days, straw for 313 days, hay for 194 days, immature green plant for 94 days and immature dry plants for 389 days. Residue samples for wheat, barley and oat grain were stored under similar conditions reported for the storage stability studies. The storage intervals for the residue samples were shorter than the storage stability demonstrated in the freezer test. Therefore, storage stability has no effect on the results of the residue studies. Sample chromatograms were provided for residue studies. The analytical procedure employed in the crop residue studies is the same as that reviewed in the analytical methodology. The chromatograms peaks were sharp and well defined with no interference peaks.

As the residue trials requirements were not met for a geographically restricted registration or a national registration, the petitioner must submit the results from additional residue trials. Since residues of florasulam in wheat, barley and oat was less than LOQ, a 25% reduction in residue trials is allowed. In the mine time, FREAS can recommend the promulgation of MRLs for wheat (0.01 ppm), barley (0.01 ppm) and oat (0.01 ppm) to cover residues of florasulam in these crops. The MRL on the RAC will cover potential residues in processed commodities. At this time, no MRL on livestock commodities will be recommended. Should the use pattern be modified in the future and this use pattern increase the dietary exposure of livestock, the agency will require sufficient studies on which to recommend residue limits in animal commodities.

III. CONCLUSION

The residue field trials conducted for wheat, barley and oat were insufficient and did not represent all the major growing zones for these crops in Canada. The limited residue data indicated that residues in wheat, barley and oat grain collected at 41-60 days following a single foliar broadcast ground application of EF-1343 SC formulation, 10 g ai/ha of florasulam (with Agral 90 Adjuvant, 0.2% v/v), equivalent to 2x the proposed Canadian maximum season rate, at BBCH 37-55 growth stage, were less than limit of quantification (<0.01 ppm). The STMaR and STMdR for wheat, barley and oat grain and immature crop fractions (straw, hay, forage) were <0.005 ppm and <0.025 ppm, respectively. This data supports an MRL of 0.01 ppm. No residues were detected in any whole plant sample collected at/after 7 days after application. Therefore, livestock grazing on wheat and barley crop can be supported 7 days after the last application of EF-13443 SC.

As the residue trials requirements were not met for a geographically restricted registration or a national registration, the petitioner must submit the results from additional residue trials. Since residues of florasulam in wheat, barley and oat was less than LOQ, a 25% reduction in residue trials is allowed. In the mine time, FREAS can recommend the promulgation of MRLs for wheat (0.01 ppm), barley (0.01 ppm) and oat (0.01 ppm) to cover residues of florasulam in these crops. The MRL on the RAC will cover potential residues in processed commodities.

IV. STUDY DEFICIENCIES

The residue field trials conducted for these crops were insufficient and did not represent all the major growing zones for wheat, barley and oat in Canada. According to the Residue Chemistry Guidelines (Regulatory Directive Dir98-02) for crops requiring eight or more field trials nationally, provincial registrations require multiple year field trial (Attachment II. Appendix V of Dir98-02). Multiple year data for provincial registration is not required if sufficient nationally representative data for the technical active ingredient is available. The petitioner has submitted residue field trials conducted over one growing season in zones common to both the USA and Canada. As the residue trials requirements were not met for a geographically restricted registration or a national registration, the petitioner must submit the results from additional residue trials. Since residue of florasulam in wheat, barley and oat was less than LOQ, a 25% reduction in residue trials is allowed. Provided that the results of these additional residue trials are consistent with the data previously reviewed (i.e., <LOQ of 0.01 ppm) the petitioner has the following options to address the deficiencies in the number of representative trials:

Option 1

NUMBER OF FIELD TRIALS BY CANADIAN/US GROWING REGION							
Crop	Residue Trials	Canadian/Canadian Equivalent US Growing Regions					Total Trials
		1	5	5A	5B	14	
Barley	Deficient		1		1	0	5
Oat	Deficient	1	1	1		0	

OR

Option 2

NUMBER OF FIELD TRIALS BY CANADIAN/US GROWING REGION							
Crop	Residue Trials	Canadian/Canadian Equivalent US Growing Regions					Total Trials
		5	5A	7	7A	14	
wheat	Deficient	1	0	0	0	2	11
Barley	Deficient	1	0	0	0	3	
Oat	Deficient	1	1	0	0	2	

In order to fulfill the data requirements, the registrant must demonstrate that the results in these additional trials are consistent with the results previously submitted. The analytical methods used in these trials must be identical to the methods used in the original trials and the sensitivity achieved (LOD and LOQ) must be equal to those reached in the original trials. In addition, the analysis of the samples must be carried out in the time frame supported by the freezer storage stability information.

Signatures:

Reviewed by: _____ _____
Ali Ismaily Date

Peer reviewed by: _____ _____
Henri Bietlot, Ph. D. Date

Section Head: _____ _____
Ariff Ally, Ph.D. Date

APPENDIX I:

Climatological Data:

PMRA Reviewer: Ali Ismaily, **Date** October 10, 2000

This DER was initially reviewed by Canada's PMRA and has been reviewed by HED. Conclusions herein agree with HED policy. In addition, this DER has been modified to include the submission MRID number.

Thurston Morton **23-May-2007**

STUDY TYPE: Nature of the Residue in Latating Goat *(Capra hircus)*; OPPTS 860.1300

TEST MATERIAL (PURITY): XDE-570 (99.7%)
[UL-aniline-^{14}C]XDE-570 (99.9%)
[triazolopyrimidine-9- ^{14}C]XDE-570 (99.7%)

SYNONYMS: **XDE-570** (Florasulam)
Common name : Florasulam (ISO-proposed)
IUPAC: **2', 6', 8-Trifluoro-5-methoxy-s-triazolo [1,5-c]pyrimidine-2-sulfonanilide**
CAS: **N-(2,6-diflurophenyl)-8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide**

CAS#: **145701-23-1**

MRID 46827902 D.E. Barnekow and M.A. Huskin, (1994), Nature of the Residues of [^{14}C]XDE-570 in Lactating Goats. North American Environmental chemical laboratory, DowElanco (9330 Zionsville Road, Indianapolis, Indiana 46268-1053) and ABC Laboratories, Inc. (7200E. ABC Lane, Columbia, MO 65202). DowElanco Laboratory Study No. MET94017, ABC Laboratories' Study No. 41502, December 23, 1994. Unpublished.

SPONSOR: DowElanco

EXECUTIVE SUMMARY:

In the lactating goat metabolism study, XDE-570, radiolabelled as either [UL-aniline-^{14}C]XDE-570, or [triazolopyrimidine-9- ^{14}C]XDE-570 was administered to two lactating goats (one per treatment) at a dose level of approximately 0.48 mg/kg bw/day. The dose was administered orally once daily in the morning for five consecutive days using a bolus gun and was equivalent to approximately11 ppm XDE-570 dietary burden at an average feed consumption of 2 kg/day. Samples of milk, urine and faeces were collected throughout the study. Approximately 24 hours after the final dose the animals were sacrificed and tissue including liver, kidneys, muscle, fat along with samples of blood, gastrointestinal contents and urine from the bladder were collected.

The results indicated that the total radioactive residues (TRRs) were almost comparable between two labelling positions for urine, faeces, muscle and fat. But a slight difference in TRR was noted for kidney, liver and milk. Recoveries of the administered dose in goat were 89% of for the aniline label (A-label) and 83% for the triazolopyrimidine label (TP-label). Majority of the radioactivity was excreted in the urine and faeces, accounting for a total of 99.8% of the recovered radioactivity. Total residues in tissues were very low. These residues in the tissues, milk and blood samples were below 0.1% of the administered dose. The highest concentration of residues in tissues were found in the kidneys, 0.069 ppm and 0.039 ppm from the A-label and TP-label experiments, respectively. The predominant radioactive component extracted from urine, milk, liver

and kidney samples was parent. One minor metabolite representing up to 1.5% of TRR was tentatively identified as 5-OH-florasulam in urine, liver and kidney samples.

Total radioactive residues in tissue (muscle, fat, skin and liver), milk and excreta samples were determined by combustion radioanalysis and/or liquid scintillation counter (LSC). Solvent extraction and subsequent fractionation were performed on the A and TP labelled milk, liver, kidney and urine samples. All aqueous and organic phase extractions were analysed by LSC. These extracts were also analysed by reverse phase HPLC to identify radioactive residues. The post solvent extracted material from milk, liver and kidney were analysed by combustion/LSC. Total radioactive residues in liver was low (0.033 ppm). Liver samples were further treated with a proteolytic enzyme to release and characterize bound residues. The proteolytic enzyme liberated 88.5% (0.029 ppm) and 85.1% (0.02 ppm) of the TRR in the A and TP treated liver tissue.

The parent compound, florasulam, is not likely to concentrate in fat, other tissues or milk as a result of feeding of treated feed. This study demonstrated low levels of radioactivity in edible tissues. These observations are supported by the low Log K_{ow} (1.00 at pH 4.00 and -1.22 at pH 7.0) which is an indication of a low potential for partition into organic solvents.

The solvent extraction efficiency tests indicated that recovery of fortified radioactivity for various fractions was excellent. The extraction efficiency of ethyl acetate was tested for milk, liver and kidney samples. Ethyl acetate extracted 88-104 % of radioactivity from spiked (0.015-0.38 ppm) samples of milk, liver and kidney. The Residue of Concern (ROC) based on the goat metabolism study may be defined as the parent compound, florasulam. The metabolism of florasulam in the rat, goat and laying hen were similar. Therefore, swine metabolism is not required. In all three species, the majority of the radioactivity was found unchanged with minor unknown metabolites at unquantifiable levels in the excreta. No significant cleavage of the sulfonanilide bridge was observed.

Based on the ruminant, laying hen and rat metabolism studies, the residue of concern (ROC) may be defined as the parent compound, florasulam.

These metabolism studies are classified acceptable and satisfy the guideline requirements for goat metabolism studies (Residue Chemistry Guidelines Dir98-02, Section 2).

COMPLIANCE:

Signed and dated GLP, Quality Assurance and no Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

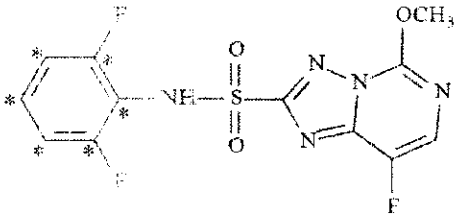
MATERIALS:

1. **Test Compound:**

[UL-aniline-^{14}C]XDE-570 ["A" labelled compound]
Radiochemical purity: 99.9% [determined by HPLC/LSC]
Specific activity: 152 µCi/mg
4.41 x 10^4 dpm/µg

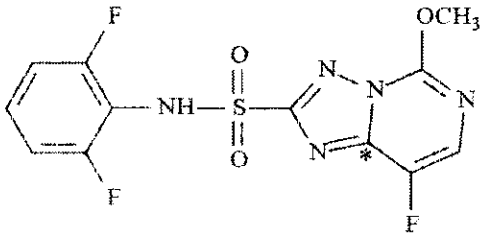
[9-triazolopyrimidine-^{14}C]DXE-570 ["TP" labelled compound]
Radiochemical purity: 99.7% [determined by HPLC/LSC]
Specific activity: 67.4 µCi/mg
4.36 x 10^4 dpm/µg

Nonradioactive DXE-570
Chemical purity: 99.7% (supplied by sponsor)



[UL-aniline-^{14}C]XDE-570

"A" label



[Triazolopyrimidine-9- ^{14}C]XDE-570

"TP" label

2. **Test animals:**

Species:	Three goats; physiological state - lactating non-pregnant *Capra hircus*
Strain/breed:	mix breed
Age:	≥ one year
Gender:	female
Weight at study initiation:	control (40 kg), "A" label (53 kg), "TP" label (51 kg)
Health status:	good health
Housing/holding areas:	goats were kept in individual elevated metabolism stalls.
Diet:	goats were fed twice daily for a total of 2 kg feed per day. The diet consists of dairy grain and alfalfa (0.60 kg alfalfa + 0.40 kg grain).
Water:	fresh water was provided *ad libitum*.
Acclimation period:	Test goats were acclimatised to conditions for at least 7 days.

During acclimation, the goats were observed for feed consumption, milk production, health

and behaviour.

Predosing: None.

METHODS:

1. **Dosing regime:**

Oral:

Level of administered dose:	0.42 mg/kg bw/day for aniline label 0.44 mg/kg bw/day for TP label
Food Consumption:	2 kg/day
Residue Intake in Diet:	11.2 ppm and 11.3 ppm
Vehicle:	capsule, using a stainless steel bolus gun.
Timing:	once daily in the morning between 10:00-10:15 a.m.
Duration:	5 consecutive days.

Dermal:

Formulation:	None
Number of treatments:	None
Application level:	N/A
Type of treatment:	N/A

Water (aquaculture):

Formulation:	None
Number of treatments:	None
Application level:	N/A
Type of treatment:	N/A

2. **Sample collection:**

Milk:

Milk was collected twice daily. A comparison of average milk production during normal production, during acclimation and during the dosing period are summarized below.

Animal	Milk Production Acclimation (kg)	Milk Production Dosing (kg)
Control	1.77	1.63
A label	1.25	1.20
TP label	1.31	1.0

The average values reported for milk production indicated that milk production was not affected by dosing with XDE-570.

Urine, faeces and cage wash: collected each morning daily.

Interval from last dose to sacrifice: 24 hours, sacrificed by electrocution.

Tissues harvested and analysed:

Blood, omental fat, perirenal fat, kidney, liver, muscle (*longissimus dorsi*, *semimembranosus* and triceps) were collected and analysed. Gall bladder contents and entire gastrointestinal (GI) tract with contents (divided into upper and lower GI tract at the pyloris) were collected , but not processed or analysed. The tissues that were analysed were collected into plastic bags, weight, cut into small pieces and immediately frozen in liquid nitrogen pending preparation for analysis. Only representative amounts of blood, muscle and fat were collected and their estimated total weight were calculated for each goat.

3. Quantification of Total Radioactive Residues (TRRs):

Total radioactive residues in tissue (muscle, fat, skin and liver), milk and excreta samples were determined by combustion radioanalysis and/or liquid scintillation counter (LSC). The radiocarbon in the samples was combusted to ^{14}C-carbon dioxide and trapped in an appropriate solvent along with scintillation fluid and quantitated by LSC. The performance of the oxidizer was determined by ^{14}C-benzoic acid standard. Minimum detectable amount (MDA) and minimum quantifiable limit (MQL) were determined for each set of samples by analysing control samples with each set of samples of tissue, milk or excreta.

4. *Extraction and Hydrolysis of Radioactive Residues (TRRs):*

Solvent extraction and subsequent fractionation were performed on the A and TP labelled samples of milk, liver, kidney and urine. Whole milk sample were initially treated with acetone to denature and remove protein. The protein pellet was lyophilized and the ^{14}C activity was quantified by combustion/LSC. The acetone was evaporated of aqueous fraction which was then defatted using hexane, acidified and extracted/partitioned with ethyl acetate resulting in organosoluble and aqueous fractions. The ethyl acetate organic fraction of the A and TP labelled milk was concentrated to dryness and the residue resolubilized in acetonitrile:water (95:5) solution. Radioactive residues in ethyl acetate organic fraction were analysed by reverse phase HPLC and normal phase TLC.

Liver and kidney samples were initially homogenized and extracted three times with acetonitrile:water (80:20). This extraction released most of the radioactivity present in these samples. The post solvent extracted tissue pellet was lyophilized and the ^{14}C activity was quantified by combustion/LSC. The acetonitrile was evaporated and the remaining aqueous fraction was then defatted using hexane, acidified and extracted/partitioned with ethyl acetate resulting in organosoluble and aqueous fractions. The ethyl acetate organic fraction of the A and TP labelled liver and kidney samples was concentrated to dryness and the residue resolubilized in acetonitrile:water (95:5) solution. Radioactive residues in ethyl acetate organic fraction were analysed by reverse phase HPLC and normal phase TLC. The extraction efficiency and stability of the parent compound was evaluated by using fortified control samples.

The lyophilized post solvent extracted Liver pellet samples were further treated with a protease digestion to release and characterize bound residues from the tissue. The lyophilized extracted pellet was mixed with protease, incubated at 37 °C for 22 hours. The mixture was filtered and the ^{14}C activity was quantified with LSC analysis. The filtrate was treated with acetone to precipitate solubilized proteins. The protein pellet was lyophilized and the ^{14}C activity was quantified by combustion/LSC. The acetone was evaporated of aqueous fraction which was then defatted using

hexane, acidified and extracted/partitioned with ethyl acetate resulting in organosoluble and aqueous fractions. The ethyl acetate organic fraction of the A and TP labelled milk was concentrated to dryness and the residue resolubilized in acetonitrile. Radioactive residues in these samples were analysed by LSC analysis.

Urine samples were acidified and extracted/partitioned with ethyl acetate. The ^{14}C activity in ethyl acetate fraction was quantified by LSC. The ethyl acetate organic fraction of the A and TP labelled urine samples was concentrated to dryness and the residue resolubilized in HPLC grade acetonitrile. These samples were analysed by reverse phase HPLC and normal phase TLC.

5. **Characterization and Identification of Residues**

All aqueous and organic phase extractions were analysed by LSC. The post solvent extracted material from milk, liver and kidney were analysed by combustion/LSC. These extracts were also analysed by reverse phase HPLC to identify radioactive residues. HPLC analysis were performed using C_{18} analytical column, an ultraviolet detector (UV) and gradient mobile phase of acetonitrile and water both with 1% acetic acid. The fortified control and treated extracts were analysed by HPLC and TLC. Reference standards were used to compare the retention times with the residues present in samples. The identity of compounds was confirmed by TLC analysis of the radioactive residues compared with the standards. TLC analysis were performed under normal phase conditions using silica gel plates developed in lined chambers with hexane-acetone (50:50). TLC plates bearing ^{14}C-compounds were scanned to determine the location and distribution of the ^{14}C-compounds.

II. RESULTS

1. Total Radioactive Residues (TRRs):

TABLE 1. Total Radioactive Residues (TRRs) of ^{14}C phenyl and ^{14}C TP labelled XDE-570 in Milk, Tissue and Excreta

Matrix	^{14}C phenyl- XDE-570 ("A" label)		^{14}C TP-XDE-570 ("TP" label)	
	ppm	% administered Dose	ppm	% administered Dose
Kidney	0.069	0.010	0.039	0.007
Liver	0.033	0.028	0.023	0.023
Milk	0.016[a]	0.052	0.033[a]	0.085
Muscle	0.0016	0.025	0.0009	0.015
Fat	0.0016	0.008	0.0017	0.009
Blood	0.007	0.014	0.0053	0.011
Total Tissue		0.137		0.150
Urine and cage wash	5.92[b]	72.6	4.46[b]	70.9
Faeces	2.65[b]	15.8	2.14[b]	12.1
Total excreta		88.4		83.0
Total Recovery		88.5		83.2

[a] residue from composite of aliquots of morning collection during 5 day study
[b] maximum residue level during 5 day of dosing

Comments:

The results indicated that the total radioactive residues (TRRs) were almost comparable between two labelling positions for urine, faeces, muscle and fat. But a slight difference in TRR was noted for kidney, liver and milk. Recoveries of the administered dose in goat were 89% of for the aniline label (A-label) and 83% for the triazolopyrimidine label (TP-label). Majority of the radioactivity was excreted in the urine and faeces, accounting for a total of 99.8% of the recovered radioactivity. Total residues in tissues were very low (up to 0.15 % of the administered dose). These residues in the tissues, milk and blood samples were below 0.1% of the applied dose. The highest concentration of residues in tissues were found in the kidneys, 0.069 ppm and 0.039 ppm in A-label and TP-label, respectively. The concentration of TRR in other tissues for A-label and TP-label were as follows: liver (0.033 ppm and 0.023 ppm); muscle (0.0016 ppm and 0.0009 ppm); fat (0.0016 ppm and 0.0017 ppm); blood (0.007 ppm and 0.0053 ppm). The residues from composite sample of morning collection during 5 day study were 0.016 ppm and 0.033 ppm in A-label and TP-label, respectively.

The parent compound, florasulam, is not likely to bioaccumulate in fat, other tissues and milk as a result of feeding of treated feed. This study demonstrated low levels of radioactivity in edible tissues. These observations are supported by the low Log K_{ow} (1.00 at pH 4.00 and -1.22 at pH 7.0) which is an indication of a low potential for partition into organic solvents.

2. Quantitative Distribution of Radioactive Residues:

TABLE 2. Quatitative Distribution of ^{14}C-Residues in Urine, Milk, Liver and Milk when Dosed with ^{14}C phenyl and ^{14}C TP labelled XDE-570

Tissues	Urine		Milk		Liver		Kidney	
Labelling group	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP
Total Radioactive Residues (TRRs)								
Total Radioactive Residues *	100 % TRR (5.92 ppm)	100 % TRR (4.46 ppm)	100 % TRR (0.016 ppm)	100 % TRR (0.033 ppm)	100 % TRR (0.033 ppm)	100 % TRR (0.023 ppm)	100 % TRR (0.069 ppm)	100 % TRR (0.039 ppm)
Total Extractable Radioactive Residues - % TRR (ppm)								
Acetone phase	Not performed		97.7 (0.016)	95.6 (0.031)	na	na	na	na
Acetonitrile/water phase			Not performed		23.2 (0.008)	22.4 (0.005)	104.4 (0.072)	104.2 (0.040)
Fractionation of Radioactive Residues - % TRR (ppm)								
Hexane phase	Not performed		< MDA (0.0001)	< MDA (0.0001)	< MQA (0.0009)	< MDA (0.0002)	< MDA (0.0016)	< MDA (0.0016)
EtoAc partition phase**	97.6 (5.78)	97.5 (4.35)	89.4 (0.015)	87.6 (0.028)	18.6 (0.006)	18.5 (0.004)	98.2 (0.068)	101.1 (0.039)
Aqueous soluble phase	-	-	2.4 (0.0004)	3.4 (0.0011)	2.8 (0.0009)	3.0 (0.0007)	1.7 (0.001)	1.4 (0.001)
Unextracted	2.4 (0.14)	2.5 (0.11)	3.8 (0.0006)	5.9 (0.0019)	82.7 (0.027)	89 (0.02)	2.2 (0.002)	2.2 (0.001)
Protease Digestion/Fractionation of Radioactive Residues - % TRR (ppm)								
Hexane phase	Not performed				<MDA (0.001)	<MDA (0.0008)	Not performed	
EtoAc partition phase					8.6 (0.0028)	8.6 (0.002)		
Aqueous soluble phase					32.2 (0.011)	45.7 (0.011)		
Unextracted					43.1 (0.014)	32.5 (0.0075)		
Identification of Radioactive Residues - % TRR (ppm)								
Parent Compound (XDE -570)	96.1 (4.31)	96.6 (5.69)	89.4 (0.015)	87.6 (0.028)	15.2 (0.005)	15.3 (0.0035)	95.8 (0.066)	98.3 (0.038)
Unidentified Metabolite ***	0.9	<MQL	-	-	1.0	1.0	1.5	1.5
Unidentified Metabolite	<MQL	<MQL	-	-	<MQL	-	0.7	<MQL
Unidentified Metabolite	<MQL	<MQL	-	-	<MQL	-	<MQL	<MQL
Unidentified Metabolite	-	-	-	-	<MQL	-	-	-
Distribution of Radioactive Residues - %TRR								
Total Extactable	97.6	97.5	91.8	90.0	62.2	75.8	99.9	102.5
Total Identified	96.1	96.6	89.4	87.6	15.2	15.3	95.8	98.3
Total Charectevized	1.4	0.9	2.4	2.4	47.1	60.5	4.1	4.2
Total Unextractable	2.4	2.5	3.8	5.9	43.1	32.5	2.2	2.2
TOTAL	100	100	95.6	95 9	105.3	108.3	102.1	104.7

* Analysed by combustion/LSC
** Fraction used for TLC and HPLC analysis.
*** Tentatively identified as 5-OH-florasulam
MDA Minimum detectable amount for each sample
MQL Minimum quantifiable limit for each sample
- Not detected

Comments:

Solvent extraction and subsequent fractionation were performed on the A and TP labelled samples of urine, milk, liver and kidney. The radioactive residues from acidified urine samples were extracted with ethyl acetate which released 97.6% (5.78 ppm) and 97.5% (4.35 ppm) of TRR from A and TP treated urine samples. The predominant radioactive component, representing 96% TRR in extracted residues from urine samples was parent, florasulam.

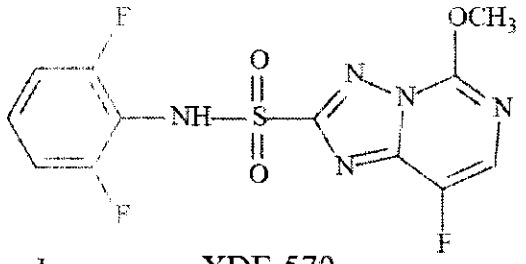
Majority of radioactivity in milk was extracted in ethyl acetate fraction. Small portions of radioactivity was soluble in hexane and aqueous phases. About 5.9% of TRR were unextractable from milk solids. The predominant radioactive component, representing >87 % TRR in extracted residues from milk samples was parent.

Liver sample were initially extracted with acetonitrile:water (80:20). The acetonitrile:water extracted only 23.2% (0.008 ppm) and 22.4% (0.005 ppm) of the TRR in A and TP treated liver samples. Further characterization of residues extracted in acetonitrile:water phase were achieved with hexane and ethyl acetate. The hexane extract of the aqueous phase contain less than MQA (0.0009 ppm) and less than MDA (0.0002 ppm) of the TRR for A and TP treated liver, respectively. The aqueous fraction after ethyl acetate fractionation represented 2.8% (0.0009 ppm) and 3% (0.0007 ppm) of the TRR for the A and TP treated liver. The ethyl acetate fractions represented 18.6% (0.006 ppm) and 18.5% (0.0043 ppm) of the TRR for A and TP treated liver. The predominant radioactive component, representing >15% TRR in extracted residues from liver samples was parent. Liver samples were further treated with a protease digestion to release and characterize bound residues from the tissue. The hexane extract of the aqueous phase contain less than MDA (0.0010 ppm) and less than MDA (0.0008 ppm) of the TRR for A and TP treated liver, respectively. The aqueous fraction after ethyl acetate fractionation represented 32.2% (0.011 ppm) and 45.7% (0.011 ppm) of the TRR for the A and TP treated liver. The ethyl acetate fractions represented 8.6% (0.0028 ppm) and 8.6% (0.002 ppm) of the TRR for A and TP treated liver. In liver tissue, up to 43% of TRR (0.014 ppm) remained unextractable. None of these fractions were analysed further.

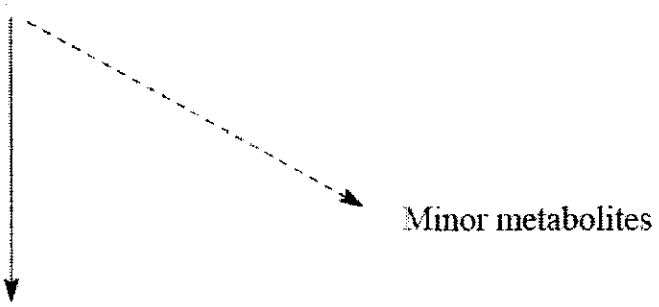
Kidney sample were initially extracted with acetonitrile:water (80:20). The acetonitrile:water extracted 104% (0.07 ppm) and 22.4% (0.04 ppm) of the TRR in A and TP treated liver samples. Further characterization of residues extracted in acetonitrile:water phase were achieved with hexane and ethyl acetate. The hexane extract of the aqueous phase contain less than MDA (0.0016 ppm) of TRR for both A and TP treated kidney, respectively. The aqueous fraction after ethyl acetate fractionation represented 1.7% (0.001 ppm) and 1.4% (0.001 ppm) of the TRR for the A and TP treated kidney. The ethyl acetate fractions represented 98.2% (0.068 ppm) and 101% (0.039 ppm) of the TRR for A and TP treated kidney. The predominant radioactive component, representing > 96% TRR in extracted residues from kidney samples was parent.

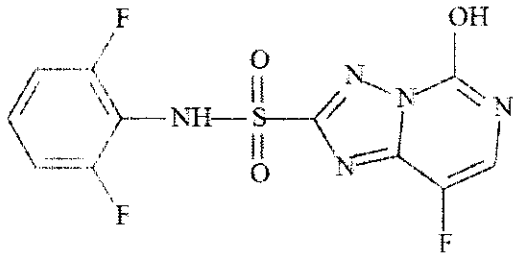
The recovery of the radioactivity for various fractions was excellent. The recovery of radioactivity added to the control milk following extraction was 92.3% in the ethyl acetate fraction and the concentration recovery of ethyl acetate fraction was 104%. The liver ethyl acetate fractions had concentration recoveries ranging from 88.5 to 88.8%. The kidney ethyl acetate fractions had concentration recovery of 103%.

Figure 1. Proposed Metabolic Profile of XDE-570 in Lactating Goat



I XDE-570





II 5-OH-XDE-570

Identification of Metabolites

Roman Numeral Identification	Common Name/Code	Chemical Name
I	XDE-570	N-(2,6-diflurophenyl)-8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide
II	5-OH-XDE-570	N-(2,6-diflurophenyl)-8-fluoro-5-hydroxyl(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide

Comments:

Most of the parent compound is eliminated by goat unchanged with minor unknown metabolites at unquantifiable levels. No significant cleavage of the sulfonanilide bridge occurred in the metabolism of florasulam in goat.

III. STORAGE STABILITY

All samples and extracts were stored frozen at approximately -20 ^{0}C during the study. All tissue and milk samples were prepared and characterized within 27 days after sacrifice. The urine samples were analysed within 51 days after sacrifice. Therefore, no storage stability tests were necessary for samples analysed in goat metabolism study.

IV. CONCLUSIONS

Majority of the administered florasulam (> 83% TRR) is excreted unchanged in urine and faeces. Residue of florasulam in tissues and milk samples was low with only a small portion of the recovered radioactivity (< 0.2% TRR) found in tissues and milk. The highest concentration was found in kidney at 0.069 ppm (0.01% TRR) of the administered dose. The major metabolite in milk and tissue was parent. In kidney, the parent accounting for > 92% of the isolated radioactivity from both phenyl and TP label florasulam. The predominant radioactive compnent, representing 15% of TRR in extracted resiues from liver samples was parent. Liver samples were further treated with a proteolytic enzyme to release and characterize bound residues. The proteolytic enzyme liberated 88.5% (0.029 ppm) and 85.1% (0.02 ppm) of the TRR in the A and TP treated liver tissue. In liver tissue, up to 43% of TRR (0.014 ppm) remained unextracted. The available methods clearly identified presence of parent compound in samples. One minor metabolite representing up to 1.5% of TRR was tentatively identified as 5-OH-florasulam in urine, liver and kidney samples. The very low residues in milk and other tissues with a major excretion of the parent compound indicated that florasulm only slightly metabolised in goat. No significant cleavage of the sulfonanilide bridge occurred (Figure 1).

Based on the data reviewed, the Residue of concern (ROC) in goat is defined as parent compound, florasulam.

VI. DEFINITION OF THE RESIDUE OF CONCERN (ROC)

The Residue of Concern (ROC) based on the goat metabolism study may be defined as the parent compound, florasulam.

VII. FINAL SUMMARY

In the lactating goat metabolism study, XDE-570, radiolabelled as either [UL-aniline-^{14}C]XDE-570, or [triazolopyrimidine-9- ^{14}C]XDE-570 was administered to two lactating goats (one per treatment) at a dose level of approximately 0.48 mg/kg bw/day. The dose was administered orally once daily in the morning for five consecutive days using a bolus gun and was equivalent to approximately11 ppm XDE-570 dietary burden at an average feed consumption of 2 kg/day. Samples of milk, urine and faeces were collected throughout the study. Approximately 24 hours after the final dose the animals were sacrificed and tissue including liver, kidneys, muscle, fat along with samples of blood, gastrointestinal contents and urine from the bladder were collected.

The results indicated that the total radioactive residues (TRRs) were almost comparable between two labelling positions for urine, faeces, muscle and fat. But a slight difference in TRR was noted for kidney, liver and milk. Recoveries of the administered dose in goat were 89% of for the aniline label (A-label) and 83% for the triazolopyrimidine label (TP-label). Majority of the radioactivity was excreted in the urine and faeces, accounting for a total of 99.8% of the recovered radioactivity. Total residues in tissues were very low. These residues in the tissues, milk and blood samples were below 0.1% of the administered dose. The highest concentration of residues in tissues were found in the kidneys, 0.069 ppm and 0.039 ppm from the A-label and TP-label experiments, respectively. The predominant radioactive component extracted from urine, milk, liver and kidney samples was parent. One minor metabolite representing up to 1.5% of TRR was tentatively identified as 5-OH-florasulam in urine, liver and kidney samples.

The parent compound, florasulam, is not likely to concentrate in fat, other tissues or milk as a result of feeding of treated feed. This study demonstrated low levels of radioactivity in edible tissues. These observations are supported by the low Log K_{ow} (1.00 at pH 4.00 and -1.22 at pH 7.0) which is an indication of a low potential for partition into organic solvents.

Total radioactive residues in tissue (muscle, fat, skin and liver), milk and excreta samples were determined by combustion radioanalysis and/or liquid scintillation counter (LSC). Solvent extraction and subsequent fractionation were performed on the A and TP labelled milk, liver, kidney and urine samples. All aqueous and organic phase extractions were analysed by LSC. These extracts were also analysed by reverse phase HPLC to identify radioactive residues. The post solvent extracted material from milk, liver and kidney were analysed by combustion/LSC. Total radioactive residues in liver was low (0.033 ppm). Liver samples were further treated with a proteolytic enzyme to release and characterize bound residues. The proteolytic enzyme liberated 88.5% (0.029 ppm) and 85.1% (0.02 ppm) of the TRR in the A and TP treated liver tissue. In liver tissue, up to 43% of TRR (0.014 ppm) remained unextractable.

The accountability of the radioactivity for various fractions was excellent. The recovery of radioactivity added to the control milk following extraction was 92.3% in the ethyl acetate fraction and the concentration recovery of ethyl acetate fraction was 104%. The liver ethyl acetate fractions had concentration recoveries ranging from 88.5 to 88.8%. The kidney ethyl acetate fractions had concentration recovery of 103%.

The Residue of Concern (ROC) based on the goat metabolism study may be defined as the parent compound, florasulam. The metabolism of florasulam in the rat, goat and laying hen were similar. Therefore, swine metabolism is not required. In all three species, the majority of the radioactivity was found unchanged with minor unknown metabolites at unquantifiable levels in excreta. No significant cleavage of the sulfonanilide bridge was observed.

The parent compound, florasulam, should be used for the ROC definition, for MRL setting and for the dietary risk assessment (DRA) purposes.

VIII. STUDY DEFICIENCIES

No deficiencies were identified in the goat metabolism study.

Signatures:

Reviewed by:

Ali Ismaily
Evaluation Officer
FREAS

Date

Peer Reviewed by:

Henri Bietlot, Ph. D.
Evaluation Officer
FREAS

Date

Approved by:

Ariff Ally, Ph. D.
Section Head
FREAS

Date

PMRA Reviewer: Ali Ismaily, **Date** September 27, 2000

This DER was initially reviewed by Canada's PMRA and has been reviewed by HED. Conclusions herein agree with HED policy. In addition, this DER has been modified to include the submission MRID number.

Thurston Morton **23-May-2007**

STUDY TYPE: Confined Accumulation in Rotational Crops - spring wheat (small grain), cabbage (leafy vegetable), carrots (root crop) and sunflowers (seed crop) ; OPPTS 860.1850

TEST MATERIAL (PURITY): [UL-phenyl-^{14}C]XDE-570 (> 97%)
[9- triaz olopyrimidine-^{14}C]XDE-570 (> 97%)

SYNONYMS: XDE-570 (Florasulam)

Common name : Florasulam (ISO-proposed)
IUPAC: 2', 6', 8-Trifluoro-5-methoxy-s-triazolo [1,5-c]pyrimidine-2-sulfonanilide
CAS: N-(2,6-diflurophenyl)-8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide

CAS#: 145701-23-1

MRID 46808208 MacDonald, A. M. G. (1997) The Uptake of XDE-570 into Four Succeeding Crops. DowElanco Europe, Letcombe Laboratory, Letcombe Regis, Oxon, OX12 9JT, UK. Laboratory Report Number: GHE-P-4889, Protocol Number: 7U, Study Completion Date December 1, 1997. Unpublished

SPONSOR: DowElanco

EXECUTIVE SUMMARY:

In the confined crop rotation study, XDE-570 (florasulam), > 97% a.i., E-1343 Suspension Concentrate labelled either as the [UL-phenyl-^{14}C]XDE-570 or the [9-triazolopyrimidine-^{14}C]XDE-570 was applied to sandy loam soil at an application rate of 7.5 g ai/ha (1.5X the maximum proposed postemergent application rate). Spring wheat, sunflower, cabbage and carrots were planted at 30 days after treatment (DAT) of soil.

Spring wheat, sunflowers, cabbage and carrots were harvested at maturity i.e., 168 DAT (spring wheat and sunflowers) 195 DAT (cabbage) and 156 DAT (carrots). Each crop was separated into fractions as spring wheat (ears and straw), sunflower (heads and stems), cabbage (shoots) and carrot (leaves and roots). The samples of crop fractions were subjected to three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash). Each wash was analysed to determine total ^{14}C-residues (TRRs) using combustion/liquid scintillation counting. None of the fraction from rotational crops had TRRs greater than 0.01 ppm . Therefore, no further attempt was made to profile TRRs.

Because levels of TRRs in the rotational crops were low (≤ 0.01 ppm), no parent and its metabolite was identified. Therefore, the confined crop rotation study supports the definition of the residue of concern (ROC) of parent only as defined in the plant and animal metabolism studies.

In addition, the soil metabolism study, reviewed by EAD, indicated that the primary transformation product was 5-OH-XDE-570. The sorption of both XDE-570 and 5-OH-XDE-570 increased with time indicating that the remaining XDE-570 in the soil is less bioavailable and less mobile. The concentration of XDE-570 and 5-OH-XDE-570 for potential uptake from soil is very low. At 30 DAT, residues of XDE-570 and 5-OH-XDE-570 in soil was low, ≤ 0.008 ppm. Therefore, it is expected that any residues translocation from the soil to the rotational crops would also be low.

Based on the results of the confined crop rotational study, field rotational crop studies are not required, and a 30-day plant back interval (PBI) can be supported for all crops. The label has a plant back interval greater than of 30 days for barley, canola, forage grasses, oats, peas, rye and wheat.

This confined crop rotation study is classified acceptable and does satisfy the guideline requirement for a crop rotation study (Residue Chemistry Guidelines Dir98-02, Section 10).

COMPLIANCE:

Signed and dated GLP and Quality Assurance were provided. No Data Confidentiality statements were provided. The study author stated that this study was conducted to meet the proposals submitted to the EC regarding Annex II and III of EC Directive 91/414/EEC; and the study reflects the current (AUG 1997) guidance for rotational crop studies as described in Lundehn (7524/VI/95 EN - rev 1).

I. MATERIALS AND METHODS

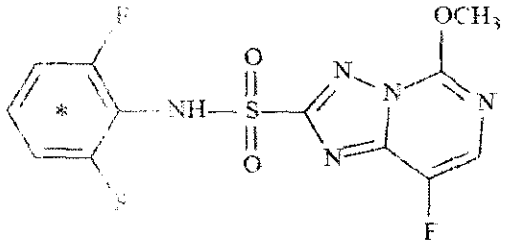
MATERIALS:

1. **Test Compound:**

[UL-phenyl-^{14}C]DXE-570 : ["phenyl" labelled compound]
Radiochemical purity: 97% and 98 % [determined by HPLC and TLC]
Specific activity: 152 µCi/mg
337400 dpm/µg

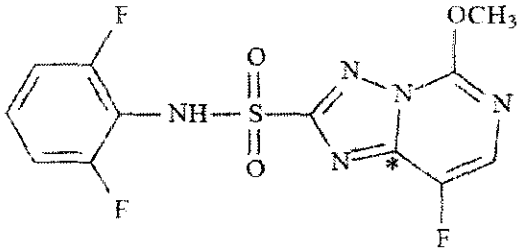
[9-triazolopyrimidine-^{14}C]DXE-570: ["TP" labelled compound]
Radiochemical purity: 97% and 98 % [determined by HPLC and TLC]
Specific activity: 155 µCi/mg
344100 dpm/µg

Nonradioactive DXE-570



[UL-phenyl-^{14}C]XDE-570

"^{14}C-Phenyl" label



[9- triazolopyrimidine-^{14}C]XDE-570

"^{14}C-TP" label

2. **Test Soil -1:** (used for spring wheat, sunflowers and cabbage)
Soil characteristics
Type: sandy loam (UK classification)
% Organic Matter (OM): 1.4
pH: in water (5.6), in 1M KCl (4.9)
Cation Exchange Capacity (CEC): (13.7)

Test Soil -2: (used for spring wheat, sunflowers and cabbage)
Soil characteristics
Type: sandy loam (UK classification)
% Organic Matter (OM): 1.1
pH: in water (7.7), in 1M KCl (7.6)
Cation Exchange Capacity (CEC): (16.9)
No information on the soil used for carrots was provided.

Treatments prior to planting (i.e., fertilizers, maintenance pesticides):

The four succeeding crops (carrots, sunflowers, cabbage and spring wheat) were grown in tubs and pots at an appropriate depth and density 30 days after applications of ^{14}C-DXE-570 formulation. The plots were prepared with sandy loam soil which was raked to simulate minimum tillage. Aphox (Primicarb) as an aphicicide, and (Dursban) chlorpyrifos as an insecticide to protect spring wheat, sunflower and cabbage crops during the study period. Vitex was used as fertilizer. Liquinure was used as fertilizer for carrot.

Subdrainage:

Tubs containing rotational crops were placed in the lysimeter complex. It is likely that the lysimeter system was set up with trays etc. to collect drainage of radioactive waste. A similar test system was reported in the plant metabolism study conducted by the same laboratory.

Rate of application:

The rate of preplant application on soil was 7.5 g ai/ha compare to the proposed maximum Canadian foliar application rate of 5 g ai/ha.

3. **Test plants:**

Species/variety::

Spring wheat *cv* Alexandria. Twelve seeds were sown per tub at depth of *ca* 2.5 cm.
Cabbage *cv* Winter Green. Eight seeds were sown per tub at a depth of *ca* 1.3 cm.
Sunflowers *cv* Sunspot. Eleven seeds were sown per tub at a depth of *ca* 2.5 cm.
Carrots *cv* Chantenay Red Cored 2. Five seeds were sown per pot. Seeds were placed on the soil surface then covered with fine white sand.

Primary/Secondary Crop:

The primary crop was not planted prior to initiation of confined crop rotation study. The ^{14}C-XDE-570 was applied to the prepared soil at 7.5 g ai/ha and aerobically aged for 30 days prior to planting of secondary (rotational) crops.

Planting interval:

Each crop was planted 30 days after soil treatment of ^{14}C-XDE-570; DAT: 30 days.

Crop parts collected and analysed:

Each crop was harvested at maturity. The spring wheat and sunflowers were harvested 168 days after treatment. The cabbage was harvested 195 days after treatment. The carrots were harvested 156 days after treatment. Each crop portion was sub-sampled as spring wheat (straw and ears), cabbage (head), sunflowers (heads and stalks) and carrots (leaves and roots).

Environmental conditions:

Weather data including information on rain fall and air temperature for the period of study were submitted. No unusual wether pattern were reported.

METHODS:

1. **Compared Use Patterns:**

Parameter	Confined Crop Rotation	Proposed Use Patterns (gap)
Formulation type	EF-1343 Soluble Concentrate	EF-1343 Suspension Concentrate
Method of application	Hand sprayer	Broadcast spray
Application rate	7.5 g ai/ha	5 g ai/ha
Number of applications	1	1
Timing of application	Preplant soil application 30 days before planting	Postemergent 2-leaf crop to flag leaf extended stage inclusive

II. TOTAL RADIOACTIVE RESIDUES (TRRs)

Soil samples were taken within 24 hours of application, 30 days after application and at crop maturity. RAC samples from the rotational crop, spring wheat, sunflowers, cabbage and carrots planted at 30 days after treatment (DAT) were harvested at maturity. Total radioactive residues (TRRs) in soil and crop samples (Table 1 and 2) were determined by combustion/LSC.

TABLE 1. Total Radioactive Residues (TRRs) in Rotational Crop Soil

Soil from the Crop	DAT	^{14}C-phenyl Treatment TRR (ppm)		^{14}C-TP Treatment TRR (ppm)	
		Fresh weight	Dry weight	Fresh weight	Dry weight
Spring wheat	0	0.027	0.028	0.03	0.031
	30	0.012	0.012	0.013	0.013
	168	0.003	0.004	0.003	0.004
Sunflowers	0	0.031	0.032	0.036	0.037
	30	0.022	0.022	0.02	0.021
	168	0.006	0.007	0.002	0.002
Cabbage	0	0.041	0.043	0.04	0.042
	30	0.03	0.033	0.016	0.016
	195	0.003	0.003	0.003	0.003
Carrots	0	0.036	0.038	0.018	0.019
	30	0.016	0.017	0.01	0.011
	156	0.004	0.004	0.006	0.007

TABLE 2. Total Radioactive Residues (TRRs) in Rotational Crop at maturity

Crop	RAC	DAT	^{14}C-phenyl (ppm)	^{14}C-TP (ppm)
Spring wheat	Ears	168	< LOD	0.001
	Straw		0.003	0.004
Sunflowers	Heads	168	< LOD	< LOD
	Stems		0.002	0.005
Cabbage	Heads	195	< LOD	0.002
Carrots	Leaves	156	< LOD	0.01
	Roots		< LOD	0.002

Comments:

The concentration of radioactivity in soil on wet weight basis was similar to the concentration on dry weight basis. At day-0, within 24 hours after application, TRRs ranged from 0.019 - 0.043 ppm. At the time of planting (30 DAT), the levels of TRRs decreased only slightly and were in the range of 0.011 - 0.033 ppm.

TRRs were observed in all fractions of rotational crops harvested at maturity; spring wheat (168 DAT), sunflowers (168 DAT), cabbage (195 DAT) and carrots (156 DAT). TRRs levels in all crop fractions, wheat (ears and straw), sunflower (heads and stems), cabbage (heads) and carrots (leaves and roots), were low (≤ 0.01 ppm). Residue levels observed ^{14}C-TP were slightly higher than the residue levels observed for ^{14}C-phenyl in all mature rotational crops. However, all TRR levels are below the levels required for further characterisation/identification of residues (Residue Chemistry Guidelines Dir98-02, Section 13).

III. EXTRACTION, CHARACTERIZATION AND IDENTIFICATION OF RESIDUES

Rotational Crop Soil:

Soil samples from each rotational crop site at 0, 30, 156 or 168 or 195 DAT were extracted with 0.01 M $CaCl_2$ solution. The supernatant was collected and residual soil was further extracted three times with acetone:water:acetic acid (90:9:1, v/v/v). Total radioactive residues (TRRs) in each extract was determined by liquid scintillation counter (LSC). TRRs in post extraction residual soil were determined by combustion/LSC. TRRs in extracts were also purified by solid phase column/methanol and identified by thin layer and high performance liquid chromatography.

TABLE 3. Extraction of Soil TRRs following Treatment with 7 g ai/ha of [phenyl-^{14}C]XDE-570 and [TP-^{14}C]XDE-570 in Rotational Crop

Fraction (Extracted from soil)	Days After Treatment (DAT)					
	0 days		30 days		156/168/195 days	
	^{14}C-phenyl	^{14}C-TP	^{14}C-phenyl	^{14}C-TP	^{14}C-phenyl	^{14}C-TP
	% TRR	% TRR	% TRR	% TRR	% TRR	% TRR
Spring Wheat						
$CaCl_2$ Extract (methanol phase)	47.7	58.5	32.5	30.9	0.76	0.45
$CaCl_2$ Extract (Aqueous phase)	0	0	0.44	1.4	0.81	1.7
Organic extract 1	59.3	41.5	48.4	33.4	7.2	12.1
Organic extract 2	0	1.3	12.7	6.4	1.2	2.2
Organic extract 3	-	-	4.2	1.9	6.5	0.48
Non extractable residue	1.7	2.4	39.2	14.6	72.7	87.9
Total recovered	109	104	121	80	82	102
Sunflowers						
$CaCl_2$ Extract (methanol phase)	60.3	52.4	35.3	21	1.8	2.7
$CaCl_2$ Extract (Aqueous phase)	0	0	0	1.3	0.11	1.5
Organic extract 1	62.4	49.6	31.6	39.2	5.6	12
Organic extract 2	0	0	6.2	7.5	1.6	2.2
Organic extract 3	-	-	2	2.9	0.34	0.65
Non extractable residue	3.1	1.8	22.4	18.3	40.7	84
Total recovered	126	104	89	80	4.82	100
Cabbage						
$CaCl_2$ Extract (methanol phase)	50.0	45.8	35.2	26.3	1	1.2
$CaCl_2$ Extract (Aqueous phase)	0	0	0	1.1	0.1	0.6
Organic extract 1	47.7	50.7	34.5	37.9	6.9	8.7
Organic extract 2	0	3.6	6.7	6.4	3.4	4.2
Organic extract 3	-	-	2.1	2.3	1	1.6
Non extractable residue	1.9	1.9	29.6	25.4	54.4	78.7
Total recovered	100	102	99	91	62	89
Carrots						
$CaCl_2$ Extract (methanol phase)	66	67	22	18.3	0.6	0.2
$CaCl_2$ Extract (Aqueous phase)	0	0.4	0.1	3.3	4.4	0.2
Organic extract 1	3.2	29.3	27.8	28.4	12.5	7.8
Organic extract 2	6.4	4.9	6.1	10.7	2.1	1.1
Organic extract 3	0 77	0	1.9	2.7	0.3	0
Non extractable residue	2.5	2.4	35.2	32.2	67.4	6.3
Total recovered	108	104	93	96	87	71

TABLE 4. Characterization and Quantification of Soil TRRs following Treatment with 7 g ai/ha of [phenyl-^{14}C]XDE-570 and [TP-^{14}C]XDE-570 in Rotational Crops

Identification	0 Days After Treatment (DAT)				30 Days After Treatment (DAT)			
	^{14}C-phenyl		^{14}C-TP		^{14}C-phenyl		^{14}C-TP	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Spring Wheat								
Total radioactivity	**TRR = 0.027 ppm**		**TRR = 0.030 ppm**		**TRR = 0.012 ppm**		**TRR = 0.013 ppm**	
Metabolite 1								
Metabolite 2			3.81	0.01				
Metabolite 3								
Metabolite 4			37.65	0.012				
5-OH XDE-570	15.03	0.005	14.68	0.005	40.86	0.005	36.8	0.005
XDE-570	91.97	0.025	43.81	0.013	28.87	0.005	23.7	0.03
Total	107	0.03	100	0.031	70	0.005	61	0.008
Sunflower								
Total radioactivity	**TRR = 0.031 ppm**		**TRR = 0.036 ppm**		**TRR = 0.022 ppm**		**TRR = 0.020 ppm**	
Metabolite 1					4.25	0.001	1.15	0
Metabolite 2	20.21	0.006						
Metabolite 3	40.13	0.013	4.76	0.002				
Metabolite 4			44.87	0.016	6.23	0.001		
5-OH XDE-570	6.24	0.002	11.9	0.004	32.19	0.007	32.17	0.007
XDE-570	56.19	0.018	40.52	0.015	19.3	0.004	24.16	0.005
Total	123	0.039	102	0.037	62	0.012	58	0.012
Cabbage								
Total radioactivity	**TRR = 0.041 ppm**		**TRR = 0.040 ppm**		**TRR = 0.030 ppm**		**TRR = 0.016 ppm**	
Metabolite 1	4.45	0.002					7.61	0.001
Metabolite 2			3.9	0.002				
Metabolite 3	3.1	0.001						
Metabolite 4	17.76	0.008	46.79	0.019	17.06	0.006		
5-OH XDE-570	30.19	0.013	9.43	0.004	24.98	0.008	19.53	0.003
XDE-570	42.19	0.018	36.37	0.015	24.53	0.008	35.23	0.006
Total	98	0.042	97	0.04	67	0.022	62	0.1
Carrots								
Total radioactivity	**TRR = 0.036 ppm**		**TRR = 0.018 ppm**		**TRR = 0.016 ppm**		**TRR = 0.010 ppm**	
Metabolite 1	2.54	0.001	11.33	0.002	Not profiled		Not profiled	
Metabolite 2								
Metabolite 3								
Metabolite 4	13.33	0.005						
5-OH XDE-570 XDE570	20.96	0.008	26.78	0.005				
XDE-570	63.34	0.025	57.34	0.011				
Total	100	0.039	96	0.018				

Comments:

At day 0, most of the radioactivity (98-123%) was extractable. The main radioactive residue was XDE-570 which accounted for 36-63% of the TRRs (0.011- 0.025 ppm). Small amounts of 5-OH-XDE-570 and four other unidentified minor metabolites were also present in soil. No single unidentified metabolite was observed > 0.006 ppm. At the day of planting (30 DAT), the levels of extractable radioactivity was declined. About 58-82% of the radioactivity was extractable, with an equivalent increase in nonextractable radioactivity of 15-39%. XDE-570 and 5-OH-XDE-570 were the main radioactive residues present at 30 DAT in soil. Therefore, these were the main components for potential uptake into the rotational crops.

The soil metabolism study reviewed by EAD, indicated that the primary transformation metabolite found in soil was 5-OH-XDE-570. In the 189 day study, the maximum levels of 5-OH-XDE-570 were reached on days 14 and 29 (one day before planting). The sorption of both XDE-570 and 5-OH-XDE-570 increased with time indicating that the remaining XDE-570 in the soil is less bioavailable and less mobile.

The concentration of XDE-570 and 5-OH-XDE-570 for potential uptake from soil is very low. At 30 DAT, residues of each of XDE-570 and 5-OH-XDE-570 was ≤ 0.008 ppm (Table 4). Therefore, it is expected that any residues translocates from the soil to the rotational crops would also be low.

Rotational Crop Fractions:

Rotational crops were harvested at maturity i.e., 168 DAT (spring wheat and sunflowers) 195 DAT (cabbage) and 156 DAT (carrots). Crop fractions of spring wheat (ears and straw), sunflower (heads and stems), cabbage (shoots) and carrot (leaves and roots) were subjected to three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash). Each wash was analysed to determine total ^{14}C-residues (TRRs) using combustion/liquid scintillation counting.

TABLE 5. Characterization of ^{14}C-phenyl-DE-570 and ^{14}C-TP-DE-570 in Selected Crop Matrices

Fraction	^{14}C phenyl		^{14}C TP		^{14}C phenyl		^{14}C TP	
	% TRR	ppm	%	ppm	%	ppm	% TRR	ppm
	Spring Wheat Ears 168-DAT				Spring Wheat Straw 168-DAT			
Total radioactivity	TRR = 0.000 ppm		TRR = 0.001 ppm		TRR = 0.003 ppm		TRR = 0.004 ppm	
Wash solvents								
water	4.7	<LOD	7.2	<LOD	7.5	<LOD	7.3	<LOD
Dichloromethane	16.3	<LOD	13.4	<LOD	7.5	<LOD	1.8	<LOD
Methanol	2.3	<LOD	3.1	<LOD	5.9	<LOD	6.8	<LOD
Total washable	23.3	<LOD	23.7	<LOD	21	<LOD	16	<LOD
Unwashable	77	<LOD	76.3	0.001	79	0.003	84	0.004
Total recovered*	100	<LOD	100	0.001	100	0.003	100	0.004
Accountability**		100		100		100		100
	Sunflower Heads 168-DAT				Sunflower Stems 168-DAT			
Total radioactivity	TRR = 0.000 ppm		TRR = 0.000 ppm		TRR = 0.002 ppm		TRR = 0.005 ppm	
Wash solvents								
water	9.1	<LOD	12..2	<LOD	3..2	<LOD	5.1	<LOD
Dichloromethane	<LOD	<LOD	0.6	<LOD	10.4	<LOD	2	<LOD
Methanol	1..2	<LOD	<LOD	<LOD	0.8	<LOD	2	<LOD
Total washable	10.3	<LOD	12.8	<LOD	14.4	<LOD	9.1	<LOD
Unwashable	89.7	<LOD	87.2	<LOD	85.6	0.002	90.8	0.001
Total recovered*	100	<LOD	100	<LOD	100	0.002	100	0.001
Accountability**						100		
	Cabbage 195-DAT							
Total radioactivity	TRR = 0.000 ppm		TRR = 0.002 ppm					
Wash solvents								
water	<LOD	<LOD	<LOD	<LOD				
Dichloromethane	<LOD	<LOD	<LOD	<LOD				
Methanol	<LOD	<LOD	16.7	<LOD				
Total washable	<LOD	<LOD	16.7	<LOD				
Unwashable	<LOD	<LOD	83.3	0.002				
Total recovered*	<LOD	<LOD	100	0.002				
Accountability**				100				
	Carrot Leaves 156-DAT				Carrot Roots 156-DAT			
Total radioactivity	TRR = 0.000 ppm		TRR = 0.010 ppm		TRR = 0.000 ppm		TRR = 0.002 ppm	
Wash solvents								
water	5.9	<LOD	29	<LOD	50	<LOD	54.1	0.001
Dichloromethane	17.7	<LOD	0.3	<LOD	<LOD	<LOD	<LOD	0.001
Methanol	<LOD	<LOD	12.4	<LOD	5	<LOD	6.6	0.001
Total washable	23.6	<LOD	41.7	0.004	55	<LOD	60.7	0.001
Unwashable	76.5	<LOD	58.3	0.006	45	<LOD	39.3	0.001
Total recovered*	100	<LOD	100	0.010	100	<LOD	100	0.002
Accountability**				166				100

* Total recovered = Total Washableleable + Remaining nonwashable
** Accountability = [Total (ppm) / TRR (ppm)] x 100

Comments:

TRRs levels in all crop fractions, wheat (ears and straw), sunflower (heads and stems), cabbage (heads) and carrots (leaves and roots), at maturity were less than 0.01 ppm. No further attempts were made to characterize TRRs. Residue levels observed in ^{14}C-TP label were slightly higher than the residue levels observed for ^{14}C-phenyl in all mature rotational crops. However, all TRR levels were below the levels required (0.01 ppm) for further characterisation/identification of residues (Residue Chemistry Guidelines Dir98-02, Section 13). No parent or metabolites were identifiable. Therefore, the confined crop rotation study supports the definition of the residue of concern (ROC) of parent only as defined in the plant and animal metabolism studies.

IV. STORAGE STABILITY

No storage stability data was provided. No information on the storage period of crop samples is provided. However, the study protocol indicated that analysis of all samples will be initiated within 3 days of sampling.

V. FINAL SUMMARY

In the confined crop rotation study, **XDE-570** (florasulam), > 97% a.i., E-1343 Suspension Concentrate labelled either as the *[UL-phenyl-^{14}C]XDE-570* or the *[9-triazolopyrimidine-^{14}C]XDE-570* was applied to sandy loam soil at an application rate of 7.5 g ai/ha (1.5X the maximum proposed postemergent application rate). Spring wheat (small grain), sunflower (seed crop), cabbage (leafy vegetable) and carrots (root crop) were planted at 30 days after treatment (DAT) of soil.

Spring wheat, sunflowers, cabbage and carrots were harvested at maturity; 168 DAT (spring wheat and sunflowers) 195 DAT (cabbage) and 156 DAT (carrots). Each crop was separated into fractions as spring wheat (ears and straw), sunflower (heads and stems), cabbage (shoots) and carrot (leaves and roots). Samples of each crop fractions were subjected to three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash). Each wash was analysed to determine total ^{14}C-residues (TRRs) using combustion/liquid scintillation counting. TRRs in all crop fractions were < 0.01 ppm. Therefore, no attempt was made to profile TRRs.

Because levels of TRRs in the rotational crops were low (≤ 0.01 ppm), no parent and its metabolite was identified. Therefore, the confined crop rotation study supports the definition of the residue of concern (ROC) of parent only as defined in the plant and animal metabolism studies.

In addition, the soil metabolism studies reviewed by EAD indicated that the primary transformation product was 5-OH-XDE-570. The sorption of both XDE-570 and 5-OH-XDE-570 increased with time indicating that the remaining XDE-570 in the soil is less bioavailable and less mobile. The concentration of XDE-570 and5-OH-XDE-570 for potential uptake from soil is very low. At 30 DAT, residues of each of XDE-570 and5-OH-XDE-570 was ≤ 0.008 ppm. Therefore, it is expected that any potential residue translocates from the soil to the rotational crops would also be low.

Based on the results of the confined crop rotational study and the soil metabolism study, no field rotational crop studies are required. A 30-day plant back interval (PBI) can be supported for all crops. The label has a plant back interval greater than of 30 days for barley, canola, forage grasses, oats, peas, rye and wheat.

VI. STUDY DEFICIENCIES

No deficiencies in the confined crop rotation study were identified.

Signatures:

Reviewed by: _____ _____
Ali Ismaily Date

Peer reviewed by: _____ _____
Henri Bietlot, Ph. D. Date

Section Head: _____ _____
Ariff Ally, Ph.D. Date

Reviewer: Ali Ismaily, Date February 13, 2001

This DER was initially reviewed by Canada's PMRA and has been reviewed by HED. Conclusions herein agree with HED policy. In addition, this DER has been modified to include the submission MRID number.

Thurston Morton **23-May-2007**

STUDY TYPE: Residue Analytical Method; OPPTS 860.1340 and 860.1360
Method II - Gas Chromatography with Mass Selective Detection

TEST MATERIAL: Florasulam (99.7%)

SYNONYMS: **XDE-570** (Florasulam)

MRID 46808019 Duebelbeis, D. O., A.D. Thomas (1998), "Residue Method Validation Report for the Determination of DE-570 (Florasulam) in Cereal Crop Commodities: Forage and Immature Green; Grain; Hay and Immature Dried; and Straw by capillary Gas Chromatography with Mass Selective Detection (GRM 98.01)", Global Environment Chemistry Laboratory, Indianapolis Lab, Dow AgroSciences LLC, Study ID: RES 98071, November 2, 1998. Unpublished.

MRID 46808020 Eckert, J. A., S. D. West (1999), "Independent Laboratory Validation Method (GRM 98.01- Determination of DE-570 (Florasulam) in Cereal Crop Commodities: Forage and Immature Green; Grain, Hay and Immature Dried; and Straw by Capillary Gas Chromatography with Mass Selective Detection", Enviro-Bio-Tech, Ltd. Bernville, PA, Study ID: DOW-05-99.
Unpublished.

MRID 46808020 Conrath, B. A., S. D. West (1998), "Multi residue methods Testing for DE-570 According to PAM I, Appendix II, as Updated January, 1994", ABC Laboratories, Inc. Columbia, MO, Study ID: ACFS-44706, October 13, 1998. Unpublished.

SPONSOR: Dow AgroSciences (DWE)

NOTE TO READER:

Two different methods were used to quantify ROC in wheat, barley and oat matrices. The petitioner first used a screening method, the immunoassay (IA) method to determine the total residues of florasulam. This method determines the residues of florasulam and related metabolites (4-hydroxyphenyl florasulam) and its glucose conjugate. In addition to this method, a gas chromatography-mass selective detection method was used that determines only the parent florasulam. This method was used to re-analyse samples when total residue of florasulam and its metabolites were found above 0.005 ppm for grain and above 0.0025 ppm for other matrices. The gas chromatography-mass selective detection method is reviewed below. Please note that immunoassay method has been reviewed in a separate document which is also available to the reader.

EXECUTIVE SUMMARY:

Methods for Residue Analysis of Plants and Plant Products - Study ID: RES 98071

The residue of concern (ROC) was defined from wheat metabolism study as the parent compound, florasulam. The petitioner is not proposing a common moiety method.

Residues of florasulam were extracted from wheat, barley and oat matrix with acidified acetone. An aliquot of the extract was purified by filtration through a graphitized carbon solid-phase extraction (SPE) column. The extract was concentrated to remove acetone, diluted with 0.01 N hydrochloric acid and partitioned onto an octadecyl (C_{18}) SPE column. The florasulam was eluted with a 30% acetonitrile in 0.01 N hydrochloride acid solution. Florasulam is partitioned, after salting, into methyl *t*-butyl ether (MTBE). The MTBE was concentrated to dryness. Residues of florasulam were dissolved in acetone and derivatized at room temperature with iodomethane and triethylamine. The acetone solution was concentrated to dryness and *N*-methyl florasulam residues were dissolved in a 5% sodium thiosulfate solution and partitioned into toluene containing the internal standard *N*-propyl florasulam. Residues of florasulam as the N-methyl florasulam derivative were determined by capillary gas chromatograph with mass selective detection (GC/MSD). This is a specific method that identifies/quantifies, florasulam, the parent compound only.

The limit of detection (LOD) was calculated as three times the standard deviation (3s) which was 0.0012 ppm in grain, 0.005 ppm in forage and immature green plant, 0.0036 ppm in hay and immature dried plant and 0.0074 ppm in straw. The limit of quantitation LOQ for florasulam was established at 0.01 ppm for grain over the concentration range of 0.01-0.10 ppm, and at 0.05 ppm for forage, hay, straw, immature green plant and immature dried plant over the concentration range of 0.05-0.50 ppm.

This method was found to give good recoveries within acceptable average range (74 ± 9% - 89 ± 8%) for the analysis of wheat (immature green and dry plant, hay, grain and straw), barley (immature green and dry plant, hay, grain and straw) and oat (immature green and dry plant, hay, grain and straw). The standard deviations measured with respect to recoveries following spiking at the LOQ appear to be indicative of the method having satisfactory repeatability. Good linearity correlation coefficient, $r^2 > 0.995$, within the range of 0.01-0.20 for florasulam analysis. The method employed *N*-propyl florasulam as an internal standard. Representative chromatograms of control matrices of wheat, barley and oat showed no interferences from crop components or from reagents, solvents and glassware. The chromatographic peaks were sharp and free of interferences in the retention areas of internal standard or *N*-methyl florasulam derivative.

The method of analysis was independently validated at the Enviro-Bio-Tech. Ltd. Bernville, PA using wheat grain, forage, hay and straw. The interlaboratory validation validated the Dow AgraSciences method GRM 98.01 for the residues of the florasulam in wheat matrices, indicating good reproducibility.

FREAS has determined that this method is valid. The development of this analytical methodology is classified acceptable as screening method and conform with the criteria of the RCG (Residue Chemistry Guidelines Dir98-02, Section 3).

Methods for Residue Analysis of Food of Animal Origin - none submitted.

The results of the animal metabolism studies in connection with very low residues detected in the crop residue studies indicated that residues will not likely be present in food of animal origin.

COMPLIANCE:

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

I. DATA GATHERING METHODS

PLANTS AND PLANT PRODUCTS

Principle of the Method

Residues of florasulam were extracted from wheat, barley and oat matrix with acidified acetone. An aliquot of the extract was purified by filtration through a graphitized carbon solid-phase extraction (SPE) column. The extract was concentrated to remove acetone, diluted with 0.01 N hydrochloric acid and partitioned onto an octadecyl (C_{18}) SPE column. The florasulam was eluted with a 30% acetonitrile in 0.01 N hydrochloride acid solution. Florasulam was partitioned, after salting, into methyl *t*-butyl ether (MTBE). The MTBE was concentrated to dryness. Residues of florasulam were dissolved in acetone and derivatized at room temperature with iodomethane and triethylamine. The acetone solution was concentrated to dryness and *N*-methyl florasulam residues were dissolved in a 5% sodium thiosulfate solution and partitioned into toluene containing the internal standard *N*-propyl florasulam. Residues of florasulam as the N-methyl florasulam derivative were determined by capillary gas chromatograph with mass selective detection (GC/MSD).

Stability of the primary and/or secondary standard solution

The primary and secondary standard solutions were prepared in acetone. These solutions were reported to be stable over the course of method development and validation. The petitioner recommended to limit the shelf life of standard to approximately six months.

Qualitative description of the method

The method employed for the detection of florasulam was a GC/MS method using an internal standard. The internal standard, N-propyl florasulam, eluted on capillary GC column (12 mx 0.2 mmi.d. with a liquid phase of DB-5MS) at 16.22 minutes. The retention time for florasulam as the N-methyl florasulam derivative was 15.35 minutes. Quantitation was based on the peak area ratio (Quantitation ratio) of the m/z 142 ion response of n-methyl florasulam to the m/z 170 ion response of the N-propyl florasulam internal standard. The signals at *m/z* (138/142), *m/z* (168/142) and *m/z* (168/138) were used as confirmation ratios.

Quantitative description of the method

Linearity

The linearity of the method/detector response was satisfactory (correlation coefficient $r^2 > 0.995$) within the range of 0.01-0.20 ppm for florasulam. The method employed N-propyl florasulam as an internal standard.

Specificity

The recoveries from control samples of wheat, barley and oat matrices (grain, forage, hay, straw, immature green plant and green dried plant) were satisfactory. Residues of florasulam were extracted from wheat, barley and oat matrices with acidified acetone. In metabolism study, residues of florasulam from these samples were initially washed with three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash). The washed samples were dried and a subsample was extracted with acetonitrile: water (90:10 v/v) and acidified acetonitrile: water (90:10: v/v).

No significant interferences (>10% LOQ) were observed at the retention time of N-methyl florasulam in control samples of grain, forage, hay, straw, immature green plant and immature dried plant. The chromatographic peaks were sharp and free of interferences in the retention areas of internal standard or N-methyl florasulam derivative.

Limit of Quantitation

The limit of quantitation (LOQ) was calculated using the standard deviation from the results of the recovery samples fortified at the targeted LOQ of 0.01 ppm for grain and of 0.05 ppm for forage, hay, straw, immature green plant and immature dried plant. The LOQ were 0.0042 ppm for grain, 0.017 ppm for forage and immature green plant, 0.012 ppm for hay and immature dried plant and 0.025 ppm for straw. These calculated values supported the validated limit of quantitation.

The limit of quantitation LOQ for florasulam was established at 0.01 ppm for grain over the concentration range of 0.01-0.10 ppm, and at 0.05 ppm for forage, hay, straw, immature green plant and immature dried plant over the concentration range of 0.05-0.50 ppm.

Limit of Detection

The limit of detection (LOD) was calculated as three times the standard deviation (3s) which was 0.0012 ppm in grain, 0.005 ppm in forage and immature green plant, 0.0036 ppm in hay and immature dried plant and 0.0074 ppm in straw.

Repeatability/Precision

The standard deviations measured with respect to recoveries following spiking at the limit of quantitation (0.01 ppm) for wheat, barley and oat grain were 2%, 8%, 2%, respectively. The standard deviations measured with respect to recoveries following spiking of other matrices of wheat, barley and oat at the limit of quantitation (0.05 ppm) for forage, hay, straw, immature green and immature dry plant ranged between 2%-9%. The mean standard deviations, at spiking levels ranging from 0.05-0.50 ppm, ranging from 2%-9% for grain, forage, hay, straw, immature green and immature dry plant, respectively. The values obtained are indicative of the method having good repeatability.

Recovery Findings

The performance of the method was checked by analysing fortified control samples of wheat, barley and oat with analytical standard solution of florasulam (99.7%) prepared in acetone. The plant matrices were ground and the samples of 10 g each were prepared by fortifying untreated control samples of wheat, barley and oat. The recovery samples were fortified at levels ranging from 0.01 to 0.10 ppm for grains and at levels ranging from 0.05 to 0.50 ppm for forage, hay, straw, immature green plants and immature dry plants. The samples were extracted and analysed to determine the concentration of florasulam. The recovery results for florasulam in wheat, barley and oats matrices are listed in the following Tables 1,2 and 3.

TABLE 1. Recovery Results from Method Validation of Gas chormatography method for florasulam in Wheat Matrices

Crop matrix	Spiking Level (ppm)	Recoveries obtained (%)	Range (%)	Mean recovery ± Std. Dev. (%)
Wheat Grain	0	- *	-	-
	0.01	83, 80	80-83	82 ± 2
	0.02	81	NA	81
	0.05	74	NA	74
	0.10	82	NA	82
		n= 5		Mean for all levels = 80 ± 4%
Wheat Forage	0	- *	-	-
	0.05	80, 76	76-80	78 ± 3
	0.25	74	NA	74
	0.50	78	NA	78
		n= 4		Mean for all levels = 74 ± 2%
Wheat Hay	0	- *	-	-
	0.05	92, 90	90-92	91 ± 1
	0.25	81	NA	81
	0.50	79	NA	79
		n= 4		Mean for all levels = 84 ± 6%
Wheat Straw	0	- *	-	-
	0.05	88, 92	88-92	90 ± 3
	0.10	90	NA	90
	0.25	85	NA	85
		n= 4		Mean for all levels = 88 ± 3%
Wheat Immature green plant	0	- *	-	-
	0.05	79, 79	NA	79
	0.25	74	NA	74
	0.50	71	NA	71
		n= 4		Mean for all levels = 75 ± 4%
Wheat Immature dry plant	0	- *	-	-
	0.05	92, 90	90-92	91 ± 1
	0.10	96	NA	96
	0.25	81	NA	81
		n= 4		Mean for all levels = 89 ± 8%

* *No residue was detected at a detection level of 0.025 ppm.* NA Not applicable

TABLE 2. Recovery Results from Method Validation of Gas chormatography method for florasulam in Barley Matrices

Crop matrix	Spiking Level (ppm)	Recoveries obtained (%)	Range (%)	Mean recovery ± Std. Dev. (%)
Barley Grain	0	- *	-	-
	0.01	91, 80	80-91	86 ± 8
	0.02	87, 90	87-90	89 ± 2
	0.10	83	NA	83
		n= 5		Mean for all levels = 86 ± 3%
Barley Hay	0	- *	-	-
	0.05	86, 87	86-87	87 ± 1
	0.10	85	NA	85
	0.50	83	NA	83
		n= 4		Mean for all levels = 85 ± 2%
Barley *Immature* green	0	- *	-	-
	0.05	76, 79	76-79	78 ± 2
	0.10	80	NA	80
	0.25	64	NA	64
		n= 4		Mean for all levels = 74 ± 9%

* No residue was detected at a detection level of 0.025 ppm.
NA Not applicable

TABLE 3. Recovery Results from Method Validation of Gas chormatography method for florasulam in Oat Matrices

Crop matrix	Spiking Level (ppm)	Recoveries obtained (%)	Range (%)	Mean recovery ± Std. Dev. (%)
Oat Grain	0	- *	-	-
	0.01	82, 85	82-85	84 ± 2
	0.02	73	NA	73
	0.05	80	NA	80
		n= 4		Mean for all levels = 79 ± 6%
Oat Forage	0	- *	-	-
	0.05	79, 70	70-79	75 ± 6
	0.10	74	NA	74
	0.50	75	NA	75
		n= 4		Mean for all levels = 75 ± 1%
Oat Straw	0	- *	-	-
	0.05	82, 82	NA	82
	0.25	80	NA	80
	0.50	82	NA	82
		n= 4		Mean for all levels = 81 ± 1%

* No residue was detected at a detection level of 0.025 ppm.
NA Not applicable.

Comments:

This method was found to give good recoveries within acceptable average range (74 ± 9% to 89 ± 8%) for the analysis of wheat (immature green and dry plant, hay, grain and straw), barley (immature green and dry plant, hay, grain and straw) and oat (immature green and dry plant, hay, grain and straw). The standard deviations ranging between 2-9% measured with respect to recoveries following spiking at the limit of quantification (0.01 ppm for grain and 0.05 ppm for all other matrices) appeared to be indicative of the method having satisfactory repeatability.

Optimization of the Analytical Method

No further experimental conditions were investigated to optimize the method recoveries.

Reproducibility

Independent method validation

The results from the supervised crop field trials indicated that residues of florasulam in wheat, barley and oat grains were less than limit of detection of 0.05 ppm. Hence, no radiovalidation of residues were carried out

An independent laboratory method validation (ILV) was conducted by CEM Analytical Services Ltd. (CEMAS) to verify the reliability and reproducibility of the Dow AgroSciences Method ERC95.6, for the determination of florasulam residues in wheat, barley and oat matrices.

Untreated controls wheat samples and control samples fortified at the LOQ (0.01 ppm for grain and 0.05 ppm for forage, hay and straw) and 2x the LOQ were analysed using method GRM 98.01. The recovery results for florasulam in wheat matrices are listed in the following Tables 4.

TABLE 4. Recovery Results Obtained by an Independent Laboratory for Gas chormatography method for the determination of florasulam Residues inWheat Matrices.

Crop matrix	Spiking Level (ppm)	Recoveries obtained (%)	Range (%)	Mean recovery ± Std. Dev. (%)
Wheat Grain	0	-	-	-
	0.01	92, 99, 102	92-101	98 ± 5
	0.02	89, 91, 91	89-91	90 ± 1
		n= 6		Mean for all levels = 94 ± 6%
Wheat Forage	0	-	-	-
	0.05	97, 97, 96	96-97	97 ± 1
	0.1	97, 95, 95	95-97	96 ± 1
		n= 6		Mean for all levels = 97 ± 1%
Wheat Hay	0	-	-	-
	0.05	106, 107, 109	106-109	107 ± 2
	0.1	102, 99, 102	99-102	101 ± 2
		n= 6		Mean for all levels = 104 ± 4%
Wheat Straw	0	-	-	-
	0.05	98, 99, 108	98-109	102 ± 6
	0.10	104, 96, 93	93-104	97 ± 6
		n= 6		Mean for all levels = 100 ± 4%

Comments:

No problems were encountered with the methodology and no changes or modifications were made. Sample extracts, purification and analysis were conducted exactly as described in for method GR 98.01. The chromatographic peaks were sharp and free of interferences in the retention areas of internal standard or N-methyl florasulam derivative. The linearity of the method/detector response was satisfactory (correlation coefficient $r^2 \geq 0.998$) within the range of 0.01-0.1 ppm for florasulam in grain, forage, hay and straw. The mean recoveries were 94 ± 6% (n=6), 97 ± 1% (n=6), 104 ± 4% (n=6) and 100 ± 4% (n=6) for grain, forage, hay and straw, respectively, when samples were spiked with florasulam at levels ranging from 0.05-1.0 ppm. The mean recovery values from the ILV were slightly higher than the ones obtained from the Dow AgroSciences analytical method. However, these recoveries were within acceptable rangeof 70-120%. The ILV analysis of method GRM 98.01 demonstrated that the method was reproducible and repeatable for the analysis of wheat grain, forage, hay and straw.

Conclusion
The ILV analysis of method GRM 98.01 demonstrated that the method was reproducible and repeatable for the analysis of wheat grain, forage, hay and straw.

FOOD OF ANIMAL ORIGIN

No methods were submitted for food of animal origin. The results of the animal metabolism studies in connection with very low residues detected in the crop residue studies indicated that residues will not likely be present in food of animal origin.

Results of the animal metabolism studies demonstrated that potential residues of florasulam in food of animal origin would unlikely be at levels above the limit of quantification (LOQ) of 0.01 ppm, if livestock consumed wheat, barley and oat crops treated at the proposed Canadian label application rate of 5 g ai/ha.

II. ENFORCEMENT METHODS

SPECIFIC METHOD

The analytical method GRM 98.01 can be used as the enforcement method for determining residues of florasulam in wheat, barley and oat.

MULTI RESIDUE METHODS

Pesticide Residue DFG Method S19:

The DFG method S19 uses gas chromatography (GC) to quantify any detectable pesticide residues. Therefore, the first part of the suitability experiments involved investigating whether standard solutions containing florasulam could be quantified using GC with either Electron Capture Detection (ECD), Nitrogen Phosphorous Detection (NPD) or Mass Selective Detection (MS). The results of the experiments indicated that florasulam behaves unpredictably during GC analysis and is therefore unsuitable for routine analysis by GC. Therefore, according to the petitioner, investigations into extractability, liquid-liquid partitioning and Gel Permeation Chromatography cleanup were not carried out. Consequently, the data presented in this report appeared to indicate that the DFG method S19 was not suitable for routine analysis of florasulam residues in wheat and barley.

Pesticide Analytical Manual Volume I (PAM Vol. 1):

A multi residue method for testing florasulam was conducted according to the Pesticide Analytical Manual Volume I (PAM Vol. 1), Appendix II (1/94) using Protocols A, C, D, E and F.

According to the petitioner, florasulam is not naturally fluorescent. At the nominal temperatures of 180 and 200 °C, florasulam does chromatography acceptably on four of the six column-detector combinations tested (4 various columns in combination with ECD and/or NPD and or electrolytic conductivity detection (ELCD)) as specified by the multi-residue testing guidelines. Florasulam also chromatographed acceptably using NPD and ELCD. However, the level of response using NPD and ELCD was insufficient, such that omitting the Florisil cleanup in Protocol D was unacceptable. Florasulam did not elute from the Florisil cleanup columns listed in Protocol E and F

Conclusions

The existing multi residue methods of analysis which are currently in common usage were not found to be suitable for the determination of florasulam residues in wheat, barley and oat.

Deficiencies

No deficiencies were identified in the submitted data for the testing of florasulam through existing multi-residue methods.

III. OVERALL STUDY DEFICIENCIES

No deficiencies were identified.

Signatures:

Reviewed by: _____ _____
Ali Ismaily Date

Peer reviewed by: _____ _____
Henri Bietlot, Ph. D. Date

Section Head: _____ _____
Ariff Ally, Ph.D. Date

Reviewer: Ali Ismaily **, Date** February 13 , 2001

This DER was initially reviewed by Canada's PMRA and has been reviewed by HED. Conclusions herein agree with HED policy. In addition, this DER has been modified to include the submission MRID number.

Thurston Morton 23-May-2007

STUDY TYPE: Residue Analytical Method; OPPTS 860.1340 and 860.1360
Method 1 - Immunoassay Screening Method

TEST MATERIAL (Purity): Florasulam (99.7%)

SYNONYMS: XDE-570 (Florasulam)

MRID 46808018 D. L.Young and D. O. Duebelbeis (1998), "Residue Method Validation Report for the Determination of Florasulam (proposed) in Grains by Immunoassay", Global Environment Chemistry Laboratory, Indianapolis Lab, Dow AgroSciences LLC, Study ID: RES 97041.01, October 12, 1998. Unpublished.

SPONSOR: Dow AgroSciences (DWE)

NOTE TO READER:

Two different methods were used to quantify ROC in wheat, barley and oat matrices. The petitioner has used the immunoassay (IA) method as a screening method which is reviewed below. This method determines the residues of florasulam and related metabolites (4-hydroxyphenyl florasulam) and its glucose conjugate. In addition to this method, a gas chromatography-mass selective detection method was used that determines only the parent florasulam. This method was used to re-analyse samples when total residue of florasulam and its metabolites were found above 0.005 ppm for grain and above 0.0025 ppm for other matrices. Please note that this method has been reviewed in a separate document which is also available to the reader.

EXECUTIVE SUMMARY:

Methods for Residue Analysis of Plants and Plant Products - Study ID: RES 97041.01

The residue of concern (ROC) was defined from wheat metabolism study as the parent compound, florasulam. The petitioner is not proposing a common moiety method.

The principle of immunoassay method is based on an enzyme linked immunosorbent assay (ELISA) for the determination of residues in barley, oat and wheat. The plant matrices were ground and recovery samples were prepared by fortifying untreated control samples of wheat (immature green and dry plant, hay, grain and straw), barley (immature green and dry plant, hay, grain and straw) and oat (immature green and dry plant, hay, grain and straw) to validate the analytical method. Residues of florasulam were extracted from all matrices with an acetic acid/acetone/water extraction solution. An aliquot of the extract is evaporated to dryness and reconstituted with 0.01 N HCl, which is then extracted using liquid/liquid partitioning or applied to a C_{18} coulmn, evaporated, reconstituted in diluent and assayed with the XDE-570 RaPID Assay test kit.
The calculated method limit of detection (LOD) for the ROC, florasulam, ranged from 0.005 to 0.022 ppm for grain and for immature plant, forage, hay and straw. The method limit of quantitation (LOQ) for the

florasulam was established at 0.010 ppm for grain and 0.005 ppm for all other crop matrices (immature green and dry plant, forage, hay and straw). This method was found to give good recoveries within acceptable average range of 93 ± 16 - 116 ± 5% for the analysis of wheat (immature green and dry plant, hay, grain and straw), barley (immature green and dry plant, hay, grain and straw) and oat (immature green and dry plant, hay, grain and straw). The standard deviations measured with respect to recoveries following spiking at the LOQ appear to be indicative of the method having satisfactory repeatability. Good linearity correlation coefficient, r > 0.990, within the range of 0.01-0.20 ppm for grain and 0.05-1.00 ppm for forage, hay, straw, immature green and immature dry plant was observed for florasulam analysis.

The method of analysis was validated at the Global Environment Chemistry Laboratory, Dow AgroSciences LLC using wheat e, barley and oat. No independent laboratory method validation for florasulm in wheat, barley and oat was conducted. However, this method was used as screening and the specific GC/MSD method was validated by independent laboratory.

FREAS has determined that this method is valid. The development of this analytical methodology is classified acceptable as screening method and conform with the criteria of the RCG (Residue Chemistry Guidelines Dir98-02, Section 3).

Methods for Residue Analysis of Food of Animal Origin - none submitted.

The results of the animal metabolism studies in connection with very low residues detected in the crop residue studies indicated that residues will not likely be present in food of animal origin.

COMPLIANCE:

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

I. DATA GATHERING METHODS

PLANTS AND PLANT PRODUCTS

Principle of the Method

The principle of the method is based on an enzyme linked immunosorbent assay (ELISA) for the determination of residues in barley, oat and wheat. The grain matrices used to validate the method include barley (immature green and dry plant, hay, grain and straw), oat (immature green and dry plant, hay, grain and straw) and wheat (immature green and dry plant, hay, grain and straw). Residues of florasulam are extracted from all matrices with an acetic acid/acetone/water extraction solution. An aliquot of the extract is evaporated to dryness and reconstituted with 0.01 N HCl, which is then extracted using liquid/liquid partitioning or applied to a C_{18} column, evaporated, reconstituted in diluent and assayed with the XDE-570 RaPID Assay test kit.

An aliquot of each extracted and diluted samples was pipetted into a disposable test tube. Enzyme-conjugated XDE-570 and paramagnetic particles coated with specific antibodies were sequentially added to the tubes. During an incubation period, the sample residue and the enzyme conjugated competed for antibody sites on the magnetic particles. At the end of the incubation period, a magnetic field was applied to the particles. The sample residues and enzyme conjugate bound to the antibodies on the particles were held in the tube by the magnetic field while the unbound reagent were decanted. After decanting, the particles were washed to remove unbound enzyme conjugate. The presence of XDE-570 was detected by adding the enzyme substrate (hydrogen peroxide) and a chromogen (3, 3', 5, 5'-tetramethylbenzidine; TMB), generating a colored product. After another incubation period, the reaction was stopped and stabilized by the addition of acid. The enzyme conjugate was in competition with the sample residues for the antibody sites, the level of color development was inversely promotional to the concentration of XDE-570 in the sample. Lower the concentration of XDE-570, the greater was the color development of the sample. The absorbence at 450nm was measured in each

tube using the RPA-1 RaPID Analyzer. A calibration curve was generated and the residue concentration in unknown samples was calculated from the regression equation.

Stability of the primary and/or secondary standard solution
No data was provided.

Qualitative description of the method
The performance of the method was checked for false positive and false negative results by analysing unfortified control samples (matrix blanks) and samples fortified at LOD. No residue was found in a control sample known to be free of florasulam and residue was detected in a control sample fortified at the LOD. There were no false positives from the unfortified control samples and no false negatives reported from LOD fortified samples analysed.

Several common pesticides, organic/inorganic compounds and solvents (Table 1, Appendix A) were tested for the potential to interfere with conjugate binding in the florasulam assay. The I_{50} concentration is used as reference value for expressing cross reactivity and determining the extent of interference. In comparison, I_{50} for florasulam in the XDE-570 RaPID Assay kit was found to be 0.52 ppb.

Quantitative description of the method

Linearity
The linearity of the method/detector response was good (correlation coefficient r > 0.990) within the range of 0.01-0.20 ppm for grain, and 0.05-1.00 ppm for immature green and dry plant, forage, hay, and straw for analysis of florasulam. The method employed external standards and a quality control sample containing 2 ppb of florasulam was also used to check the performance of the analytical method.

Specificity

This method was also tested on metabolites of florasulam (5-OH XDE-570 and 4-OH XDE-570). The method was found to be very sensitive to the 4-OH XDE-570 metabolite (I_{50} ~ 0.8 ng/ml) and not sensitive to the 5-OH XDE-570 metabolite (I_{50} ~ 10, 000 ng/ml). The 4-OH XDE-570 metabolite was available in purified form and used to approximate reactivity of the antibody to the glucose conjugate of this metabolite found in grain matrices.

Limit of Quantitation

The limit of quantification (LOQ) was calculated using the standard deviation from the results of the recovery samples fortified at the targeted limit of quantification of 0.05 ppm for forage, hay, straw, immature green and immature dry plant and 0.01 ppm for grain. The LOQ was calculated as ten times the standard deviation (10s). The validated Limit of Quantitation (LOQ) for florasulam in barley, oats and wheat grain was established at 0.01ppm over the concentration range of 0.01-0.20 ppm for all grain. The calculated limit of quntification was 0.039 ppm in forage, 0.054 ppm in hay, 0.070 ppm in straw; 0.040 ppm in immature green plant and 0.033 ppm in immature dry plant, and 0.018 ppm in grain of wheat, barley, and oats. These calculated values generally supported the validated limit of quantification.

The Limit of Quantitation (LOQ) for florasulam was established at 0.01 ppm for grain and for all other crop matrices (forage, hay, straw, immature green and immature dry plant) was established at 0.05 ppm over the concentration range of 0.05-1.20 ppm for these commodities.

Limit of Detection

The limit of detection (LOD) was calculated using the standard deviation from the results of the recovery samples fortified at the targeted limit of quantification of 0.05 ppm for forage, hay, straw, immature green and immature dry plant and 0.01 ppm for grain. The LOD was calculated as three times the standard deviation (3s). The calculated LOD was 0.012 ppm in forage, 0.016 ppm in hay,0.021 ppm in straw; 0.012 ppm in immature green and 0.010 ppm in immature dry plant, and 0.054 ppm in grain of wheat, barley, and oats.

Repeatability/Precision

The standard deviations measured with respect to recoveries following spiking at the limit of quantitation (0.01 ppm) for wheat, barley and oat grain were 34%, 9%, 12%, respectively. The standard deviations measured with respect to recoveries following spiking of other matrices of wheat, barley and oat at the limit of quantitation (0.05 ppm) for forage, hay, straw, immature green and immature dry plant ranged between 2%-12%. The mean standard deviations, at spiking levels ranging from 0.025-1.00 ppm, ranged between 4%-13% for grain, forage, hay, straw, immature green and immature dry plant, respectively. The values obtained are indicative of the method having good repeatability.

Recovery Findings

The performance of the method was checked by analysing fortified control samples of wheat, barley and oat with analytical standard solution of florasulam (99.7%) prepared in acetone. The plant matrices were ground and recovery samples of 10 g each were prepared by fortifying untreated control samples of wheat, barley and oat. The recovery samples were fortified at levels ranging from 0.005 to 0.20 ppm for all grains and at levels ranging from 0.025 to 1.0 ppm for immature green plants and dry plants, forage, hay, and straw. The samples were extracted and analysed to determine the concentration of florasulam. The recovery results for florasulam in wheat, barley and oats matrices are listed in the following Tables 1, 2 and 3.

TABLE 1. Recovery Results from Method Validation of Immunoassay method for florasulam in wheat Matrices

Crop matrix	Spiking Level (ppm)	Recoveries obtained (%)	Range (%)	Mean recovery ± Std. Dev. (%)
Wheat Grain	0	-*	-	-
	0.005	-**	-	-
	0.010	76, 136, 80	76-136	97 ± 34
	0.020	100, 112, 94	94-112	102 ± 9
	0.100	82, 86, 89	82-89	86 ± 4
	0.200	100, 102, 106	100-106	103 ± 3
		n=12		Mean for all levels = 97 ± 13
Wheat Forage	0	-	-	-
	0.025	-	-	-
	0.050	96, 90, 90	90-96	92 ± 4
	0.100	102, 111, 108	102-111	107 ± 5
	0.500	104, 108, 107	104-108	106 ± 2
	1.00	120, 114, 111	111-120	115 ± 5
		n=12		Mean for all levels = 105 ± 4
Wheat Hay	0	-	-	-
	0.025	-	-	-
	0.050	84, 96, 100	84-100	93 ± 8
	0.100	93, 96, 110	93-110	97 ± 9
	0.500	84, 81, 81	81-84	82 ± 2
	1.00	95, 108, 98	95-108	100 ± 7
		n=12		Mean for all levels = 93 ± 6
Wheat Straw	0	-	-	-
	0.025	-	-	-
	0.050	90, 88, 96	88-96	91 ± 4
	0.100	92, 102, 96	92-102	97 ± 5
	0.500	90, 93, 105	90-105	96 ± 8
	1.00	114, 105, 101	101-114	107 ± 7
		n=12		Mean for all levels = 98 ± 5

Crop matrix	Spiking Level (ppm)	Recoveries obtained (%)	Range (%)	Mean recovery ± Std. Dev. (%)
Wheat Immature green plant	0	-	-	-
	0.025	-	-	-
	0.050	108, 118, 108	108-118	111 (6)
	0.100	114, 105, 110	105-114	110 (5)
	0.500	120, 117, 117	117-120	118 ± 2
	1.00	110, 96, 122	96-122	110 ± 15
		n=12		Mean for all levels = 113 ± 7
Wheat Immature dry plant	0	-	-	-
	0.25	-	-	-
	0.050	120, 112, 108	108-120	113 ± 6
	1.00	117, 114, 119	114-119	117 ± 3
	0.500	117, 111, 108	111-117	112 ± 5
	1.00	114, 123, 126	114-126	121 ± 6
		n=12		Mean for all levels = 116 ± 5

* No residue was detected at a detection level of 0.025 ppm.
** Residue was detected but it was below the 0.050 ppm limit of quantification.

TABLE 2. Recovery Results from Method Validation of Immunoassay method for florasulam in Barley Matrices

Crop matrix	Spiking Level (ppm)	Recoveries obtained (%)	Range (%)	Mean recovery ± Std. Dev. (%)
Barley Grain	0	-*	-	-
	0.005	-**	-	-
	0.010	104, 92, 92	92-104	98 ± 9
	0.020	88, 88, 76	76-88	84 ± 7
	0.100	81, 78, 90	78-90	83 ± 6
	0.200	110, 120, 80	80-120	115 ± 7
		n=12		Mean for all levels = 95 ± 7
Barley Hay	0	-	-	-
	0.025	-	-	-
	0.050	108, 112, 90	90-112	103 ± 12
	0.100	111, 96, 87	87-111	98 ± 12
	0.500	99, 84, 87	420-495	90 ± 8
	1.00	122, 98, 98	975-1215	106 ± 14
		n=12		Mean for all levels = 99 ± 12
Barley Straw	0	-	-	-
	0.025	-	-	-
	0.050	100, 96, 106	96-106	101 ± 5
	0.100	101, 95, 98	95-101	98 ± 3
	0.500	114, 105, 114	105-114	111 ± 5
	1.00	120, 105, 105	105-120	110 ± 9
		n=12		Mean for all levels = 105 ± 4
Barley Immature green plant	0	-	-	-
	0.025	-	-	-
	0.050	100, 94, 112	94-112	102 ± 9
	0.100	108, 113, 119	108-119	113 ± 6
	0.500	105, 102, 114	102-114	107 ± 6
	1.00	117, 113, 117	113-117	116 ± 2
		n=12		Mean for all levels = 107 ± 5

Crop matrix	Spiking Level (ppm)	Recoveries obtained (%)	Range (%)	Mean recovery ± Std. Dev. (%)
Barley Immature dry plant	0	-	-	-
	0.025	-	-	-
	0.050	100, 106, 108	100-108	105 ± 4
	0.100	111, 105, 102	102-111	106 ± 5
	0.500	108, 114, 99	99-114	107 ± 8
	1.00	111, 108, 113	108-113	111 ± 3
		n=12		Mean for all levels = 107 ± 5

* No residue was detected at a detection level of 0.025 ppm.
** Residue was detected but it was below the 0.050 ppm limit of quantification.

TABLE 3. Recovery Results from Method Validation of Immunoassay method for florasulam in Oat Matrices

Crop matrix	Spiking Level (ppm)	Recoveries obtained (%)	Range (%)	Mean recovery ± Std. Dev. (%)
Oat Grain	0	-	-	-
	0.005	-	-	-
	0.010	92, 92, 112	92-112	99 ± 12
	0.020	110, 72, 78	72-110	87 ± 21
	0.100	82, 78, 85	78-85	82 ± 4
	0.200	122, 112, 112	112-122	115 ± 5
		n=12		Mean for all levels = 96 ± 10
Oat Forage		-	-	-
	0.025	-	-	-
	0.050	96, 96, 102	96-102	98 ± 4
	0.100	108, 126, 117	108-126	117 ± 9
	0.500	103, 104, 101	101-104	103 ± 2
	1.00	85, 90, 89, 126, 99, 126	85-126	103 ± 19
		n=12		Mean for all levels = 105 ± 8
Oat Hay	0	-	-	-
	0.025	-	-	-
	0.050	108, 100, 108	100-108	105 ± 5
	0.100	111, 113, 116	111-116	113 ± 3
	0.500	111, 111, 105	105-111	109 ± 4
	1.00	120, 125, 117	117-120	121 ± 4
		n=12		Mean for all levels = 112 ± 4
Oat Straw	0	-	-	-
	0.025	-	-	-
	0.050	108, 112, 108	108-112	109 ± 2
	0.100	114, 117, 105	105-117	112 ± 6
	0.500	114, 93, 99	93-114	102 ± 11
	1.00	114, 90, 102	90-114	102 ± 12
		n=12		Mean for all levels = 106 ± 7

Crop matrix	Spiking Level (ppm)	Recoveries obtained (%)	Range (%)	Mean recovery ± Std. Dev. (%)
Oat Immature green	0	-*	-	-
	0.025	-**	-	-
	0.050	93, 102, 105	93-105	100 ± 6
	0.100	113, 105, 113	105-113	110 ± 5
	0.500	111, 132, 114	111-132	119 ± 11
	1.00	116, 122, 125	116-125	121 ± 5
		n=12		Mean for all levels = 113 ± 7
Oat Immature dry plant	0	-	-	-
	0.025	-	-	-
	0.050	106, 120, 118	106-120	115 ± 8
	0.100	105, 110, 119	105-119	111 ± 7
	0.500	102, 96, 114	96-114	104 ± 9
	1.00	113, 105, 113	105-113	110 ± 5
		n=12		Mean for all levels = 110 ± 7

* No residue was detected at a detection level of 0.025 ppm.
** Residue was detected but it was below the 0.050 ppm limit of quantification.

Comments:

This method was found to give good recoveries within acceptable average range (93 ± 16% to 116 ± 5%) for the analysis of wheat (immature green and dry plant, hay, grain and straw), barley (immature green and dry plant, hay, grain and straw) and oat (immature green and dry plant, hay, grain and straw). The standard deviations measured with respect to recoveries following spiking at the LOQ appear to be indicative of the method having satisfactory repeatability.

Independent Laboratory Validation

The Dow AgroSciences analytical method GRM 97.01 was validated at the Global Environment Chemical Laboratory, Dow AgroSciences LLC using wheat, barley and oat matrices fortified with florasulam. No Independent Laboratory Validation (ILV) was conducted to verify the reliability and reproducibility of this method for the determination of florasulam in wheat, barley and oat matrices. However, this method was used as a screening method to detect florasulam in wheat, barley and oat samples. Samples found to contain residues above LOQ were re-analysed by a capillary gas chromatography, the GRM 98.01 method which is validated by an independent laboratory. This method is also developed by Dow AgroSciences.

Confirmation of the Identity of the Residues

The results from the supervised crop field trials indicated that residues of florasulam in wheat, barley and oat grains were less than limit of detection of 0.05 ppm. Hence, no radiovalidation of residues were carried out. However, the analytical method GRM 98.01 using GC-MSD system can be used to confirm the identity of the florasulam residues in wheat, barley and oat commodities. Residues of florasulam in this method are extracted from wheat, barley and oat matrix with acidified acetone. An aliquot of the extract is purified by filtration through a graphitized carbon solid-phase extraction (SPE) column. The extract is concentrated to remove acetone, diluted with 0.01 N hydrochloric acid and partitioned onto an octadecyl (C_{18}) SPE column. The florasulam is eluted with a 30% acetonitrile in 0.01 N hydrochloride acid solution. Florasulam is partitioned, after salting, into methyl *t*-butyl ether (MTBE). The MTBE is concentrated to dryness and *N*-methyl florasulam residues were dissolved in a 5% sodium thiosulfate solution and partitioned into toluene containing the internal standard *N*-propyl florasulam. Residues of florasulam as the N-methyl florasulam derivative are determined by capillary gas chromatography with mass selective detection (GC/MSD).

Optimization of the Analytical Method

No further experimental conditions were investigated to optimize the method recoveries. Modifications to the assay procedures are not recommended.

Conclusions

Based on the validation data , the Immunoassy method GRM 97.01 was assessed to be acceptable for use in determining/screening residues of florasulam in wheat (immature green and dry plant, hay, grain and straw), barley (immature green and dry plant, hay, grain and straw) and oat (immature green and dry plant, hay, grain and straw). The limit of quantitation was sufficiently low and recoveries for all samples of wheat, barley and oat were within acceptable limits.

Deficiencies

No deficience were noted.

II. ENFORCEMENT METHODS

SPECIFIC METHOD

The analytical method GRM 98.01 can be used as the enforcement method for determining residues of florasulam in wheat, barley and oat commodities.

III. OVERALL STUDY DEFICIENCIES

No deficiencies were identified.

Signatures:

Reviewed by: _____ _____
Ali Ismaily Date

Peer reviewed by: _____ _____
Henri Bietlot, Ph. D. Date

Section Head: _____ _____
Ariff Ally, Ph.D. Date

APPENDIX A:

Table I. Compounds Tested for the Potential to Interfere in the XDE-570 RaPID Assay Test Kit

Pesticides	Solvents (max Tolerated)	Organic/Inorganic compounds
Alachlor	Acetone (15%)	Calcium (chloride dihydrate)
Aldicarb	Acetonitrile (5%)	Copper (chloride)
Atrazine	DFM (20%)	Humic Acid
Benomyl	Methanol (10%)	Iron (chloride hexahydrate)
Butylate		Magnesium (chloride hexahydrate)
Captan		Maganese (chloride)
Carbaryl		Mercuric (chloride)
Carbaryl		Nikel (sulfate hexahydrate)
Carbendazim		Nitrate (sodium)
Carbofuran		Peroxide (hydrogen, 30%)
Chlorpyrifos		Phosphate (sodium, heptahydrate)
Chlorsulfuron		Silicates (sodium meta-)
Cloransulam-methyl		Sodium chloride
1,1-dichloro-1-propene		Sulfate (sodium)
2,4-D		Sulfite (sodium)
Diacamba		Thiosulfate (sodium, pentahydrate)
Dichloropropene		Zinc (chloride)
Diclosulam		
Dinoseb		
Ethylene bisdithiocarbamate		
Fenoxaprop-ethyl		
Flamprop-methyl		
Fluazifop-p-butyl		
Flumetsulam		
Fluroxypyr		
Glyphosate		
Lindane		
Malathion		
MCPA		
MCPP		
Metolachlor		
Metribuzin		
Metosulam		
Metsulfuron-methyl		
Methomyl		
Pentachlorophenyl		
Picoloram		
Propachlor		
Propanil		
Tebuconazole		
Terbufos		
Thiabendazole		
Thiophanate-methyl		
Tilt		
3,5,6-Trichloro-2-pyridinol		
Tralkoxydim		
Triallate		
Trifluralin		
Triclopyr		

PMRA Reviewer: Ali Ismaily **Date:** September 6, 2000

This DER was initially reviewed by Canada's PMRA and has been reviewed by HED. Conclusions herein agree with HED policy. In addition, this DER has been modified to include the submission MRID number.

Thurston Morton **23-May-2007**

STUDY TYPE: Nature of the Residue in Plants - Winter Wheat; OPPTS 860.1300

TEST MATERIAL (PURITY): [UL-phenyl-^{14}C]XDE-570 (> 99.3%)
[9- triazolopyrimidine-^{14}C]XDE-570 (> 98.3%)

SYNONYMS: **XDE-570** (Florasulam)

Common name : Florasulam (ISO-proposed)
IUPAC: **2', 6', 8-Trifluoro-5-methoxy-s-triazolo [1,5-c]pyrimidine-2-sulfonanilide**
CAS: **N-(2,6-difluorophenyl)-8-fluoro-5-methoxy(1,2,4)*triazolo*(1,5-c)pyrimidine-2-sulphonamide**

CAS RN: ***145701-23-1***

MRID 46808003 Fiona Pillar. (1997) The Metabolism of XDE-570 in Winter Wheat - Final Report. DowElanco Europe, Letcombe Laboratory, UK. Laboratory report number: GHE-P-5729, Protocol number: 5U, Study Completion date Oct, 24, 1997. Unpublished

SPONSOR: DowElanco

COMMENTS ON THE USE OF EU DER:

The contents of Tables 2, 3, 4 and 5 indicating the nature and amounts of residue of florasulam in winter wheat plants was directly taken from the EU DER provided by the petitioner. The data presented in these tables was found comparable with those presented by the petitioner in the original study.

EXECUTIVE SUMMARY:

In the metabolism study, [^{14}C]-DE-570 (>98%) formulated with *EF 1343 blank formulation*, radiolabeled as [^{14}C]-phenyl-XDE-570 and [^{14}C]-TP-XDE-570 was applied to winter wheat at crop growth stages of BBCH30 (stem elongation-early application) and BBCH49 (postflag leaf emergence/first awns visible-late application) at 50 g ai/ha. The rate used herein was equivalent to 10X the proposed Canadian label rate of 5 g ai/ha. The formulation used in metabolism study was identical to that used in the residue studies and that of proposed for registration. Winter wheat plants (10 plants/tub) were planted in sandy loam soil contained in tubs. ^{14}C-DE-570 formulations were applied to run-off to wheat plants using a spray gun. All tubs were placed outdoors, for the duration of the in-life phase of the study, in the lysimeter complex. In addition to natural precipitations, the plants were watered at the soil surface as required. Plants were harvested within 18 hours of treatment (day 0), 30 days after treatment and finally at crop maturity (129 days after BBCH 30 application and 65 days after BBCH 49)

The early application (BBCH 30 crop stage) sampling of immature whole wheat plant (0 day after application), the parent (71%, 2.9 ppm phenyl and 63%, 2.0 ppm TP labelled TRR) and one other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (19%, 0.79 ppm phenyl and 24.6%, 0.027 ppm TP labelled TRR) and 4-OH-(phenyl)-DXD-570 (0.9%, 0.038 ppm phenyl and 0.84%, 0.027 ppm TP labelled TRR). A total of 91% of the phenyl and TP labelled TRR was identified. A total of 97% of phenyl and TP labelled TRR was extractable. A total of 5.3% (0.22 ppm) phenyl and 4.9% (0.16 ppm) TP labelled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam. In addition, a minor metabolite, 2-sulphonamide (1.5%, 0.048 ppm TP labelled TRR) was also identified.

The late application (BBCH 49 crop stage) sampling of immature whole wheat plant (0 day after application), the parent (84%, 0.57 ppm phenyl and 81%, 0.61 ppm TP labelled TRR) and one other major metabolite was identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (8.5%, 0.058 ppm phenyl and 8.5%, 0.064 ppm TP labelled TRR). A total of 90% of the TRR was identified. A total of 94% of the phenyl and TP labelled TRR was extractable. A total of 1.9% (0.014 ppm) phenyl labelled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam. In addition, minor metabolites 4-OH-(phenyl)-DXD-570 (1.2%, 0.0087 ppm phenyl and 0.4%, 0.003 ppm labelled TRR) and 2-sulphonamide (0.7%, 0.005 ppm TP labelled TRR) were also identified.

The early application (BBCH 30 crop stage) sampling of immature whole wheat plant (30 days after application), the parent (28%, 0.12 ppm phenyl and 27%, 0.11 ppm TP labelled TRR) and one other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (21%, 0.083 ppm phenyl and 12.8%, 0.051 ppm TP labelled TRR) and 4-OH-(phenyl)-DXD-570 (6.8%, 0.027 ppm phenyl and 15.1%, 0.060 ppm TP labelled TRR). A total of 56% the phenyl and TP labelled TRR was identified. A total of 63% of the phenyl and 77% of the TP labelled TRR was extractable. A total of 2.7% (0.011ppm) phenyl labelled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam. In addition, a minor metabolite, 2-sulphonamide (1%, 0.051 ppm TP labelled TRR) was also identified.

The late application (BBCH 49 crop stage) sampling of immature whole wheat plant (30 days after application), the parent (27%, 0.03 ppm phenyl and 32%, 0.041ppm TP labelled TRR) and one other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (41.5%, 0.051 ppm phenyl and 19%, 0.024 ppm TP labelled TRR). A total of 69% phenyl and 51% of TP labelled TRR was identified. A total of 69% of the phenyl and 78% of TP labelled TRR was extractable. A total of 26% (0.034 ppm) TP labelled TRR consisted of several minor components. Each of these component was estimated to be less than 0.01 ppm. No other metabolite was identified.

The early application (BBCH 30 crop stage) sampling of mature wheat straw (129 days after application), no parent compound was identified. However, some metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (6.3%, 0.003 ppm phenyl and 2.5%, 0.0018 ppm TP labelled TRR,), 4-OH-(phenyl)-DXD-570 (8.4%, 0.0041 ppm phenyl and 1.6%, 0.0012 ppm TP labelled TRR) and 2-sulphonamide (4.7%, 0.0034 ppm TP labelled TRR). A total of 15% of phenyl and 8.8% of the TRR was identified. A total of 61.4% of the phenyl and 78.2% TP labelled TRR was extractable. A total of 45.8% (0.02 ppm) phenyl and 43% (0.03 ppm) TP labelled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam. Each of these metabolite was estimated to be less than 0.01 ppm.

The late application (BBCH 49 crop stage) sampling of mature wheat straw (65 days after application), the parent (14%, 0.057 ppm phenyl and 7%, 0.02 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (21.5%, 0.088 ppm phenyl and 13%, 0.041 ppm TP labelled TRR), 4-OH-(phenyl)-DXD-570 (14%, 0.059 ppm phenyl and 5.5%, 0.017 ppm labelled TRR) and 2-sulphonamide (19%, 0.058 ppm TP labelled TRR). A total of 50% phenyl and 44% TP labelled TRR was identified. A total of 59% of the phenyl and 79% TP labelled TRR was extractable. A total of 9.4% (0.039 ppm) phenyl and 5.3% (0.017 ppm) TP labelled TRR consisted of several minor components, more polar than florasulam. Each of these metabolite was estimated to be less than 0.01 ppm.

Total radioactive residue level in grain was determined by combustion/LSC. The ^{14}C-residues were too low to elucidate the nature of the TRRs in mature wheat ears (up to 0.03 ppm) and grain (up to 0.008 ppm), therefore, no further attempts to characterize/identify the ^{14}C-residues were carried out.

The analysis of wheat plant samples was started within 3 days of sampling. In addition, the petitioner reported that the results of analyses of intact plant samples after 6, 8 and 9 months show that the chromatographic profiles between the initial and storage stability samples are very similar. From these comparison of chromatographic profiles, the petitioner concluded that radioactive residues of XDE-570 in winter wheat are stable under conditions of storage for up to 9 months.

The metabolism of XDE-570 in wheat proceeded via hydroxylation in the 4-position of phenyl ring with subsequent glucose conjugation. Additional degradation was followed by tentative cleavage of the sulphonamide bridge. The metabolites detected in wheat matrices were 4-OH-(phenyl)-florasulam, glucose conjugate of 4-OH-(phenyl)-florasulam and 2-sulphonamide. The 4-OH-(phenyl)-florasulam and glucose conjugate of 4-OH-(phenyl)-florasulam were both present in rat metabolism. The metabolism study was conducted at 10x the proposed Canadian label rate (5 g ai/ha) and 2-sulphonamide metabolite was detected only in winter wheat straw (0.059 ppm) and not in the grain. The 2-sulphonamide metabolite is not considered to be of toxicological significance.

Based on the winter wheat metabolism study, the low levels of residues observed in grain (0.008 ppm) and considering exaggerated application rate (10X the proposed Canadian Application rate), the residue of concern (ROC) was defined as the parent compound, XDE-570 (florasulam).

The winter wheat metabolism study is classified as acceptable and it satisfies the guideline requirement for a plant metabolism study (Residue Chemistry Guidelines Dir98-02, Section 2).

COMPLIANCE:

Signed and dated GLP and Quality Assurance Data statements were provided. This study was conducted by Dow Elanco Europe, Letcombe Laboratories, Letcombe Regis, Wantage, Oxon, United Kingdom. The author indicated that this study reflects the current (Aug 1997) guidance for plant metabolism studies as described in Luden (7028/VI/95 EN - rev2.6/1/97) and in EC Directive 96/98 amending Annex II and II of 91/414.

MATERIALS AND METHODS

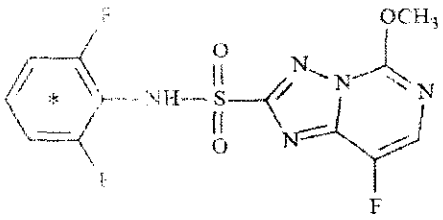
MATERIALS

1. **Test Compound:**

[UL-phenyl-^{14}C]DXE-570 ["phenyl" labelled compound]
Radiochemical purity: (99.39, 99.55) % [determined by TLC]
Specific activity: 152.1 µCi/mg
3.37662 x 10^8 dpm/mg

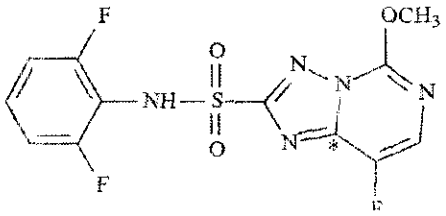
[9-triazolopyrimidine-^{14}C]DXE-570 ["TP" labelled compound]
Radiochemical purity: (98.36, 98.59) % [determined by TLC]
Specific activity: 155.4 µCi/mg
3.44988 dpm/mg

Nonradioactive DXE-570



[UL-phenyl-^{14}C]XDE-570

"Phenyl" label



[9- triazolopyrimidine-^{14}C]XDE-570

"TP" label

2. **Test Site:**

Testing environment: Winter wheat plants were grown in tubs and pots prepared with sandy loam soil and were setup outdoor. Fenpropimorph, tenbuconazole and epoxiconazole were used as fungicide and aphox was used as an insecticide to protect crop during the study period.
Environmental conditions (temperature, rainfall, sunlight, etc.): The information on rain fall, wind speed, air temperature and soil temperature were for the period of study were submitted. No unusual wether pattern were reported.
Soil characteristics
Type: sandy loam
% Organic Matter (%OM): Not reported.
pH: Not reported.
Cation Exchange Capacity (CEC): Not reported.

3. **Test Crop:**

Type/Variety: winter wheat (*cv Avalon*)
Crop group: Group 15 - cereal grain group
Group 16 - forage, fodder, and straw of cereal grains group.
Crop part(s) harvested entire aerial part in immature plants and ears and straw at maturity.
Crop growth stage at time of application and harvest:

Crop growth stages at time of application: BBCH30 (stem elongation-early application)
BBCH49 (postflag leaf emergence/first awns visible-late application)

Crop growth stages at time of harvest: 18 hours of treatment: immature, fresh
30 days after treatment: immature, fresh
129 days after treatment (BBCH 30): mature, fresh
65 days after treatment BBCH 49: mature, fresh

METHODS:

1. **Compared Use Patterns:**

Parameter	Metabolism Study	Proposed Use patterns (gap)
Type of application	Postemergent foliar	Postemergent foliar
Formulation type	EF 1343 Suspension Concentration with/without Agral 90 surfactant at a rate of 0.2% v/v	EF 1343 Suspension Concentration with Agral 90 surfactant at a rate of 0.2% v/v
Method of application	Hand sprayer	Broadcast spray
Actual dosage rate	50 g ai/ha	50 g ai/ha
Number of applications	1	1
Timing of application/growth stage	BBCH30 growth stage BBCH49 growth stage	Postemergent 2-leaf crop upto and including the flag leaf extended stage
PHI (foliar) - days	129 days for BBCH 30 65 days for BBCH 49	60 days

2. **Sample Harvest:**

Harvest procedures (mechanical/hand, etc.): Not reported but likely harvest by hand.
Type of equipment used: None
Number/weight of samples collected per replication: The study protocol stated that at least 2 plants will be sampled from each treatment. The weight of samples was not reported.
Number of replications/treatment level: Two groups of approximately10 plants treated at growth stages of BCCH 30 and BBCH 49 at treatment level of 50 g ai/ha.

II. TOTAL RADIOACTIVE RESIDUES (TRRs):

Disposition ^{14}C-Residues of Florasulam (XDE-570)

Grain samples were mixed with dry ice and milled to a fine powder. TRR in the grain samples were determined by combustion in a biological oxidizer and analyzed by liquid scintillation counting (LSC). The efficiency of the oxidizer was assessed using carbon-14 standards for oxidizers. Immature whole wheat plant, mature wheat straw and mature wheat ear samples were subjected to three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash) and an extraction with acetonitrile: water mixture. Total ^{14}C-residues in each wash, extract and nonextractable tissue samples were determined by combustion/LSC. The petitioner summed the radioactivity in surface washes, extracts and nonextractable residues to account for the total TRRs in each crop sample.

TABLE 1. Total Radioactive Residues (TRRs) in immature whole wheat plant, mature wheat straw, mature wheat ears and mature wheat grain from winter wheat plants treated at BBCH 30 and BBCH 49 growth stages with [UL-phenyl-^{14}C]XDE-570 and [9-triazolopyrimidine-^{14}C]XDE-570 at a rate of 50 g ai/ha (all TRRs expressed on a wet weight basis).

Timing/Method of application	Matrix	PHI (days)	Total Radioactive Residues of XDE-570 (ppm)			
			Phenyl-label		TP-label	
			Actual 10x GAP	Anticipated 1x GAP	Actual 10x GAP	Anticipated 1x GAP
BBCH 30 growth stage/ foliar spray	immature whole wheat plant	0	4.1	0.4	3	0.3
		30	0.4	0.04	0.4	0.04
	mature wheat straw	129	0.048	0.0048	0.07	0.007
	mature wheat ears	129	0.003	0.0003	0.008	0.0008
	mature wheat grain	129	0.001	0.0001	0.002	0.0002
BBCH 49 growth stage/ foliar spray	immature whole wheat plant	0	0.68	0.068	0.76	0.076
		30	0.12	0.012	0.13	0.013
	mature wheat straw	65	0.41	0.041	0.3	0.032
	mature wheat ears	65	0.03	0.003	0.03	0.003
	mature wheat grain	65	0.002	0.0002	0.008	0.0008

Total radioactive residue (TRR) in wheat samples from metabolism study conducted with phenyl label was similar to TRR from metabolism study conducted with TP label in both growth stages. As expected, concentration of TRR in the wheat samples in early growth stage was lower than in late growth stage, due to continue metabolism while wheat plant grew.

It is anticipated that TRR at the proposed Canadian application rate (5 g ai/ha) will be considerably lower than the actual TRR seen in the metabolism studies at 10x the proposed Canadian label rate.

II. RESULTS

A. Extraction and Hydrolysis of Residues:

Immature Whole Wheat plant 0-day:
There were sufficient TRRs in 0-day sampling of the immature whole wheat plant at BBCH 30 and BBCH 49 growth stage to characterize and identify the ^{14}C-residues.

Extractable TRRs: The 0-day samples of immature whole wheat plant collected at BBCH 30 and BBCH 49 stages were subjected to three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash). The washed plant sample was dried and homogenised and then it was extracted with acetonitrile: water mixture (90:10 v/v). Total ^{14}C-residues in each wash, extract, washed and extracted plant tissue samples were determined by combustion/LSC.

Bound TRRs: No further analysis of the extracted plant tissue was carried out to characterize bound TRRs.

Immature Whole Wheat plant 30-day:
There were sufficient TRRs in 30-day sampling of the immature whole wheat plant from BBCH 30 and BBCH 49 growth stage applications to characterize and identify the ^{14}C-residues.

Extractable TRRs: The 30-day samples of immature whole wheat plant collected from BBCH 30 and BBCH 49 stage applications were subjected to three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash). The washed sample was dried and a subsamples was extracted with acetonitrile: water (90:10 v/v) and acidified acetonitrile: water (90:10: v/v) mixtures. Total ^{14}C-residues in each wash and extract were determined by combustion/LSC. The nonextractable residues were further extracted with acid (0.1M HCl) and base (1M NaOH).

Bound TRRs: The extracted plant tissue was dried and homogenised. A sample was further extracted with hydrochloride acid and sodium hydroxide to characterize bound residues. In order to quantify the incorporation of non extractable residues into lignin and cellulose, the 30-day samples of immature whole wheat plant collected from BBCH 30 stage application which had previously been surface washed and dried were extracted with acidified acetonitrile followed by an extraction with Potassium Permanganate. The radioactive content of the remaining residue and of the fibres fractions was determined by combustion analysis and the radioactivity in the filtrate was determined by LSC.

Mature Wheat Straw:
There were sufficient TRRs in mature wheat straw samples from BBCH 30 and BBCH 49 growth stage applications to characterize and identify the ^{14}C-residues.

Extractable TRRs: The samples of mature straw collected from BBCH 30 and BBCH 49 stage applications were subjected to three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash). The washed sample was dried and a subsamples was extracted with acetonitrile: water (90:10 v/v) and acidified acetonitrile: water (90:10: v/v) mixtures. Total ^{14}C-residues in each wash and extract were determined by combustion/LSC. The nonextractable residues were further extracted with acid (0.1M HCl) and base (1M NaOH).

Bound TRRs: The extracted plant tissue was dried and homogenised. The plant tissue was further subjected to hydrochloric acid extraction and sodium hydroxide extraction to characterize bound TRRs. In order to quantify the incorporation of non extractable residues into lignin and cellulose, mature straw collected from BBCH 30 stage application which had previously been surface washed and dried were extracted with acidified acetonitrile were submitted to NaOH digestion. The radioactive content of the remaining residue and of the fibres fractions was determined by combustion analysis and the radioactivity in the filtrate was determined by LSC.

Mature Wheat Ears:
There were sufficient TRRs in mature wheat ear samples from BBCH 30 and BBCH 49 growth stage applications to characterize and identify the ^{14}C-residues.

Extractable TRRs: The samples of mature wheat ears collected from BBCH 30 and BBCH 49 stage applications were subjected to three sequential surface washes (an aqueous wash, a dichloromethane wash and a methanol wash). The washed sample was dried and a subsamples was extracted with acetonitrile: water (90:10 v/v) mixture. Total ^{14}C-residues in each wash and extract were determined by combustion/LSC.

Bound TRRs: No further analysis of the extracted plant tissue was carried out to characterize bound TRRs.

Mature Wheat Grain:
Total radioactive residue level in grain was determined by combustion/LSC. The ^{14}C-residues were too low to elucidate the nature of the TRR in mature wheat grain samples. Therefore, no further attempts were made to characterize/identify the TRR.

TABLE 2. Fractionation and Extraction/Hydrolysis of ^{14}C-Residues from immature whole wheat plant, mature wheat straw and mature wheat ears of winter wheat plants treated, at BBCH 30 growth stage, with [UL-phenyl-^{14}C]XDE-570 and 9-triazolopyrimidine-^{14}C]XDE-570 at a rate of 50 g ai/ha (10x GAP).
(all TRRs listed in the table are expressed on a wet weight basis).

Commodity		Immature whole wheat plant PHI : 0 day		Immature whole wheat plant PHI : 30 days		Mature wheat straw PHI : 129 days		Mature wheat ears PHI : 129 days	
Labeling group		^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP
Total radioactive residues									
mg florasulam equiv./kg		4.1	3.2	0.40	0.4	0.048	0.073	0.0027	0.008
Washable radioactive residues									
Aqueous wash	mg/kg	2.7	1.8	0.12	0.14	0.006	0.021	0.0004	0.004
	%TRR	65	57	29	36	13	28	16	47
DCM wash	mg/kg	0.23	0.21	0.031	0.045	0.0004	0.001	0.00002	0.0002
	%TRR	5.6	6.6	7.6	11	0.9	1.7	0.66	2.3
Methanol wash	mg/kg	0.74	0.75	0.068	0.062	0.006	0.014	0.0003	0.0002
	%TRR	18	23	16.9	15.6	13.4	19.5	9.4	2.0
Residues	mg/kg	0.44	0.42	0.19	0.15	0.035	0.036	0.002	0.004
	%TRR	11	13	46	37	73	50	74	48
Combined solvent extracted residues	mg/kg	0.31	0.32	0.18	0.13	0.013	0.019	0.0007	0.0015
	%TRR	7.6	10	45	37	27	26.0	25	19
Non extractable radioactive residues									
	mg/kg	0.135	0.099	0.0039	0.0027	0.022	0.018	0.001	0.002
	%TRR	3.3	3.1	1.0	0.7	46	24	49	29
Total recovery (washed fractions + extracted fractions + residual radioactivity)									
Total	mg/kg	4.1	3.2	0.4	0.41	0.048	0.073	0.0027	0.008
	%TRR	100	99	100	100	99.9	99.9	100	100

TABLE 3. Fractionation and Extraction/Hydrolysis of ^{14}C-Residues from immature whole wheat plant, mature wheat straw and mature wheat ears of winter wheat plants treated, at BBCH 49 growth stage, with [UL-phenyl-^{14}C]XDE-570 and 9-triazolopyrimidine-^{14}C]XDE-570 at a rate of 50 g ai/ha (10x GAP)
(all TRRs expressed on a wet weight basis).

Commodity		Immature whole wheat plant PHI : 0 day		Immature whole wheat plant PHI : 30 days		Mature wheat straw PHI : 65 days		Mature wheat ears PHI : 65 days	
Labeling group		^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP
Total radioactive residues									
mg Florasulam equiv./kg		0.68	0.76	0.12	0.13	0.41	0.32	0.031	0.03
Washable radioactive residues									
Aqueous wash	mg/kg	0.32	0.48	0.042	0.060	0.14	0.16	0.0085	0.014
	%TRR	48	64	35	48	33	50	28	46
DCM wash	mg/kg	0.21	0.15	0.005	0.006	0.009	0.01	0.0006	0.0006
	%TRR	30	20	4.1	5.2	2.2	3.6	2.1	2.1
Methanol wash	mg/kg	0.059	0.037	0.025	0.022	0.054	0.041	0.0052	0.003
	%TRR	8.7	5.0	20	18	13	13	17	7.9
Residues	mg/kg	0.091	0.083	0.05	0.037	0.21	0.11	0.016	0.013
	%TRR	13	11	41	30	52	33	53	44
Combined solvent extracted residues	mg/kg	0.048	0.036	0.034	0.029	0.044	0.062	0.0019	0.0035
	%TRR	7	4.7	27	23	11	20	6	11.5
Non extractable radioactive residues									
	mg/kg	0.043	0.047	0.017	0.0085	0.17	0.042	0.014	0.01
	%TRR	6.4	6.2	13.6	6.7	41	13.6	47	33
Total recovery (washed fractions + extracted fractions + residual radioactivity)									
	mg/kg	0.68	0.75	0.12	0.12	0.41	0.31	0.031	0.03
	%TRR	100	100	100	100	100	100	100	100

Immature Whole Wheat plant 0-day:
At day 0, within 18 hours of application, most of the TRR (phenyl and TP label) in both early and late applications were washed off the surfaces of leaves with water, dichloromethane and methanol. In the early application (BBCH 30 growth stage), these washes removed 89% and 87% of phenyl and TP labeled TRRs, respectively. In the late application (BCCH 49 growth stage), TRRs removed with these washes were 86% and 89% for phenyl and TP labels, respectively. In the early application, acetonitrile:water treatment extracted another 7.6% and 10% phenyl and TP labeled TRRs, respectively. In the late application, acetonitrile:water treatment extracted 7.0% and 4.7% phenyl and TP labeled TRRs, respectively. The remaining nonextracted TRRs were about 3% for phenyl and TP labels and about 6% for phenyl and TP labels in early and late applications, respectively.

Immature Whole Wheat plant 30-day:
By 30 days after application, less of the TRRs would wash off from the surface of the plant with water, dichloromethane and methonal in both early and late application plants. The washed TRRs were 54% and 63% for early application and 59% and 70% for late application for phenyl and TP labels, respectively. In the early application, further treatment with acetonitrile:water, acidified acetonitrile:water, hydrochloric acid, and sodium hydroxide extracted another 45% and 35% of the phenyl and TP labeled TRRs, respectively. In the late application, further treatment with acetonitrile:water, acidified acetonitrile:water, hydrochloric acid, and sodium hydroxide extracted 37% and 29% of the phenyl and TP labeled TRRs, respectively. The remaining nonextracted TRRs were about 4% and 17% for phenyl and 3% and 8% TP labels in early and late applications, respectively.

Mature Wheat Straw:
In maturity straw, 129 days after the early application, the washed TRRs with water, dichloromethane and methonal were 28% for phenyl and 50% TP label. Whereas, in maturity straw, 65 days after late application, the washed TRRs with water, dichloromethane and methonal were 48% of phenyl and 67% TP label. In the early application, further treatment with acetonitrile:water, acidified acetonitrile:water, hydrochloric acid, and sodium hydroxide extracted another 27% and 26% of the phenyl and TP labeled TRRs, respectively. In the late application, further treatment with acetonitrile:water, acidified acetonitrile:water, hydrochloric acid, and sodium hydroxide extracted 11% and 20% of the phenyl and TP labeled TRRs, respectively. The remaining nonextracted TRRs were about 46% and 41% for phenyl, and 24% and 14% TP labels in early and late applications, respectively.

Mature Wheat Ears:
In maturity wheat ears, 129 days after the early application, the washed TRRs with water, dichloromethane and methonal were 26% for phenyl and 52% TP label. In maturity wheat ears, 65 days after late application, the washed TRRs with water, dichloromethane and methonal were 47% of phenyl and 56 % TP label. In the early application, acetonitrile:water treatment extracted another 25% and 19% phenyl and TP labeled TRRs, respectively. In the late application, acetonitrile:water treatment extracted 6% and 12% phenyl and TP labeled TRRs, respectively. The remaining nonextracted TRRs were about 49% and 47% for phenyl, and 19% and 33% for TP labels in early and late applications, respectively.

Mature Wheat Grain:
Total radioactive residue level in grain was determined by combustion/LSC. The ^{14}C-residues were too low (0.008 ppm) to elucidate the nature of the TRR in mature wheat grain samples. Therefore, no further attempts were made to characterize/identify the TRR.

B. Characterization and Identification of Residues

The TRRs in wash and extracts of wheat samples were analysed using two separate chromatographic analytical methods, an analytical normal phase TLC using a non radiolabeled florasulam, and HPLC/UV systems using reference standards. Two extraction methods involving oxidatition with potassium permanganate and hydrolysis with sodium hydroxide were used to invetigate incorporation of non extractable radioactive residues into lignin and cellulose. Immature 30-day whole wheat plant and mature straw samples from BBCH 30 application were studied. These samples were previously surface washed, dried and then extracted with acidified acetonitrile. The radioactive content of the solid fractions from these methods was determined by combustion analysis and the radioactivity in the filtrate was determined by LSC.

An unknown metabolite was detected in day 0 and day 30 methanol wash and acetonitrile/water extract of wheat plants treated with both radiolabelled forms of XDE-570. The structure of this metabolite was investigated using ESP LC-MS analytical methods. The petitioner assigned the structure as the glucose conjugate of XDE-570. The metabolite was incubated with a specific β-glucosidase enzyme to confirm the structure.

TABLE 4. Summary of Characterization/Identification of ^{14}C-Residues in immature whole wheat plant and mature wheat straw from winter wheat plants treated, at BBCH 30 growth stage, with [UL-phenyl-^{14}C]XDE-570 and 9-triazolopyrimidine-^{14}C]XDE-570 at a rate of 50 g ai/ha (10x GAP).

Commodity		Immature wheat plant PHI : 0 day		Immature wheat plant PHI : 30 days		Mature wheat straw PHI : 129 days	
Labeling group		^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP
Parent compound	mg/kg	2.9	2.0	0.12	0.11	-	-
	% TRR	71	63	29	27	-	-
2-sulphonamide*	mg/kg	-	0.048	-	0.004	-	0.003
	% TRR	-	1.5	-	1.0	-	4.7
Glucose conjugate of 4-HO (phenyl) - DE- 570	mg/kg	0.8	0.79	0.083	0.051	0.003	0.0018
	% TRR	19	24	21	13	6.3	2.5
4-OH-phenyl-DE-570*	mg/kg	0.039	0.027	0.027	0.06	0.0041	0.0012
	%TRR	0.9	0.84	6.8	15.1	8.4	1.6
Polar components	mg/kg	0.011	0.062	0.019	0.084	0.0004	0.019
	% TRR	0.3	1.9	4.6	21	0.9	27
Unidentified metabolites**	mg/kg	0.22	0.16	0.011	-	0.022	0.031
	% TRR	5.3	4.9	2.7	-	46	43
Total Extractable	mg/kg	4	3.1	0.26	0.31	0.03	0.057
	% TRR	97	97	63	77	61	78
Total identified metabolites	mg/kg	3.75	2.91	0.23	0.23	0.007	0.006
	% TRR	91	90	56	56	15	9

- : Not radiodetected.
* : The tentative assignment results from comparison of retention times with a reference standard on HPLC.
** : This fraction contains several minor components, more polar than Florasulam.

TABLE 5. Summary of Characterization/Identification of ^{14}C-Residues in immature whole wheat plant and mature wheat straw from winter wheat plants treated, at BBCH 49 growth stage, with [UL-phenyl-^{14}C]XDE-570 and 9-triazolopyrimidine-^{14}C]XDE-570 at a rate of 50 g ai/ha (10x GAP)

Commodity		Immature wheat plant PHI : 0 day		Immature wheat plant PHI : 30 days		Mature wheat straw PHI : 65 days	
Labeling group		^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP	^{14}C phenyl	^{14}C TP
Parent compound	mg/kg	0.57	0.61	0.034	0.041	0.057	0.022
	% TRR	84	80	27	32	14	7
2-sulphonamide*	mg/kg	-	0.005	-	-***	-	0.059
	% TRR	-	0.7	-	-***	-	18
Glucose conjugate of 4-OH-(phenyl) -DE-570	mg/kg	0.058	0.064	0.051	0.024	0.088	0.041
	% TRR	8.5	8.5	42	19	22	13
4-OH-(phenyl) -DE-570*	mg/kg	0.0087	0.0029	-	-	0.059	0.017
	%TRR	1.2	0.4	-	-	14.4	5.5
Polar components	mg/kg	-	0.012	-	0.034	-	0.093
	% TRR	-	1.6	-	27	-	29
Unidentified metabolites**	mg/kg	-	0.0142	-	-	0.039	0.017
	% TRR	-	1.9	-	-	9.4	5.3
Total Extractable	mg/kg	0.64	0.71	0.085	0.099	0.24	0.25
	% TRR	94	94	69	78	59	79
Total identified metabolites	mg/kg	0.64	0.68	0.085	0.065	0.21	0.14
	% TRR	94	90	69	51	50	44

- : Not radiodetected.
* : The tentative assignment results from comparison of retention times with a reference standard on HPLC.
** : This fraction contains several minor components, more polar than Florasulam.
*** : The 2-sulphonamide metabolite was not radiodetected at late application in the case of the ^{14}C TP labeling in immature wheat plants (PHI : 30 days).

Immature Whole Wheat plant 0-day:
The early application (BBCH 30 crop stage) sampling of immature whole wheat plant (0 day after application), the parent (71%, 2.9 ppm phenyl and 63%, 2 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (19%, 0.8 ppm phenyl and 24.6%, 0.027 ppm TP labelled TRR) and 4-OH-(phenyl)-DXD-570 (0.9%, 0.039 ppm phenyl and 0.84%, 0.027 ppm labelled TRR). A total of 91% of the phenyl and TP labelled TRR was identified. A total of 97% of phenyl and TP labelled TRR was extractable. A total of 5.3% (0.22 ppm) phenyl and 4.9% (0.16 ppm) TP labelled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam. In addition, a minor metabolite, 2-sulphonamide (1.5%, 0.048 ppm TP labelled TRR) was also identified.

The late application (BBCH 49 crop stage) sampling of immature whole wheat plant (0 day after application), the parent (84%, 0.570 ppm phenyl and 81%, 0.610 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (8.5%, 0.058 ppm phenyl and 8.5%, 0.064 ppm TP labelled TRR). A total of 90% of the TRR was identified. A total of 93% of the phenyl and TP labelled TRR was extractable. A total of 1.9% (0.014 ppm) phenyl labelled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam. In addition, minor metabolites 4-OH-(phenyl)-DXD-570 (1.2%, 0.009 ppm phenyl and 0.4%, 0.003 ppm labelled TRR) and 2-sulphonamide (0.7%, 0.005 ppm TP labelled TRR) were also identified.

Immature Whole Wheat plant 30-day:
The early application (BBCH 30 crop stage) sampling of immature whole wheat plant (30 days after application), the parent (29%, 0.12 ppm phenyl and 27%, 0.11 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (21%, 0.08 ppm phenyl and 12.8%, 0.051 ppm TP labelled TRR), 4-OH-(phenyl)-DXD-570 (6.8%, 0.027 ppm phenyl and 15.1%, 0.06 ppm labelled TRR). A total of 56% the phenyl and TP labelled TRR was identified. A total of 63% of the phenyl and 77% of the TP labelled TRR was extractable. A total of 2.7% (0.011ppm) phenyl labelled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam. In addition, a minor metabolite, 2-sulphonamide (1%, 0.051 ppm TP labelled TRR) was also identified.

The late application (BBCH 49 crop stage) sampling of immature whole wheat plant (30 days after application), the parent (27%, 0.034 ppm phenyl and 32%, 0.041 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (42%, 0.051 ppm phenyl and 19.1%, 0.0243 ppm TP labelled TRR). A total of 69% phenyl and 51% of TP labelled TRR was identified. A total of 69% of the phenyl and 78% of TP labelled TRR was extractable. A total of 26% (0.034 ppm) TP labelled TRR consisted of several minor components, more polar than florasulam. Each of these components was estimated to be less than 0.01 ppm. No other metabolite was detected.

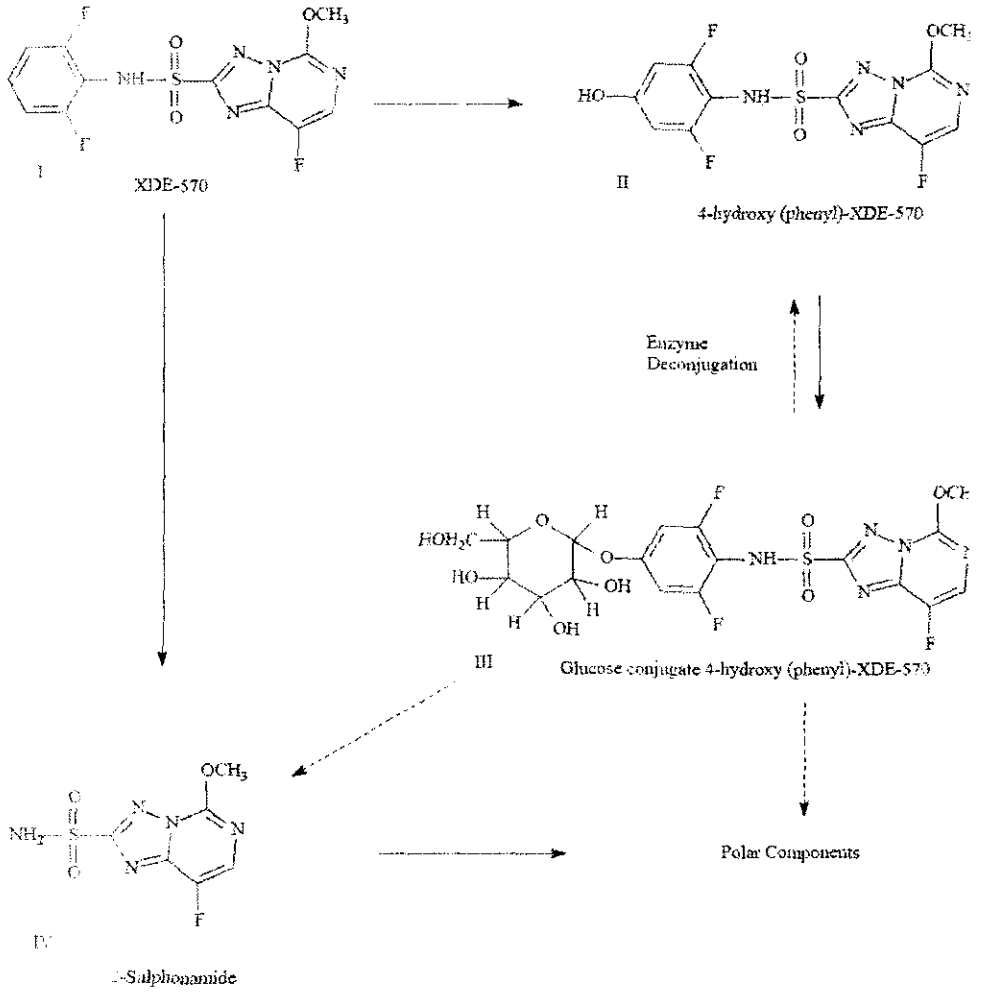
Mature Wheat Straw:
The early application (BBCH 30 crop stage) sampling of mature wheat straw (129 days after application), no parent compound was identified. However, some metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (6.3%, 0.003 ppm phenyl and 2.5%, 0.0018 ppm TP labelled TRR,), 4-OH-(phenyl)-DXD-570 (8.4%, 0.0041 ppm phenyl and 1.6%, 0.001 ppm labelled TRR) and 2-sulphonamide (4.7%, 0.003 ppm TP labelled TRR). A total of 15% of phenyl and 8.8% of the TRR was identified. A total of 61.4% of the phenyl and 78% TP labelled TRR was extractable. A total of 45.8% (0.02 ppm) phenyl and 43% (0.03 ppm) TP labelled TRR was consisted of several minor components, more polar than florasulam. Each of these component was estimated to be less than 0.01 ppm.

The late application (BBCH 49 crop stage) sampling of mature wheat straw (65 days after application), the parent (14%, 0.057 ppm phenyl and 7.1%, 0.022 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (21.5%, 0.09 ppm phenyl and 13%, 0.041 ppm TP labelled TRR), 4-OH-(phenyl)-DXD-570 (14%, 0.059 ppm phenyl and 5.5%, 0.017 ppm labelled TRR) and 2-sulphonamide (18.6%, 0.059 ppm TP labelled TRR). A total of 50% phenyl and 44% TP labelled TRR was identified. A total of 59% of the phenyl and 79% TP labelled TRR was extractable. A total of 9.4% (0.039 ppm) phenyl and 5.3% (0.017 ppm) TP labelled TRR was consisted of several minor components, more polar than florasulam. Each of these component was estimated to be less than 0.01 ppm.

Mature Wheat Ears:
Total radioactive residue level in wheat ears (0.003-0.03 ppm) was determined by combustion/LSC. The concentration of ^{14}C-residues were too low to elucidate the nature of the TRRs in mature wheat ears. Therefore, no further attempt to characterize and identify the ^{14}C-residues was made.

Mature Wheat Grain:
Total radioactive residue level in grain (0.001-0.008 ppm) was determined by combustion/LSC. The concentration of ^{14}C-residues were too low to elucidate the nature of the TRRs in mature wheat grain. Therefore, no further attempt to characterize and identify the ^{14}C-residues was made.

Figure 1. Proposed Metabolic Profile of XDE-570 (florasulam) in Winter Wheat Plants.



Identification of Metabolites

Identification	Common Name/Code	Chemical Name
I	XDE-570	**N-(2,6-difluorophenyl)-8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide**
II	4-OH-(phenyl)-XDE-570	N-(2,6-difluro-4-hydroxyphenyl)-8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide
III	glucose conjugate 4-OH-(phenyl)-XDE-570	-
IV	2-sulphonamide	8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-

		sulphonamide

The metabolism of XDE-570 in winter wheat proceeded via hydroxylation in the 4-position of phenyl ring with subsequent glucose conjugation. Additional degradation was followed by possible cleavage across the sulphonamide bridge forming a number of small polar components.

C . Storage Stability

The analysis of wheat plant samples was started within 3 days of sampling. A selection of duplicate plants from each of the sampling point intervals (Day 0, day 30 and maturity) were selected at random and frozen. These were then under deep-freeze conditions and washed and extracted 6, 8 or 9 months after storage. The samples were treated in exactly the same way as samples analyzed earlier. The petitioner reported that the results of analyses of intact plant samples after 6, 8 and 9 months show that the chromatographic profiles between the initial and storage stability samples are very similar. From these comparison of chromatographic profiles, the petitioner concluded that radioactive residues of XDE-570 in winter wheat are stable under conditions of storage for up to 9 months.

III. FINAL SUMMARY

In the metabolism study, [^{14}C]-DE-570 (>98%) formulated with EF 1343 blank formulation, radiolabeled as [^{14}C]-phenyl-XDE-570 and [^{14}C]-TP-XDE-570 was applied to winter wheat at crop growth stages of BBCH30 (stem elongation-early application) and BBCH49 (postflag leaf emergence/first awns visible-late application) at 50 g ai/ha. The rate used herein was equivalent to 10X the proposed Canadian label rate of 5 g ai/ha. The formulation used in metabolism study was identical to that used in the residue studies and that of proposed for registration. Winter wheat plants (10 plants/tub) were planted in sandy loam soil contained in tubs. ^{14}C-DE-570 formulation was applied to run-off to wheat plants using a spray gun. All tubs were placed outdoors, for the duration of the in-life phase of the study, in the lysimeter complex. In addition to natural precipitation, the plants were watered at the soil surface as required. Plants were harvested within 18 hours of treatment (day 0), 30 days after treatment and finally at crop maturity (129 days after BBCH 30 application and 65 days after BBCH 49).

The early application (BBCH 30 crop stage) sampling of immature whole wheat plant (0 day after application), the parent (71%, 2.9 ppm phenyl and 63%, 2.0 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (19%, 0.79 ppm phenyl and 24.6%, 0.027 ppm TP labelled TRR) and 4-OH-(phenyl)-DXD-570 (0.9%, 0.038 ppm phenyl and 0.84%, 0.027 ppm TP labelled TRR). A total of 91% of the phenyl and TP labelled TRR was identified. A total of 97% of phenyl and TP labelled TRR was extractable. A total of 5.3% (0.22 ppm) phenyl and 4.9%
(0.16 ppm) TP labelled TRR was not identified. However, this TRR consisted of several minor components, more polar than florasulam. In addition, a minor metabolite, 2-sulphonamide (< 1.5%, 0.048 ppm TP labelled TRR) was also identified.

The late application (BBCH 49 crop stage) sampling of immature whole wheat plant (0 day after application), the parent (84%, 0.57 ppm phenyl and 81%, 0.61 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (8.5%, 0.058 ppm phenyl and 8.5%, 0.064 ppm TP labelled TRR). A total of 90% of the TRR was identified. A total of 94% of the phenyl and TP labelled TRR was extractable. A total of 1.9% (0.014 ppm) phenyl labelled TRR was not identified. However, this

TRR consisted of several minor components, more polar than florasulam. In addition, minor metabolites 4-OH-(phenyl)-DXD-570 (1.2%, 0.0087 ppm phenyl and 0.4%, 0.003 ppm labelled TRR) and 2-sulphonamide (0.7%, 0.005 ppm TP labelled TRR) were also identified.

The early application (BBCH 30 crop stage) sampling of immature whole wheat plant (30 days after application), the parent (28.6%, 0.115 ppm phenyl and 27.4%, 0.109 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (20.6%, 0.083 ppm phenyl and 12.8%, 0.0513 ppm TP labelled TRR,), 4-OH-(phenyl)-DXD-570 (6.8%, 0.0274 ppm phenyl and 15.1%, 0.060 ppm TP labelled TRR). A total of 56% the phenyl and TP labelled TRR was identified. A total of 63.3% of the phenyl and 77.3% of the TP labelled TRR was extractable. A total of 2.7% (0.011ppm) phenyl labelled TRR consisted of unidentified metabolite. In addition, a minor metabolite, 2-sulphonamide (1%, 0.051 ppm TP labelled TRR) was also identified.

The late application (BBCH 49 crop stage) sampling of immature whole wheat plant (30 days after application), the parent (27%, 0.03 ppm phenyl and 32%, 0.041 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (41.5%, 0.051 ppm phenyl and 19%, 0.024 ppm TP labelled TRR). A total of 69% phenyl and 51% of TP labelled TRR was identified. A total of 69% of the phenyl and 78% of TP labelled TRR was extractable. A total of 26.5% (0.034 ppm) TP labelled TRR consisted of several minor components, more polar than florasulam. Each of these component was estimated to be less than 0.01 ppm. No other metabolite was detected.

The early application (BBCH 30 crop stage) sampling of mature wheat straw (129 days after application), no parent compound was identified. However, some metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (6.3%, 0.003 ppm phenyl and 2.5%, 0.0018 ppm TP labelled TRR,), 4-OH-(phenyl)-DXD-570 (8.4%, 0.0041 ppm phenyl and 1.6%, 0.0012 ppm labelled TRR) and 2-sulphonamide (4.7%, 0.0034 ppm TP labelled TRR). A total of 15% of phenyl and 8.8% of the TRR was identified. A total of 61.4% of the phenyl and 78.2% TP labelled TRR was extractable. A total of 45.8% (0.02 ppm) phenyl and 43% (0.03 ppm) TP labelled TRR consisted of several minor components, more polar than florasulam. Each of these component was estimated to be less than 0.01 ppm.

The late application (BBCH 49 crop stage) sampling of mature wheat straw (65 days after application), the parent (14%, 0.057 ppm phenyl and 7%, 0.02 ppm TP labelled TRR) and other major metabolites were identified as glucose conjugate of 4-OH-(phenyl)-DXD-570 (21.5%, 0.088 ppm phenyl and 13%, 0.041 ppm TP labelled TRR), 4-OH-(phenyl)-DXD-570 (14%, 0.059 ppm phenyl and 5.5%, 0.017 ppm labelled TRR) and 2-sulphonamide (19%, 0.058 ppm TP labelled TRR). A total of 50% phenyl and 44% TP labelled TRR was identified. A total of 59% of the phenyl and 79% TP labelled TRR was extractable. A total of 9.4% (0.039 ppm) phenyl and 5.3% (0.017 ppm) TP labelled TRR consisted of several minor components, more polar than florasulam. Each of these component was estimated to be less than 0.01 ppm.

Total radioactive residue level in grain was determined by combustion/LSC. The ^{14}C-residues were too low (0.03 ppm) to elucidate the nature of the TRRs in mature wheat ears and grain, therefore, no further attempt to characterize and identify the ^{14}C-residues was made.

The metabolism of XDE-570 in wheat proceeded via hydroxylation in the 4-position of phenyl ring with subsequent glucose conjugation. Additional degradation was followed by tentative cleavage of the sulphonamide bridge. The metabolites detected in wheat matrices were 4-OH-(phenyl)-florasulam, glucose conjugate of 4-OH-(phenyl)-florasulam and 2-sulphonamide. The 4-OH-(phenyl)-florasulam and glucose

conjugate of 4-OH-(phenyl)-florasulam were both present in rat metabolism. The metabolism study was conducted at 10x the proposed Canadian label rate (5 g ai/ha) and 2-sulphonamide metabolite was detected only in winter wheat straw (0.059 ppm) and not in the grain. The 2-sulphonamide metabolite is not considered to be of toxicological significance.

Based on the winter wheat metabolism study, the low levels of residues observed and considering exaggerated application rate (10X the proposed Canadian application rate), the residue of concern (ROC) may be defined as the parent compound, XD-570 (florasulam).

IV. CONCLUSIONS

Wheat plants were treated with [UL-phenyl-^{14}C]XDE-570 and [9- triazolopyrimidine-^{14}C]XDE-570 at the rate of 50 g ai/ha (10 x maximum Canadian proposed rate) at early and late applications at BBCH 30 and BBCH 49 growth stages, respectively. The wheat samples were collected and analysed for radioactive residues to determine the metabolic fate of XDE-570. The TRR found in the wheat samples in early application plants (BBCH 30) were found in immature plant (0 day application) at 4.1ppm and 3.2 ppm; immature plant at (30 days application) 0.4 ppm and 0.4 ppm; mature straw at 0.048 ppm and 0.073 ppm; mature ears at 0.0027 ppm and 0.008 ppm; and grain at 0.0013 ppm and 0.0022 ppm, for phenyl and TP labelled samples, respectively. The TRR found in the wheat samples in late application plants (BBCH 49) were found in immature plant (0 day application) at 0.68 ppm and 0.76 ppm; immature plant at (30 days application) 0.12 ppm and 0.13 ppm; mature straw at 0.41 ppm and 0.32 ppm; mature ears at 0.031 ppm and 0.03 ppm; and grain at 0.0024 ppm and 0.008 ppm, for phenyl and TP labelled samples, respectively. If the residues were extrapolated to the maximum Canadian proposed application rate of 10 g ai/ha, the values would be equivalent to 0.41 ppm and 0.32; 0.04 ppm and 0.04ppm; 0.0048ppm and 0.007 ppm; 0.0003 ppm and 0.0008 ppm; 0.0001 ppm and 0.0002 ppm in immature plant (0 day application), immature plant (30 day application), mature straw, mature ears and grain, for phenyl and TP labelled samples, respectively. A similar reduction of TRRs was noticed in the late application plant samples.

Therefore, the metabolism of XD-570 in winter wheat proceeded via hydroxylation in the 4-position of phenyl ring with subsequent glucose conjugation. Additional degradation was followed by possible cleavage across the sulphonamide bridge forming a number of small polar components. **Based on the winter wheat metabolism study, the low levels of residues observed and considering exaggerated application rate (10X the proposed Canadian Application rate), the Residue of Concern (ROC) may be defined as the parent compound, XD-570 (florasulam).**

V. DEFINITION OF THE RESIDUE OF CONCERN (ROC)

Based on the winter wheat metabolism study, the low levels of residues observed in grain (0.008 ppm) and considering exaggerated application rate (10X the proposed Canadian Application rate), the Residue of Concern (ROC) may be defined as the parent compound, XD-570 (florasulam).

VI. STUDY DEFICIENCIES

No deficiency was identified in the winter weat metabolism study.

Signatures:

Reviewed by: _____ _____
Ali Ismaily Date

Peer reviewed by: _____ _____
Henri Bietlot, Ph. D. Date

Section Head: _____ _____
Ariff Ally, Ph.D. Date