ANNEX B

Florasulam

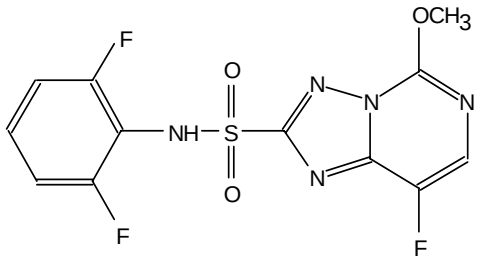
B.6 Residue data

Introductory Remarks :

Florasulam (DE-570) is a member of the 1,5c triazolopyrimidine sulfonanilides, a class of post-emergence herbicides known to inhibit the plant enzyme acetolactate synthase enzyme (ALS) which is a key enzyme in the biosynthesis of the branched chained amino acids isoleucine, leucine and valine.

This herbicide (N-(2,6-difluorophenyl)-8-fluoro-5-methoxy-(1,2,4)-triazolo-(1,5c)-pyrimidine-2-sulphonamide) is developed in Europe for the control of broadleaf weeds in cereals.

Figure : Structure of Florasulam (DE-570).



Two different forms of ^{14}C radiolabel were used, one uniformly labeled in the phenyl ring and the other labeled at the 9-position of the triazolopyrimidine (TP) ring.

Appendix D to this section contains the metabolic pathways with the structure of the metabolites as well as the chemical names of synthetic reference compounds used in the metabolism studies.

B.6.1. Metabolism, distribution and expression of residues in plants (Annex IIA 6.1)

B.6.1.1. Metabolism, distribution and expression of residues in winter wheat

The Metabolism of DE-570 in Winter Wheat - Final report (Pillar F., 1997)
Guidelines :
This study was conducted to meet the proposals submitted to the EC regarding Annex II and III of EC Directive 91/414/EEC.
GLP :
Yes.
Material and methods :
Test substances :
^{14}C-phenyl-Florasulam and ^{14}C -TP-Florasulam.
Experimental design :
Winter Wheat plants were treated at an application rate equivalent to 50 g a.s./ha at growth stages BBCH30 (stem elongation-early application) and BBCH49 (post flag leaf emergence/first awns visible-late application); 10 plants were treated respectively with each test substance and 10 other plants were left untreated as a control.
The rate used herein was equivalent to 6.7-10 times the proposed field rate.
The test substances were formulated as a suspension concentrate and were applied once to run-off to wheat plants using a spray gun.
Plants were harvested at days 0, 30 after treatment and finally at crop maturity (129 days and 65 days after BBCH 30 and BBCH 49 applications respectively).
At days 0 and 30, the immature plants were separated into shoot and root; this latter was not evaluated.
At maturity, the crops were sampled into straw, grain and chaff.

Extraction procedures :
The immature wheat plants were subjected to 3 sequential washes : an aqueous wash, a dichloromethane wash and a methanol wash.
Samples of maturity intact ears and straw were subjected to the same washing procedure.
The washed residues of the immature plants (day 0) and of the maturity ears were dried and homogenised prior to be extracted with acetonitrile/water.
The washed residues of the immature wheat plants (day 30) and of the mature straw were treated with solvents mixtures followed by further acid and base treatments.
The radioactivity associated with washed and extracted tissue samples was determined by combustion analysis.
Radioactivity in the extracts was measured by Liquid Scintillation Counting.
The grain and chaff were directly combusted to determine total radioactive residue levels.
The concentrated solvent washes and extracts were investigated by TLC using a non radiolabeled florasulam underspot and by HPLC (florasulam, 4-hydroxy(phenyl) florasulam and 2-sulphonamide were used as reference standards).
In order to quantify the incorporation of non extractable residues into lignin and cellulose, mature straw residues that had previously been surface washed and dried were extracted with acidified acetonitrile followed by an extraction with Potassium Permanganate or submitted to a 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.
Mass spectrometry was used for isolation of a glucose conjugate with confirmation of its identity by enzymatic hydrolysis using β-glucosidase.

Findings :

Table B.6.1-1 : Investigation of the nature and amounts of residues of Florasulam (DE-570) in winter wheat plants following foliar spray treatments at a rate corresponding to 50 g a.s./ha - Application growth stage : BBCH 30 (Residues expressed as mg Florasulam equiv./kg).

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	4.116	3.221	0.404	0.4	0.048	0.073	0.0027	0.00797
Washable radioactive residues									
Aqueous wash	mg/kg	2.697	1.833	0.117	0.143	0.0063	0.0207	0.00044	0.00376
	%TRR	65.53	56.92	28.99	35.88	13.11	28.36	16.16	47.38
DCM wash	mg/kg	0.231	0.212	0.031	0.045	0.00044	0.00123	0.00002	0.00018
	%TRR	5.64	6.59	7.67	11.29	0.91	1.68	0.66	2.30
Methanol wash	mg/kg	0.740	0.752	0.068	0.0625	0.0065	0.0143	0.00025	0.00016
	%TRR	17.99	23.37	16.96	15.62	13.47	19.53	9.38	2.01
Residues	mg/kg	0.446	0.422	0.187	0.148	0.035	0.036	0.00199	0.0038
	%TRR	10.85	13.12	46.38	37.21	72.51	50.44	73.80	48.31
Combined solvent extracted residues	mg/kg	0.310	0.323	0.184	0.133	0.013	0.019	0.00068	0.00154

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
	%TRR	7.6	10	45.4	36.6	26.8	26.0	25.22	19.19
Non extractable radioactive residues									
	mg/kg	0.135	0.099	0.0039	0.0027	0.022	0.0179	0.00131	0.00233
	%TRR	3.3	3.1	1.0	0.7	45.6	24.4	48.58	29.12
Total recovery (washed fractions + extracted fractions + residual radioactivity)									
Total	mg/kg	4.113	3.219	0.4039	0.4055	0.0482	0.073	0.0027	0.00797
	%TRR	100.06	99.98	100.02	100.09	99.89	99.97	100.0	100.0

B.6.1-2 : Elucidation of total extractable radioactive residues - Residues expressed as mg Florasulam equiv./kg - BBCH 30

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	2.919	2.033	0.115	0.109	-	-
	% TRR	70.9	63.1	28.6	27.4	-	-
2-sulphonamide*	mg/kg	-	0.048	-	0.0042	-	0.0034
	% TRR	-	1.5	-	1.0	-	4.7
Glucose conjugate of 4-HO (phenyl) - DE- 570	mg/kg	0.795	0.794	0.083	0.0513	0.003	0.0018
	% TRR	19.4	24.6	20.6	12.8	6.3	2.5
4-OH-phenyl-DE-570*	mg/kg	0.0386	0.0271	0.0274	0.0604	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	0.0185	0.084	0.0004	0.0194
	% TRR	0.3	1.9	4.6	21	0.9	26.5
Unidentified metabolites**	mg/kg	0.216	0.1578	0.0112	-	0.0222	0.0313
	% TRR	5.3	4.9	2.7	-	45.8	42.9
Total Extractable	mg/kg	3.979	3.121	0.2551	0.308	0.0297	0.0571
	% TRR	96.8	96.8	63.3	77.3	61.4	78.2
Total identified metabolites	mg/kg	3.752	2.902	0.2254	0.2249	0.0071	0.0064
	% TRR	91.2	90.04	56	56.3	14.7	8.8

- : 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 B.6.1-3 : Investigation of the nature and amounts of residues of Florasulam (DE-570) in winter wheat plants following foliar spray treatments at a rate corresponding to 50 g a.s./ha - Application growth stage : BBCH 49 (Residues expressed as mg Florasulam equiv./kg).

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	0.680	0.756	0.123	0.126	0.412	0.315	0.0307	0.0303
Washable radioactive residues									
Aqueous wash	mg/kg	0.323	0.482	0.042	0.060	0.136	0.157	0.00851	0.0139
	%TRR	47.6	63.8	34.6	47.7	33.1	49.8	27.69	46.02
DCM wash	mg/kg	0.206	0.153	0.005	0.006	0.0089	0.0112	0.00064	0.00062
	%TRR	30.3	20.2	4.1	5.2	2.2	3.6	2.09	2.06
Methanol wash	mg/kg	0.059	0.037	0.025	0.022	0.0539	0.041	0.0052	0.0024
	%TRR	8.7	5.0	20.4	17.6	13.1	13.3	17.10	7.93
Residues	mg/kg	0.0913	0.0827	0.0503	0.0374	0.213	0.105	0.0163	0.0133
	%TRR	13.41	10.94	40.88	29.53	51.68	33.36	53.12	44.0
Combined solvent extracted residues	mg/kg	0.0477	0.0356	0.0335	0.029	0.0444	0.062	0.00187	0.00349
	%TRR	7.01	4.72	27.3	22.9	10.8	19.9	6.08	11.49
Non extractable radioactive residues									
	mg/kg	0.043	0.047	0.0168	0.0085	0.168	0.042	0.0144	0.0098
	%TRR	6.4	6.22	13.6	6.7	41	13.6	47.04	32.51
Total recovery (washed fractions + extracted fractions + residual radioactivity)									
	mg/kg	0.678	0.754	0.122	0.125	0.411	0.313	0.0306	0.0302
	%TRR	100.01	99.94	100.0	100.1	100.2	100.2	100.0	100.01

B.6.1-4 : Elucidation of total extractable radioactive residues - Residues expressed as mg Florasulam equiv./kg - BBCH 49

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	0.570	0.610	0.0336	0.0409	0.0572	0.0224
	% TRR	83.9	80.7	27.3	32.3	13.9	7.1
2-sulphonamide*	mg/kg	-	0.0053	-	-***	-	0.0587
	% TRR	-	0.7	-	-***	-	18.6
Glucose conjugate of 4-HO(phenyl) - DE-570	mg/kg	0.0577	0.0639	0.0511	0.0243	0.0883	0.0411
	% TRR	8.5	8.5	41.5	19.1	21.5	13.1
4-OH-(phenyl)-DE-570*	mg/kg	0.0087	0.0029	-	-	0.0593	0.0173
	%TRR	1.2	0.4	-	-	14.4	5.5
Polar components	mg/kg	-	0.0117	-	0.0336	-	0.0925
	% TRR	-	1.6	-	26.5	-	29.3
Unidentified metabolites**	mg/kg	-	0.0142	-	-	0.0387	0.0167
	% TRR	-	1.9	-	-	9.4	5.3
Total Extractable	mg/kg	0.6364	0.708	0.0847	0.0988	0.2435	0.2487
	% TRR	93.6	93.7	68.8	77.9	59.2	78.9
Total identified metabolites	mg/kg	0.6364	0.6821	0.0847	0.0652	0.2048	0.1395
	% TRR	93.6	90.3	68.8	51.4	49.8	44.3

- : 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 curiously not radiodetected at late application in the case of the ^{14}C TP labeling in immature wheat plants (PHI : 30 days).

Aqueous and organic soluble radioactive residues from plants harvested at day 0 indicated that up to 86% TRR could be washed from the surface of the plants.
63% to 84% TRR were recovered as unchanged Florasulam while the glucose conjugate of the hydroxylated florasulam accounted for between 9% to 25% TRR. A small amount of radioactivity was tentatively assigned as the 2-sulphonamide.
At 30 days application, in early application plants, the total radioactive residues comprised predominantly the parent compound (28% TRR) with increased amounts of the glucose conjugate moiety (13% to 21% TRR) and also the tentative 4-OH(phenyl)-Florasulam (7% to 15% TRR).
In plants harvested at maturity, residues levels in the mature wheat grains were extremely low considering the elevated application rate used in this study (values ranging between 0.0008 mg/kg and 0.00238 mg/kg for both the 2 application timings). Due to these low levels, it was not possible to complete further investigation of the nature of the residues in grain.
In straw at maturity, the parent compound was not present in early application plants while small amounts of the glucose conjugate was observed (2.5%TRR). Polar components including a few quantity of the tentative 2-sulphonamide metabolite formed the major part of the residues.

In plants treated at the late application, the glucose conjugate moiety remained the predominant single component with 21% TRR. The parent compound and the tentatively assigned 2-sulphonamide were present at respectively 14% and 18% TRR.

Investigation of incorporation of non extractable radioactive residues into natural matrices (lignin and cellulose)

2 immature wheat plants (day 30) and 2 maturity wheat straw samples at early plants application were selected at random and were investigated for the determination of "bound" radioactivity in the natural matrices.
The results showed that approximately 4 % TRR was associated with cellulose regardless of harvest interval and radiolabeled treatment.
Material associated with lignin corresponded to 25% and 27% TRR respectively in maturity straw samples and in wheat plants harvested 30 days after the treatment.
Conclusion :
The metabolic pathway of florasulam in winter wheat has been established (See figure 2 in appendix D to this section).
The parent compound is shown to be rapidly metabolized through hydroxylation in the 4-position of the phenyl ring followed by glucose conjugation.
The metabolism of Florasulam in wheat plants consists in a rapid hydroxylation and subsequent glucose conjugation of the hydroxylated phenyl parent molecule. These reactions are followed by possible cleavage across the sulphonamide bridge forming a number of small polar components.
Only the tentative 4-OH-(phenyl)-Florasulam was a metabolite found both in wheat and rat.
The glucose conjugate moiety and the tentative 2-sulphonamide were not recovered in rat metabolism.
Finally, residue levels in the grain were extremely low in plants treated at either application timing.
It can be concluded that there is minimal transport or storage of Florasulam in the grain.

B.6.2 Metabolism, distribution and expression of residues in livestock

B.6.2.1 Metabolism, distribution and expression of residues in lactating goats

Nature of the residues of (^{14}C)Florasulam in Lactating Goats (Barnekow D.E., Huskin M.A., 1994a)
Guidelines :
EPA/OECD Subdivision O, Residue Chemistry, Section 171-4 (b) (3).
GLP :
Yes.
Material and methods :
Test substances : ^{14}C-aniline-Florasulam and ^{14}C-TP-Florasulam. These were refered as ^{14}C"A" and ^{14}C"TP" labels respectively.
Experimental design :
Two lactating dairy goats (*Capra hircus*) were orally dosed once daily for 5 consecutive days.
Each animal received a dietary exposure equivalent to approximately 11 mg/animal/day of test material which represented nearly 340 x the dietary exposure calculated for dairy animals.
A third goat served as a control and was similarly dosed with a placebo capsule.
Within 24 hours after the last dose, the 3 goats were sacrificed and tissues (fat, muscle, liver and kidney) were collected for residue analysis and metabolites characterization.
Milk was collected twice daily; the excreta (feces and urine) were also collected daily.
Extraction and analysis procedures :
Total radioactive residues in the tissues, milk, urine and faeces were determined by combustion analysis and/or liquid scintillation counting.
Appropriate biphasic extractions of tissue samples were made to give organic, aqueous and non extractable fractions.
The aqueous fraction was partitioned against ethyl acetate following by chromatographic analysis by reverse phase HPLC and normal phase TLC (non-labeled standards of Florasulam, 5-OH(phenyl) Florasulam, 2-sulphonamide were used as references).
Enzymatic action (protease) and EtoAc partitioning were applied on the post extraction solids of liver as this fraction

contained high amounts of radioactivity. The EtoAc soluble residues released by this way were submitted to the same analytical methods.

Findings :

Table B.6.2.1-1 : Recovery of radioactivity from goats after oral administration of ^{14}C-aniline or ^{14}C-Triazolopyrimidine-9-Florasulam (in mg Florasulam equiv./kg).

	^{14}C"A" treated goat I		^{14}C"TP" treated goat II	
Tissues	**mg/kg**	**% of total dose**	**mg/kg**	**% of total dose**
Urine	4.61	72.6	3.52	70.9
Cage washing	0.265	0.072	0.587	0.122
Faeces	2.33	15.8	2.34	12.1
Total excretion	*7.205*	*88.472*	*6.447*	*83.122*
Milk	0.016	0.052	0.033	0.085
Liver	0.033	0.0275	0.023	0.023
Kidney	0.069	0.0096	0.039	0.0073
Muscle	0.0016	0.024	0.0009	0.0153
Fat	0.0016	0.0079	0.0017	0.0092
Blood	0.007	0.0135	0.00528	0.0109
Total recovery	7.33	88.60	6.54	83.27

24 hours after the last dose, more than 83% of the total administered radioactivity was recovered in excreta, milk and tissues from both the 2 treated goats.

There is no explanation for the lacking of 12% and 17% of the total dose in the case respectively of goat I and goat II.

The amount of radioactivity recovered in milk and in edible tissues was only 0.15% of the total dose.

The residue levels in tissues were the highest in liver and kidney (respectively 0.023-0.033 mg and 0.039-0.069 mg Florasulam equiv./kg for the 2 labeling positions).

Table B.6.2.1-2 : Investigation of the nature and amount of residues of Florasulam in excreta, milk and edible tissues of goats. (Residues expressed as mg Florasulam equiv./kg).

Tissues	**Urine**		**Milk**		**Liver**		**Kidney**	
Goat reference	^{14}C"A"	^{14}C"TP"	^{14}C"A"	^{14}C"TP"	^{14}C"A"	^{14}C"TP"	^{14}C"A"	^{14}C"TP"
Total radioactive residues (mg Florasulam equiv./kg)	4.61	3.526	0.016	0.033	0.033	0.023	0.069	0.039
Extractability of radioactive residues (% TRR)								
Acetone phase	na	na	97.7	95.6	na	na	na	na
(Acetonitrile/water : 80/20) phase	na	na	na	na	23.2	22.4	104.4	102.5
Hexane phase	na	na	<0.62	<0.3	<2.7	<0.86	<2.3	<4.1

Tissues	Urine		Milk		Liver		Kidney	
Goat reference	^{14}C"A"	^{14}C"TP"	^{14}C"A"	^{14}C"TP"	^{14}C"A"	^{14}C"TP"	^{14}C"A"	^{14}C"TP"
Ethyl acetate partition of extracted residues (% TRR)								
EtoAc partition phase*	97.6	97.5	89.4	87.6	18.6	18.5	98.2	101.1
Elucidation of radioactive residues (% TRR)								
Parent compound	96.1	96.6	89.4	87.6	15.22	15.27	95.79	98.31
Tentative 5-OH-Florasulam	0.90	-	-	-	1.01	1.04	2.25	1.48
Aqueous soluble phase	-	-	2.4	3.4	2.8	3.0	1.7	1.4
Post extraction residues (%TRR)	na	na	3.8	5.9	81.8	86.95	2.2	2.2
Protease digestion (%TRR)								
	Not performed				71.87	75.55	Not performed	
Ethyl acetate partition of released residues (%TRR)								
EtoAc soluble released residues	Not performed				7.55	7.47	Not performed	
Aqueous soluble released residues					29.26	41.57		
Final solid residues (%TRR)					37.25	28.34		
Balance : extracted phases + post extraction residues (%TRR)								
	97.6	97.5	101.5	101.5	105	109.35	106.6	104.7

- : Not radiodetected.
na : Not applicable.
* : Fraction used for TLC and reverse phase HPLC analysis.

97% TRR were extracted with ethyl acetate from urine and up to 95%TRR with acetone from milk.
Extractability of radioactivity in liver and kidney were 23% and 104%TRR respectively.
A protease digestion on the post extraction solids of liver released up to 71%TRR for both the 2 treated goats.
The parent compound was identified as the major constituant of the residue in urine (96%TRR), in milk (more than 87%TRR), in liver (15%TRR) and in kidney (up to 95%TRR).
No further investigation on the released radioactive fraction in liver following protease digestion was conducted.
The metabolite 5-OH-Florasulam was tentatively identified in liver and in kidney but its structure was not confirmed.

Conclusion :

Up to 83% of the total administered radioactivity was eliminated in excreta (urine+faeces).
The parent compound was slightly metabolized and remained the major constituant of the residue in urine, milk and kidney.
The metabolic pathway of Florasulam in goats is presented in figure 3 in appendix D to this section.
No significant cleavage of the sulfonanilide bridge occurred in the metabolism of Florasulam in goats.
The very low residue levels in milk and edible tissues combined with a major excretion of the parent compound demonstrated that the residues of Florasulam did not bioconcentrate in the goat tissues.
The metabolism of Florasulam in lactating goat is considered as similar to the metabolism in rat.

B.6.2.2 Metabolism, distribution and expression of residues in laying hens.

Nature of the Residue of ^{14}C-Florasulam in Laying Hens (Barnekow D.E., Huskin M.A., 1994b)

Guidelines :

EPA/Guideline Subdivision O, Residue Chemistry, Section 171-4 (b) (3).

GLP :

Yes.

Material and methods :

Test substances : ^{14}C-aniline-Florasulam and ^{14}C-TP-Florasulam. These were refered as ^{14}C"A" and ^{14}C"TP" labels respectively.

Experimental design :

Two groups of 10 laying hens each were orally dosed once daily with either the ^{14}C"A" treated or the ^{14}C"TP" treated Florasulam for 5 consecutive days.

Each hen received a dietary exposure of 11 mg/animal/day of test material which corresponded to approximately 10000 x the maximum dietary exposure for poultry consuming diets with the expected levels of residues of Florasulam in grain.

An other group of 10 hens served as a control group and was dosed with placebo capsules twice daily for 5 consecutive days.

The hens were sacrificed within 24 hours after the last administration.

Skin, liver, fat and composite muscle were collected for residue analysis and metabolites identification.

Eggs and excreta were collected twice a day from each group.

Extraction and analysis procedures :

The total radioactive residues in the edible tissues, eggs and excreta were determined by combustion analysis and/or Liquid Scintillation Counting. The metabolism of Florasulam in liver, fat and muscle was not further investigated due to the extremely low radioactivity.

A balance of the administered dose was established for the hens of the 2 groups.

Eggs (yolk and white were not dissociated), skin and excreta (urine, faeces and cage washings) were extracted with acetonitrile/water (80/20) with subsequent ethyl acetate partitioning for eggs and skin.

The ethyl acetate extracts of eggs and skin and the excreta extracts were analysed by reverse phase HPLC and normal phase TLC using reference substances (non-labeled Florasulam, 5-OH-(phenyl)-Florasulam, 2-sulphonamide).

Findings :

Table B.6.2.2-1 : Recovery of radioactivity from hens after oral administration of ^{14}C-aniline or ^{14}C-Triazolopyrimidine-9-Florasulam (in mg Florasulam equiv./kg).

	^{14}C"A" Hens I		**^{14}C"TP" Hens II**	
Tissues	**TRR (mg a.s. equiv./kg)**	**% of total dose**	**TRR (mg a.s. equiv./kg)**	**% of total dose**
Excreta	10	91.3	11.5	96.9
Eggs	0.0038	0.013	0.0043	0.013
Skin	0.0066	0.002	0.0050	0.002
Liver	<0.0014*	<0.001	<0.00097*	<0.001
Composite fat	<0.00043*	<0.001	<0.00059*	<0.001
Composite muscle	<0.00048*	<0.001	<0.00078*	<0.001
TOTAL	10.010	91.31	11.50	96.91

* : Tissue residue levels below the experimental minimum quantifiable amount.

Notes :

- The egg samples were selected from those with the highest dpm/g value in the preliminary tissue combustion analysis.
-Skin, although not considered as an edible tissue, was analysed because of its higher level of radioactive residues.

Table B.6.2.2-2 : Investigation of the nature and amount of residues of Florasulam in excreta, skin and eggs of the ^{14}C"A" and ^{14}C"TP" treated laying hens.

Sample	Excreta		Eggs		Skin	
Hen reference	^{14}C"A"	^{14}C"TP"	^{14}C"A"	^{14}C"TP"	^{14}C"A"	^{14}C"TP"
TRR (mg/kg)	10.0	11.5	0.0038	0.0043	0.0066	0.0050
Extractability of radioactive residues (% TRR)						
Acetonitrile/water : 80/20 phase	103	84.7	98.2	102	95.4	96.4
Ethyl acetate partition of extracted residues (%TRR)						
EtoAc partition phase*	na	na	95.6	96.2	89.7	89.9
Elucidation of radioactive residues (% TRR)						
Parent compound	95.1	79.7	95.1	95.2	85.9	80.7
5-OH-Florasulam	-	-	-	-	-	-
2-sulphonamide	-	-	-	-	-	-
Unidentified metabolites 1	-	-	-	<1.7	<1.7	4.8
Unidentified metabolites 2	-	-	-	-	<1.7	<2.9
Unidentified metabolites 3	6.8	4.5	-	-	-	-
Unidentified metabolites 4	<1.0	-	<1.7	-	<1.7	<2.9
Total	101.9	84.2	95.1	95.2	85.9	85.5
Aqueous soluble phase	na	na	-	-	-	-
Residual radioactive residues (% TRR)						
	1.2	2.1	-	-	-	-
Balance : extracted phase + residual radioactive residues (%TRR)						
	104.2	86.8	98.2	102	95.4	96.4

na : Not applicable.
- : Not radiodetected.
(*) : Fraction used for TLC and HPLC analysis.

24 hours after the last dose, up to 91% of the total administered radioactivity were recovered in excreta, eggs and tissues (Table B.6.2.2-1) for both the 2 labeling positions.
The amount of radioactivity recovered in eggs and tissues was 0.017% of the total dose.
Total radioactive residues in edible tissues demonstrated the presence of very low levels of residues ranging between 0.004 and 0.007 mg Florasulam equiv./kg in skin and eggs.
The other tissue residue levels were below the experimental limit of quantification.
The extractability of radioactive residues ranged between 84% and 103% of TRR for excreta, eggs and skin (Table B.6.2.2-2).
The parent compound was found to be the major constituant of the residues in tissues samples with amounts ranging from 80% to 95% of TRR.

Conclusion :
The major amount of the radioactivity was eliminated in the excreta (91.3-96.9% of the total dose) as unchanged parent compound. This reflected a slight metabolization of the active substance.
The highest level of radioactive residues was recovered in the eggs with 0.013 % of the total dose for both the 2 treated hens groups.
Therefore, the residues of Florasulam have no tendency to bioconcentrate.
The metabolic pathway of Florasulam in hens is similar to the metabolic pathways described in goat and in rat and is presented in figure 3 in appendix D to this section.

B.6.2.3 Metabolism, distribution and expression of residues in pigs

No particular degradation pathway has been observed in goats and hens in comparison to rats.
Consequently, a pig metabolism study is not required.

B.6.3 Definition of the residue

In plants :

Total radioactive residues in wheat grain at maturity were exceptionally low and as a result, no further investigation of the nature of the residues was conducted.
In straw at maturity, no Florasulam was observed in early application plants with only small amounts of the glucose conjugate moiety.
Several polar components were observed including tentative 2-sulphonamide and 4-OH-(phenyl)-Florasulam suggesting a rapid metabolization of Florasulam with a cleavage across the sulphonamide bridge.
In late application plants, the parent molecule, the glucose conjugate moiety and the tentatively identified metabolites were present accounting for very low levels.

In view of these low levels of residue and considering exaggerated application rate, the residue definition for monitoring for wheat grain and straw is proposed as the parent compound.

A method of analysis is available for the parent compound in plants products.

No conversion factor for assessment of consumer safety (calculation based on the ratio extractable residues/residue to be monitored) could be established as the characterization of the metabolites in mature wheat grain was not possible.

In livestock :

The metabolism in lactating goats and laying hens indicated a slight metabolization of Florasulam.
Quantifiable levels of radioactivity in edible tissues were found in goat milk, liver and kidney and in hen eggs, skin. The major constituant of the total residues was the parent molecule in excreta, milk, eggs and edible tissues.
Unknown metabolites were also observed in goats and hens but their amounts were too low for further characterization.
There was no major difference in the behaviour of Florasulam between the phenyl and the triazolopyrimidine labels. Therefore, the sulphonamide bridge cleavage did not seem to occur to any significant extent.

The residue definition for monitoring is proposed as the parent compound alone although residue levels in edible tissues are predicted to be very low.

No method of analysis is submitted for foodstuffs of animal origin. The notifier states that the residue levels in edible tissues are predicted to be very low and not present at levels which would be appropriate for monitoring (Livestock feeding studies are not required).

The conversion factors for assessment of consumer safety (calculation based on the ratio extractable residues/residue to be monitored) is :
-For milk, liver and kidney : 1
-Eggs : 1

Regarding the liposolubility of the defined residue (parent compound alone), no fat soluble Florasulam residue could be drawed with the value of the partition coefficient n-octanol/water of Florasulam which is <3 (Log P*ow* = 1.00 at PH4 and Log P*ow* = -1.22 at PH 7).

B.6.4 Use pattern

Florasulam is a post-emergence herbicide effective against broadleaf weeds (mainly *Galium aparine*, *Stellaria media, Matricaria spp.*). Spray concentrations were calculated taking into account a broadcast application with medium volume.

Table B.6.4-1 : Intended uses of Florasulam - Spray formulations - **SC (50 g a.s./L)**

Crop Disease	**Country (Northern/Southern Europe)**	**Rate of application (g a.s./ha)**	**Maximum rate per season (g a.s./ha)**	**Spray concentration (g/hl)**	***Maximum nber of applic. / season *Growth stage at last application**	**Spray interval in days**	**Pre-harvest interval in days**
Spring &winter Wheat/Barley/ Oats/Rye Triticale (*)	N	4.0-7.5	4.0-7.5	1.875-2	1 EC 39(?)	-	NA
Spring &winter Wheat/Barley/ Oats/Rye Triticale	S	0.5-7.5	0.5-7.5	1.25-1.66	1 (Treatment may be split when range of emergence of weeds Maximum treatment to crop is 7.5 g a.s./ha) BBCH 49 (first awns visible)	-	NA
Spring &winter Wheat/Barley/ Oats/Rye Triticale	N	2.5-7.5	2.5-7.5	1.875-2.5	1 BBCH 39 (Flag leaf stage : flag leaf fully unrolled, ligule just visible)	-	NA
Spring &winter Wheat/Barley/ Oats/Rye Triticale	N	0.5-7.5	0.5-7.5	1.25-1.66	1 (Treatment may be split when range of emergence of weeds maximum treatment to crop is 7.5 g a.s./ha) BBCH 49 (first awns visible)	-	NA

Crop Disease	Country (Northern/Southern Europe)	Rate of application (g a.s./ha)	Maximum rate per season (g a.s./ha)	Spray concentration (g/hl)	*Maximum nber of applic. / season *Growth stage at last application	Spray interval in days	Pre-harvest interval in days
Spring &winter Wheat/Barley/ Oats/Rye Triticale	N	2.5-7.5	2.5-7.5	1.25-1.875	1 BBCH 39 (Flag leaf stage : flag leaf fully unrolled, ligule just visible)	-	**NA**
Spring &winter Wheat/Barley/ Oats/Rye Triticale Undersown cereals	N	2.5-7.5	2.5-7.5	1.875-5	1 (Treatment may be split when range of emergence of weeds Maximum treatment to crop is 7.5 g a.s./ha) BBCH 49 (first awns visible)	-	**NA**
Winter Wheat/Barley/ Oats/Rye Triticale	N	2.5-5.0	2.5-5.0	1.66-2.5	1 BBCH 32 (Node 2 at least 2 cm above node 1)	-	**NA**
Spring &winter wheat	S	5.0-7.5	5.0-7.5	1.5-1.66	1 BBCH 49 (first awns visible)	-	**NA**
Spring &winter wheat/Barley	S	3.75-5.0	3.75-5.0	1.25-1.875	1 BBCH 36 (Node 6 at least 2 cm above node 5)	-	**NA**
Winter wheat/Spring &winter Barley Durum wheat	S	3.75-5.0	3.75-5.0	1.0-1.25	1 BBCH 36 (Node 6 at least 2 cm above node 5)	-	NA

NA : Not applicable for these GAPs - PHI determined by the stage of application.

B.6.5 Identification of critical GAPs

The conditions leading to realistic worst-cases for residue levels in grain and straw are indicated in the table herebelow. These critical GAPs were taken into consideration during the evaluation of supervised field trials.

Crop	N/S Europe	Application rate (g a.s./ha), Number of applic., PHI	Treatment stage
Spring & winter wheat	N/S	7.5, 1 applic., PHI determined by the stage of application	BBCH 49
Spring & winter barley, oat, rye, triticale	N/S	7.5, 1 applic., PHI determined by the stage of application	BBCH 49
Durum wheat	S	5.0, 1 applic., PHI determined by the stage of application	BBCH 36

B.6.6 Residues resulting from supervised trials (Annex IIA 6.3; Annex IIIA 8.1)

Preliminary remarks.

A total number of 42, 38 and 5 trials were provided respectively for winter wheat, winter barley and durum wheat
Samples of green plants were taken at different PHIs up to normal harvest time. Grain and straw were sampled at maturity.
The residues of Florasulam in whole plant, grain and straw were determined using the Analytical Method ERC 95.6 (HPLC using UV absorbance detection at 260 nm) which had a lowest validated level of quantification of 0.01 mg/kg for grain and 0.05 mg/kg for whole plant and straw.
All residue values which were < 20 % of the lowest validated level-LOQ (<0.002 mg/kg and <0.01 mg/kg respectively for grain and straw/whole plant) were classified as “not detected” in the residue trials.
All these studies were conducted under GLP conditions.

The intended uses and the residue data are summarized according to the standard summary sheets in appendix F to this section. The figures selected for MRL proposals are in bold and underlined in the summary sheets.

Table B.6.6-1 : Summary and characterization of the supervised residue trials

Application rate (g a.s./ha)	Number of applications	Growth stage at application	Zone	Number of trials		
				winter wheat	winter barley	durum wheat
4.6	1	31	S	-	1	-
5	1	30,31,32-33	S	8(1)	-	-
5	1	31,32,33-43	S	-	8(5)	-
5	1	23-32,32-33	S	-	-	2
7.5	1	32	N	11	11(2)	-
			S	3	3	1
7.5	1	49	N	7	6	-
			S	1	2(1)	-
7.5	2: Split treatment with a total rate of 7.5 g a.s./ha/season	32 and 49	N	5	1	-
			S	1	-	-
7.5	2	32 and 49	N	4	5	-
			S	-	1	-
10	1	31,43	N	2	-	-
10	1	31-32,34	S	-	-	2
Total number of trials			N	29	23	-
			S	13	15	5

( ) : Number of the trials in which 0.1% polyglycol or Agral adjuvant was added as a tank mix.

B.6.6.1 Residues resulting from supervised trials - Winter wheat

Residues of XDE-570 in Winter Soft Wheat at Intervals Following a Single or Double Application of EF-1343, Northern France - 1995 (Butcher S., Gibson R., 1996b)
Residues of XDE-570 in Winter Wheat at Intervals Following a Single or Double Application of EF-1343, UK - 1995 (Butcher S., Gibson R., 1996a)
Residues of XDE-570 in Winter Wheat at Intervals Following a Single or Double Application of EF-1343, Germany - 1996 (Gambie A., Butler R.E., 1997aa)
Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single or Double Application of EF-1343, UK - 1995 (Final Report)(Gambie A., Butler R.E., 1997j)
Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single or Double Application of EF-1343, Germany - 1996 (Gambie A., Butler R.E., 1997l)
Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single or Double Application of EF-1343, UK - 1996 (Gambie A., Butler R.E., 1997m)
Residues of DE-570 in Winter Soft Wheat at Intervals Following a Single Application of EF-1343, Northern France - 1996 (Gambie A., Butler R.E., 1997c)
Residues of XDE-570 in Winter Wheat at Intervals Following a Single Application of EF-1343, Germany - 1995 (Butcher S., 1996g)
Residues of XDE-570 in Winter Soft Wheat and Soil at Harvest Following a Single Application of EF-1343, Northern France - 1996 (Gambie A., Butler R.E., 1997n)
Residues of XDE-570 in Grain, Straw and Soil at Harvest Following a Single Application of EF-1343 to Winter Wheat, Germany - 1995 (Gambie A., Butler R.E., 1997o)
Residues of XDE-570 in Winter Wheat at Harvest Following a Single Application of EF-1289, UK - 1994 (Butcher S., 1996a)
Residues of XDE-570 in Winter Soft Wheat at Intervals Following a Single or Double Application of EF-1343, Southern France - 1995 (Butcher S., 1996d)
Residues of DE-570 in Winter Soft Wheat at Intervals Following a Single Application of EF-1343, Southern France - 1996 (Gambie A., Butler R.E., 1997d)
Residues of XDE-570 in Winter Soft Wheat and Soil at Harvest Following a Single Application of EF-1343, Southern France - 1996 (Gambie A., Butler R.E., 1997p)
Residues of DE-570 in Winter Durum Wheat at Harvest Following a Single Application of EF-1343, Southern France - 1996 (Gambie A., Butler R.E., 1997e)
Residues of XDE-570 in Winter Wheat at Intervals Following a Single Application of EF-1343, Italy - 1995 (Butcher S., 1996e)
Residues of XDE-570 in Winter Wheat at Intervals Following a Single Application of EF-1343, Italy - 1996 (Gambie A., Butler R.E., 1997f)
Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single Application of EF-1343, Italy - 1995 (Gambie A., Butler R.E., 1997q)
Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single Application of EF-1343, Spain - 1995 (Gambie A., Butler R.E., 1997k)
Residues of DE-570 in Winter Wheat at Harvest Following a Single Application of EF-1343, Spain - 1996 (Gambie A., Butler R.E., 1997a)
Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single Application of EF-1343, Italy - 1996 (Gambie A., Butler R.E., 1997r)

North :
11 residue trials are in accordance with the critical GAP of 7.5 g a.s./ha, 1 application at BBCH 49.
The residue values are :
11 x <0.002 mg/kg for grain and 11 x <0.01 mg/kg for straw.

South :
2 residue values supported the critical GAP of 7.5 g a.s./ha, 1 application at BBCH 49.

The residue values are :
<0.002, <0.002 mg/kg for grain,
<0.01, <0.01 mg/kg for straw.

In all trials covering Northern and Southern Europe, the residues of Florasulam in grain and straw were below the LOQ (0.01* mg/kg and 0.05* mg/kg respectively).

MRL proposal for grains : 0.01* mg/kg.

B.6.6.2 Residues resulting from supervised trials - Durum Wheat

Residues of XDE-570 in Durum Wheat at Harvest Following a Single Application of EF-1289, Southern France - 1994 (Butcher S., 1996f)
Residues of DE-570 in Winter Durum Wheat at Harvest Following a Single Application of EF-1343, Southern France - 1996 (Gambie A., Butler R.E., 1997e)

South :
3 residue values supported the critical GAP of 5.0 g a.s./ha, 1 application at BBCH 36.
The residue values are :
<0.002, <0.002, <0.002 mg/kg for grain,
<0.01, <0.01, <0.01 mg/kg for straw.

The residues of Florasulam in grain and straw were below the LOQ (0.01* mg/kg and 0.05* mg/kg respectively).

MRL proposal for grains : 0.01* mg/kg.

B.6.6.3 Residues resulting from supervised trials - Winter Barley

Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, Northern France - 1995 (Butcher S., Gibson R., 1996c)
Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, Germany - 1996 (Gambie A., Butler R.E., 1997ab)
Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, UK - 1996 (Gambie A., Butler R.E., 1997g)
Residues of XDE-570 in Winter Barley at Harvest Following a Single or Double Application of EF-1343, Germany - 1996 (Gambie A., Butler R.E., 1997s)
Residues of XDE-570 in Winter Barley at Harvest Following a Single or Double Application of EF-1343, UK - 1995 (Final Report)(Gambie A., Butler R.E., 1997t)
Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single or Double Application of EF-1343, UK - 1996 (Gambie A., Butler R.E., 1997u)
Residues of XDE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Germany - 1995 (Butcher S., 1996h)
Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Northern France - 1996 (Gambie A., Butler R.E., 1997v)
Residues of XDE-570 in Grain, Straw and Soil at Harvest Following a Single Application of EF-1343 to Winter Barley, Germany - 1995 (Gambie A., Butler R.E., 1997w)
Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, Southern France - 1995 (Butcher S., 1996b)
Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single or Double Application of EF-1343, Southern France - 1995 (Gambie A., Butler R.E., 1997x)

Residues of DE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Southern France - 1996 (Gambie A., Butler R.E., 1997h)
Residues of XDE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Italy - 1995 (Butcher S., 1996c)
Residues of DE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Italy - 1996 (Gambie A., Butler R.E., 1997b)
Residues of DE-570 in Winter Barley at Harvest Following a Single Application of EF-1343, Italy - 1996 (Gambie A., Butler R.E., 1997i)
Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Italy - 1995 (Gambie A., Butler R.E., 1997y)
Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Spain - 1995 (Gambie A., Butcher S., Gibson R., 1996)
Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Spain - 1996 (Gambie A., Butler R.E., 1997z)

North :
6 residue trials were in accordance with the critical GAP of 7.5 g a.s./ha, 1 application at BBCH 49.
The residue values are :
6 x <0.002 mg/kg for grain and 6 x <0.01 mg/kg for straw.

South :
6 residue values supported the critical GAP of 7.5 g a.s./ha, 1 application at BBCH 49.
The residue values are :
6 x <0.002 mg/kg for grain and 6 x <0.01mg/kg for straw.

The residues of Florasulam in grain and straw for Northern and Southern Europe were below the LOQ (0.01* mg/kg and 0.05* mg/kg respectively).

MRL proposal for grains : 0.01* mg/kg.

Conclusion :
The supervised trials which were realized in cereal crops according to the critical GAP (1 applic., 7.5 g a.s./ha at BBCH 49) revealed that no residues were detected in the straw and the grain (below the LOQ of the analytical method).
Data from trials in conditions slightly different from the critical GAP conditions (1 applic. at 5 g a.s./ha, 1 applic. at 10 g a.s./ha, 2 treatments totalling 15 g a.s./ha, ...) showed that residues were not detected in either grain or straw.

B.6.7 Effects of industrial processing and /or household preparation on the residue (Annex IIA 6.5; Annex IIIA 8.4)

Since the residue level in the wheat or barley grain was below the LOQ (0.01*) and as the TMDI values are below 10% of the ADI, the investigation of the effects of industrial processing on the nature and the level of the residues is not required.

B.6.8. Livestock feeding studies (Annex IIA 6.4; Annex IIIA 8.3)

- The supervised residue trials indicated that the residues in crop parts (grain and straw) fed to animals didn't exceed 0.1 mg/kg of diet as received (Residues in grain and straw were less than 0.002 mg/kg and 0.01 mg/kg respectively).

-Residues in edible tissues in the goat do exceed 0.01 mg/kg; however, the dose levels in this study were 340 times higher than the potential exposure in the diet. Therefore, actual residues in edible animal products would be considerably less than 0.01 mg/kg.

-Residues in edible tissues in laying hens do not exceed 0.01 mg/kg.
Livestock feeding studies are not required.

Intake calculations for livestock (according to appendix G of the "Guidelines for the establishment of Community Maximum Residue Levels (MRLs) of Plant Protection Products in Food and Feedingstuffs of Plant and Animal Origin") are presented herebelow

Table B.6.8 -1 : Intake calculations for dairy cattle (maximum daily intake of dry matter : 20 kg for 550 kg body weight).

Material	% of total DM/day	Intake of DM from material (kg/anim al/d)	% dry matter in material	Intake of material (kg/animal/d)	Residue in material (mg/kg)	Residue intake (mg/animal/d)
Cereal grain	40	8	86	9.3	0.01*	0.093
Cereal straw	20	4	86	4.7	0.05*	0.235
Total						0.328

The potential intake of residues of Florasulam by dairy cattle is 0.0006 mg/kg b.w/day.

Table B.6.8 -2 : Intake calculations for beef cattle (maximum daily intake of dry matter : 15 kg for 350 kg body weight).

Material	% of total DM/day	Intake of DM from material (kg/anim al/d)	% dry matter in material	Intake of material (kg/animal/d)	Residue in material (mg/kg)	Residue intake (mg/animal/d)
Cereal grain (Bran)	20	3	89	3.4	0.01*	0.034
Cereal straw	50	7.5	86	8.7	0.05*	0.435
Total						0.469

The potential intake of residues of Florasulam by beef cattle is 0.00134 mg/kg b.w/day.

Table B.6.8 -3 : Intake calculations for pig (maximum daily intake of dry matter : 3 kg for 75 kg body weight).

Material	% of total DM/day	Intake of DM from material (kg/anim al/d)	% dry matter in material	Intake of material (kg/animal/d)	Residue in material (mg/kg)	Residue intake (mg/animal/d)
Cereal grain	80	2.4	86	2.8	0.01*	0.028
Total						0.028

The potential intake of residues of Florasulam by pig is 0.00037 mg/kg b.w/day.

Table B.6.8 -4 : Intake calculations for chicken (maximum daily intake of dry matter : 0.12 kg for 1.9 kg body weight).

Material	% of total DM/day	Intake of DM from material (kg/anim al/d)	% dry matter in material	Intake of material (kg/ani mal/d)	Residue in material (mg/kg)	Residue intake (mg/animal/d)
Cereal grain	70	0.084	86	0.098	0.01*	0.00098
Total						0.00098

The potential intake of residues of Florasulam by chicken is 0.00051 mg/kg b.w/day.

Conclusion :
The potential intake of residues of Florasulam by dairy cattle, beef cattle, pig and chicken can be considered as negligible.

B.6.9 Residues in succeeding or rotational crops (Annex IIA 6.6; Annex IIIA 8.5)

The uptake of Florasulam (DE-570) into Four Succeeding Crops (MacDonald, A.M.G., 1997)
Guidelines :
The study was conducted to meet the proposals submitted to the EC regarding Annex II and III of EC Directive 91/414/EEC.
GLP :
Yes
Material and methods :
Test substances : Phenyl label (Florasulam- Ph-UL-(^{14}C)) and Triazolopyrimidine label (Florasulam-9-(^{14}C)).
Prior to sowing of representative crops (spring wheat, sunflower, cabbage and carrot), the active substance was applied to bare soil at the use rate of 7.5 g a.s./ha and was aerobically aged for 30 days.
Seeding and planting were done 30 days after soil treatment.
Each crop was harvested at maturity. Spring wheat was separated into straw and ears; the cabbage heads only were collected; sunflowers were separated into heads and stalks; the carrots were separated into leaves and roots.
All these subsamples were subjected to washes with water, dichloromethane and methanol.
Soil and plant samples were dosed by liquid scintillation counting and by combustion analysis.
Metabolites in soil were identified by HPLC using reference standards (Florasulam and 5-hydroxy-Florasulam).
Findings :
The following total radioactive residues (TRR expressed in mg Florasulam equiv./kg) were determined :
-soil, after treatment (day 0): 0.019-0.043 mg/kg.
-soil, after ageing (day 30) : 0.011-0.033 mg/kg.
-soil at maturity (harvest time) : 0.002-0.007 mg/kg.
Florasulam and metabolite 5-hydroxy were detected in soil at concentrations ranging from 0.003 to 0.008 mg/kg at sowing date (day 30). These were the main components for potential uptake into the crops.

Table B.6.9-1 : Total radioactive residues in the combined washes fractions and the washed tissues of the succeeding crops (expressed as mg Florasulam equiv./kg).

Crop	Fraction	Phenyl labeled Florasulam	Triazolopyrimidine labeled Florasulam
Spring wheat (168 days after soil treatment)	Ears	nd	0.001
	Straw	0.003	0.004
Sunflowers (168 days after soil treatment)	Heads	nd	nd
	Stems	0.002	0.001
Cabbage (195 days after soil treatment)	Heads	nd	0.002
Carrots (156 days after soil treatment)	Leaves	0.004	0.006
	Roots	0.001	0.001

nd : Not radiodetected

Conclusion :
The levels of radioactivity taken up into these succeeding crops were below 0.006 mg/kg Florasulam equivalent. Therefore, the uptake of Florasulam in edible plant parts of leafy vegetables, root vegetables, oil seed crop and cereals, installed as succeeding crops is not sufficient to reach measurable levels in monitoring.

B.6.10 Proposed pre-harvest intervals, re-entry intervals or withholding periods to minimize residues in crops, plants, plant products, treated areas or spaces (Annex IIA 6.8; Annex IIIA 8.7)

Pre-harvest interval :
Pre-harvest interval is not required. The application time is determined by the crop growth stage of the last application (BBCH 49).

Re-entry period for livestock :
In cases where livestock may be fed immature cereal crops following crop failure, a re-entry period of 7 days is proposed. This is based on data from decline trials which demonstrate that there are no residues detectable (<0.05 mg/kg) in immature plant at a maximum of 6 days after application.

Re-entry period for man to crops :
No re-entry period for man to treated crops is required.

Withholding period for animal feedingstuffs :
In cases where livestock may be fed immature cereal crops following crop failure, a re-entry period of 7 days is proposed (No residues were detected in any whole plant taken more than 6 days after the final application).

Waiting period between application and handling treated products :
Not required.

Waiting periods between last application and sowing or planting succeeding crops :
Not required.

B.6.11 Estimates of the potential and actual exposure through diet and other means (Annex IIA 6.9; Annex IIIA 8.8)

Adult consumer

The following TMDI calculations are carried out using :
-the FAO/WHO cultural diet for the European (August 1994);
-the MRL proposals for individual commodities established in section B.6.6 (Residues resulting from supervised trials);
-the conversion factors to apply for assessment of consumer safety in section B.6.3 (Residue definition);
-the residue levels in processed commodities were not determined in section B.6.7 as no investigation on the effect of industrial processing on the level and the nature of the residue was required.

Additionnally, the intake calculations rely on the following assumptions :
-for each crop, the % of ADI consumed is based on a body weight of 60 kg;
-the ADI of Florasulam is 0.05 mg/kg bw/day.

Commodity	Consumption (kg/day)	MRL (mg/kg)	Conversion factor	Intake (mg/kg)
Cereals (1)	0.2233	0.01*	-	0.002233

(1) : including oats/barley/rye/wheat/triticale.

Taking into account a person of 60 kg body weight, the TMDI is 3.7×10^{-5} mg/kg bw/day. This represents 0.07 % of the ADI.

German 4-6 years old girl

The following TMDI calculations are carried out using :
-the German diet for a 4-6 years old girl;
-the MRL proposal for individual commodities;.
-the ADI of Florasulam is 0.05 mg/kg bw/day.

Commodity	Consumption (kg/day)	MRL (mg/kg)	Conversion factor	Intake (mg/kg)
Cereals (1)	0.108	0.01*	-	0.00108

(1) : including raw and processed cereals

Taking into account a body weight of 13.5 kg, the TMDI of the German 4-6 years old girl is 0.00008 mg/ kg bw/day. This represents 0.16 % of the ADI.

Children and infants from United Kingdom

The following TMDI calculations are carried out using :
-the Pesticides Safety Directorate Consumer Exposure Model;
-the MRL proposal for individual commodities;
-the ADI of Florasulam is 0.05 mg/kg bw/day.

Commodity	**Child 30 kg bw**		**Infant 7.5 kg bw**	
	"High level" intakes from single commodities			
	97.5th percentile consumption (kg/day)	TMDI for single commodity (mg/kg bw/day)	97.5th percentile consumption (kg/day)	TMDI for single commodity (mg/kg bw/day)
Wheat	0.2199	0.000073	0.0614	0.000082
Barley (assuming 1% beer consumption)	0.0036	0.000001	na	na
Oat	0.0305	0.00001	0.0182	0.000024
	Total dietary intakes from combinations of commodities (total TMDI) (mg/kg bw/day)			
Total	0.000083		0.000106	

na : Not applicable.

The TMDIs of UK children and infants are respectively 0.17 and 0.20 % of the ADI.

The contribution of animal products was considered as negligible and therefore was not included in the intake calculations.

B.6.12 Community MRLs and MRLs in EU Member States (Document E-4)

Florasulam is a new herbicide. There is currently no community MRL.

B.6.13 Proposed MRLs and justification for the acceptability of those residues (Annex IIA 6.7; Annex IIIA 8.6)

Based on the wheat and animal metabolism studies, the only relevant residue was the parent molecule.
Supervised crop residue trials in winter cereals (winter wheat, winter barley, durum wheat) indicated that there were no quantifiable residues in grain. Therefore, a single MRL is proposed for all the cereal crops.

MRL proposal for cereal grains : 0.01* mg/kg.

B.6.14 Storage stability of residue samples

The Stability of Florasulam in Wheat Under Frozen Storage Conditions over 18 months -Interim Report (Butler R.E. and Gambie, A.; 1997)
The Stability of Florasulam in Wheat Under Frozen Storage Conditions over 18 months -Final Report (Gambie, A.; 1999)

Guidelines :
In accordance with Appendix H : Storage stability of residue samples (7032/VI/95 rev.4) of "Guidelines for the generation of data concerning residues as provided in Annex II Part A, section 6 and Annex III, Part A, section 8 of Directive 91/414/EEC.

GLP :
Yes.

Material and methods :
Test substance : Florasulam (DE-570).
Experimental design :
Whole wheat plant, wheat grain and wheat straw were stored frozen 0 days, 1, 3, 6, 13...23 months. (freezer temperature ranged from -18°C to -25°C for the majority of the storage period).
Weighed aliquots of untreated samples were fortified at the rates of 0.5 mg/kg for whole plant and straw, and 0.1 mg/kg for grain.These fortification levels were 10 times the lowest validated level of the analytical method in use.
In addition, aliquots of untreated substrates were stored for procedural recovery determinations.
The concentrations of residues of Florasulam in all samples were quantified by HPLC using UV absorbance detection at 260 nm (Florasulam as analytical standard).
The results for the stored fortified samples were corrected using the mean recoveries obtained for the procedural recoveries on the day of analysis.

Findings :

Substrate	Storage Period (days)	Procedural Recovery (%)	Respective Nominal Recovery (%)
Whole plant	0,35,80,172,411,579	73-104	98,86,92,86,100,94
Grain	0,34,105,174,390,683	79-98	100,98,104,102,103,104
Straw	0,22,101,170,394,562	83-106	101,98,106,106,90,110

Conclusion
There was no loss of Florasulam residues from fortified wheat whole plant, grain or straw during frozen storage over a period of 562 to 683 days.

B.6.15 Summary and evaluation of residue behaviour

***In plants* :**

The metabolism of Florasulam was investigated in winter wheat plants.

Total radioactive residues in the grain at maturity were very low (maximum of 0.002 mg/kg). As a result of these extremely low levels of radioactivity it was not possible to complete further investigation of the presence and the nature of the residues.

In straw at maturity, no Florasulam was detected in plants treated at BBCH 30 with only small amounts of the glucose conjugate moiety. Several polar components were observed including a small quantity of the tentative 2-sulphonamide and the 4-position hydroxylated -phenyl -parent molecule.

In late application plants, Florasulam was detected in straw at maturity with non negligible amounts of the glucose conjugate of the hydroxylated -Florasulam and the tentative metabolites : 2-sulphonamide and the 4-OH-(phenyl)-Florasulam.

The metabolic pathway suggested a rapid metabolization of the parent compound via hydroxylation of the phenyl ring with subsequent sugar conjugation followed by cleavage across the sulphonamide bridge.

Two metabolites were not present in the rat metabolism but their concentration was found to be very low considering the exaggerated application rate.
Therefore, their toxicological significance is negligible.

In livestock :

Metabolism studies in lactating goats and laying hens demonstrated that the majority of the applied radioactivity was recovered as unchanged Florasulam in excreta.
Residues in the edible tissues have been shown to be primarily the parent compound.
Florasulam undergoes a very slight metabolization with no significant sulphonamide bridge cleavage.
The very low level of residues in edible tissues demonstrated that the residues of Florasulam did not bioconcentrate in livestock.

Similar metabolism is seen in lactating goats and laying hens.

Supervised residue trials :

Wheat and barley residue trials data under field conditions were provided allowing the MRL proposal for wheat and barley grain of 0.01* mg/kg.

The method of analysis provided allows the enforcement of the proposed MRL.

Industrial processing studies :

Not required.

Livestock feeding studies :

Not required.

Florasulam in animal products can be considered as non liposoluble.

Residues in rotational crops :

The residues in rotational crops are very low and the fixing of MRLs for these crops is not necessary.

Potential and actual exposure through diets :

Assessment of the safety of the consumer indicates that the intake of residues of Florasulam is well below the maximum acceptable level for the three cultural diets.

B.6.16 References relied on

Residue data for the active substance (Annex IIA 6)

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
IIA 6.2	Barnekow, DE, Huskin, MA, Nature of the Residue of [^{14}C]XDE-570 in Lactating Goats DowElanco, Indianapolis, USA and ABC Laboratories Inc, Columbia, USA MET94017, December 1994a	GH-C 3478	Yes	Unpublished Protected
IIA 6.2	Barnekow, DE, Huskin, MA, Nature of the Residue of [^{14}C]XDE-570 in Laying Hens DowElanco, Indianapolis, USA and ABC Laboratories Inc, Columbia, USA MET94018, December 1994b	GH-C 3481	Yes	Unpublished Protected
IIA 6.3	Butcher, S, Residues of XDE-570 in Winter Wheat at Harvest Following a Single Application of EF-1289, UK - 1994 DowElanco Europe, Letcombe Regis, Oxon, UK R94-115, February 1996a	GHE-P-4813	Yes	Unpublished Protected
IIA 6.3	Butcher, S, Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, Southern France - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-047, May 1996b	GHE-P-5037	Yes	Unpublished Protected
IIA 6.3	Butcher, S, Residues of XDE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Italy - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-013, May 1996c	GHE-P-5178	Yes	Unpublished Protected
IIA 6.3	Butcher, S, Residues of XDE-570 in Winter Soft Wheat at Intervals Following a Single or Double Application of EF-1343, Southern France - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-048, May 1996d	GHE-P-5118	Yes	Unpublished Protected
IIA 6.3	Butcher, S, Residues of XDE-570 in Winter Wheat at Intervals Following a Single Application of EF-1343, Italy - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK	GHE-P-5133	Yes	Unpublished Protected

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
	R95-010, May 1996e			
IIA6.3	Butcher, S, Residues of XDE-570 in Durum Wheat at Harvest Following a Single Application of EF-1289, Southern France - 1994 DowElanco Europe, Letcombe Regis, Oxon, UK R94-114, June 1996f	GHE-P-5007	Yes	Unpublished Protected
IIA 6.3	Butcher, S, Residues of XDE-570 in Winter Wheat at Intervals Following a Single Application of EF-1343, Germany - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK RL95-008, August 1996g	GHE-P-5180	Yes	Unpublished Protected
IIA 6.3	Butcher, S, Residues of XDE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Germany - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK RL95-007, August 1996h	GHE-P-5179	Yes	Unpublished Protected
IIA 6.3	Butcher, S, Gibson, R, Residues of XDE-570 in Winter Wheat at Intervals Following a Single or Double Application of EF-1343, UK - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-050, January 1996a	GHE-P-4811	Yes	Unpublished Protected
IIA 6.3	Butcher, S, Gibson, R, Residues of XDE-570 in Winter Soft Wheat at Intervals Following a Single or Double Application of EF-1343, Northern France - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-016, February 1996b	GHE-P-4812	Yes	Unpublished Protected
IIA 6.3	Butcher, S, Gibson, R, Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, Northern France - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-017, February 1996c	GHE-P-4869	Yes	Unpublished Protected
IIA 6.3	Butler, RE, Gambie, A, The Stability of DE-570 in Wheat Under Frozen Storage Conditions over 18 months (Interim Report) DowElanco Europe, Letcombe Regis, Oxon, UK ST96-001, November 1997	GHE-P-6782	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Teasdale R, The Stability of DE-570 in Wheat Under Frozen Storage Conditions over 18 months (Final Report) DowElanco Europe, Letcombe Regis, Oxon, UK	GHE-P-7904	Yes	Unpublished Protected

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
	ST96-001, May 1999			
IIA 6.3	Gambie, A, Butcher, S, Gibson, R, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Spain - 1995 Dow AgroSciences, Letcombe Regis, Oxon, UK R95-045, October 1996	GHE-P-5385	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, RE, Residues of DE-570 in Winter Wheat at Harvest Following a Single Application of EF-1343, Spain - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-005, August 1997a	GHE-P-6332	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, RE, Residues of DE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Italy - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-008, August 1997b	GHE-P-6335	Yes	Unpublished Protected
IIA 6.3	Gambie, A,Butler, R, Residues of DE-570 in Winter Soft Wheat at Intervals Following a Single Application of EF-1343, Northern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-115, September 1997c	GHE-P-6343	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of DE-570 in Winter Soft Wheat at Intervals Following a Single Application of EF-1343, Southern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-111, September 1997d	GHE-P-6339	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, RE, Residues of DE-570 in Winter Durum Wheat at Harvest Following a Single Application of EF-1343, Southern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-113, September 1997e	GHE-P-6341	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Wheat at Intervals Following a Single Application of EF-1343, Italy - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-007, September 1997f	GHE-P-6334	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, UK - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-004, September 1997g	GHE-P-6331	Yes	Unpublished Protected
	Gambie, A, Butler, R, Residues of DE-570 in Winter			Unpublished

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
IIA 6.3	Barley at Intervals Following a Single Application of EF-1343, Southern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-110, September 1997h	GHE-P-6338	Yes	Protected
IIA 6.3	Gambie, A, Butler, R, Residues of DE-570 in Winter Barley at Harvest Following a Single Application of EF-1343, Italy - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-009, September 1997i	GHE-P-6336	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single or Double Application of EF-1343, UK - 1995 (Final Report) DowElanco Europe, Letcombe Regis, Oxon, UK R95-049, October 1997j	GHE-P-5390	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single Application of EF-1343, Spain - 1995 Dow AgroSciences, Letcombe Regis, Oxon, UK R95-046, October 1997k	GHE-P-5386	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single or Double Application of EF-1343, Germany - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK RL96-011, November 1997l	GHE-P-6345	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single or Double Application of EF-1343, UK - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-003, November 1997m	GHE-P-6330	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Soft Wheat and Soil at Harvest Following a Single Application of EF-1343, Northern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-116, November 1997n	GHE-P-6344	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Grain, Straw and Soil at Harvest Following a Single Application of EF-1343 to Winter Wheat, Germany-1995 DowElanco Europe, Letcombe Regis, Oxon, UK RL95-006, November 1997o	GHE-P-5476	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Soft Wheat and Soil at Harvest Following a Single	GHE-P-6340	Yes	Unpublished Protected

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
	Application of EF-1343, Southern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-112, November 1997p			Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single Application of EF-1343, Italy - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-011, November 1997q	GHE-P-5387	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter wheat and Soil at Harvest Following a Single Application of EF-1343, Italy - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-010, November 1997r	GHE-P-6337	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Barley at Harvest Following a Single or Double Application of EF-1343, Germany - 1996 Dow AgroSciences, Letcombe Regis, Oxon, UK RL96-012, November 1997s	GHE-P-6346	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Barley at Harvest Following a Single or Double Application of EF-1343, UK - 1995 (Final Report) DowElanco Europe, Letcombe Regis, Oxon, UK R95-051, November 1997t	GHE-P-5391	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single or Double Application of EF-1343, UK - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-002, November 1997u	GHE-P-6329	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Northern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-114, November 1997v	GHE-P-6342	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Grain, Straw and Soil at Harvest Following a Single Application of EF-1343 to Winter Barley, Germany - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK RF95-009, RL95-009, November 1997w	GHE-P-5477	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single or Double Application of EF-1343, Southern France - 1995	GHE-P-5389	Yes	Unpublished Protected

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
	DowElanco Europe, Letcombe Regis, Oxon, UK R95-015, November 1997x			
IIA 6.3	Gambie, A, Butler, R, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Italy - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-012, November 1997y	GHE-P-5388	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Spain - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-006, November 1997z	GHE-P-6333	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Wheat at Intervals Following a Single or Double Application of EF-1343, Germany - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK RL96-013, December 1997aa	GHE-P-6347	Yes	Unpublished Protected
IIA 6.3	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, Germany - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK RL96-014, December 1997ab	GHE-P-6348	Yes	Unpublished Protected
IIA 6.6	MacDonald, A, The Uptake of XDE-570 into Four Succeeding Crops DowElanco Europe, Letcombe Regis, Oxon, UK 7U, December 1997	GHE-P-4889	Yes	Unpublished Protected
IIA 6.1	Pillar, F, The Metabolism of XDE-570 in Winter Wheat - Final Report DowElanco Europe, Letcombe Regis, Oxon, UK 5U, October 1997	GHE-P-5729	Yes	Unpublished Protected

Residue data for the formulation EF-1343 (Annex IIIA 8)

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
IIIA 8.1 (see IIA 6.2)	Barnekow, DE, Huskin, MA, Nature of the Residue of [^{14}C]XDE-570 in Lactating Goats DowElanco, Indianapolis, USA and ABC Laboratories Inc, Columbia, USA MET94017, December 1994a	GH-C 3478	Yes	Unpublished Protected
IIIA 8.1 (see IIA 6.2)	Barnekow, DE, Huskin, MA, Nature of the Residue of [^{14}C]XDE-570 in Laying Hens DowElanco, Indianapolis, USA and ABC Laboratories Inc, Columbia, USA MET94018, December 1994b	GH-C 3481	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Residues of XDE-570 in Winter Wheat at Harvest Following a Single Application of EF-1289, UK - 1994 DowElanco Europe, Letcombe Regis, Oxon, UK R94-115, February 1996a	GHE-P-4813	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, Southern France - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-047, May 1996b	GHE-P-5037	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Residues of XDE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Italy - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-013, May 1996c	GHE-P-5178	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Residues of XDE-570 in Winter Soft Wheat at Intervals Following a Single or Double Application of EF-1343, Southern France - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-048, May 1996d	GHE-P-5118	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Residues of XDE-570 in Winter Wheat at Intervals Following a Single Application of EF-1343, Italy - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-010, May 1996e	GHE-P-5133	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Residues of XDE-570 in Durum Wheat at Harvest Following a Single Application of EF-1289, Southern France - 1994 DowElanco Europe, Letcombe Regis, Oxon, UK R94-114, June 1996f	GHE-P-5007	Yes	Unpublished Protected

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Residues of XDE-570 in Winter Wheat at Intervals Following a Single Application of EF-1343, Germany - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK RL95-008, August 1996g	GHE-P-5180	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Residues of XDE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Germany - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK RL95-007, August 1996h	GHE-P-5179	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Gibson, R, Residues of XDE-570 in Winter Wheat at Intervals Following a Single or Double Application of EF-1343, UK - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-050, January 1996a	GHE-P-4811	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Gibson, R, Residues of XDE-570 in Winter Soft Wheat at Intervals Following a Single or Double Application of EF-1343, Northern France - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-016, February 1996b	GHE-P-4812	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butcher, S, Gibson, R, Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, Northern France - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-017, February 1996c	GHE-P-4869	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Butler, RE, Gambie, A, The Stability of DE-570 in Wheat Under Frozen Storage Conditions over 18 months (Interim Report) DowElanco Europe, Letcombe Regis, Oxon, UK ST96-001, November 1997	GHE-P-6782	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butcher, S, Gibson, R, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Spain - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-045, October 1996	GHE-P-5385	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, RE, Residues of DE-570 in Winter Wheat at Harvest Following a Single Application of EF-1343, Spain - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-005, August 1997a	GHE-P-6332	Yes	Unpublished Protected

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, RE, Residues of DE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Italy - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-008, August 1997b	GHE-P-6335	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of DE-570 in Winter Soft Wheat at Intervals Following a Single Application of EF-1343, Northern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-115, September 1997c	GHE-P-6343	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of DE-570 in Winter Soft Wheat at Intervals Following a Single Application of EF-1343, Southern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-111, September 1997d	GHE-P-6339	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, RE, Residues of DE-570 in Winter Durum Wheat at Harvest Following a Single Application of EF-1343, Southern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-113, September 1997e	GHE-P-6341	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Wheat at Intervals Following a Single Application of EF-1343, Italy - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-007, September 1997f	GHE-P-6334	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, UK - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-004, September 1997g	GHE-P-6331	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of DE-570 in Winter Barley at Intervals Following a Single Application of EF-1343, Southern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-110, September 1997h	GHE-P-6338	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of DE-570 in Winter Barley at Harvest Following a Single Application of EF-1343, Italy - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-009, September 1997i	GHE-P-6336	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single or Double Application of EF-1343, UK - 1995 (Final	GHE-P-5390	Yes	Unpublished Protected

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
	Report) DowElanco Europe, Letcombe Regis, Oxon, UK R95-049, October 1997j			
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single Application of EF-1343, Spain - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-046, October 1997k	GHE-P-5386	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single or Double Application of EF-1343, Germany - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK RL96-011, November 1997l	GHE-P-6345	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single or Double Application of EF-1343, UK - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-003, November 1997m	GHE-P-6330	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Soft Wheat and Soil at Harvest Following a Single Application of EF-1343, Northern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-116, November 1997n	GHE-P-6344	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Grain, Straw and Soil at Harvest Following a Single Application of EF-1343 to Winter Wheat, Germany-1995 DowElanco Europe, Letcombe Regis, Oxon, UK RL95-006, November 1997o	GHE-P-5476	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Soft Wheat and Soil at Harvest Following a Single Application of EF-1343, Southern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-112, November 1997p	GHE-P-6340	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Wheat and Soil at Harvest Following a Single Application of EF-1343, Italy - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-011, November 1997q	GHE-P-5387	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter wheat and Soil at Harvest Following a Single Application of EF-1343, Italy - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK	GHE-P-6337	Yes	Unpublished Protected

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
	R96-010, November 1997r			
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Barley at Harvest Following a Single or Double Application of EF-1343, Germany - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK RL96-012, November 1997s	GHE-P-6346	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Barley at Harvest Following a Single or Double Application of EF-1343, UK - 1995 (Final Report) DowElanco Europe, Letcombe Regis, Oxon, UK R95-051, November 1997t	GHE-P-5391	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single or Double Application of EF-1343, UK - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-002, November 1997u	R96-002	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Northern France - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK R96-114, November 1997v	GHE-P-6342	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Grain, Straw and Soil at Harvest Following a Single Application of EF-1343 to Winter Barley, Germany - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK RF95-009, RL95-009, November 1997w	GHE-P-5477	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single or Double Application of EF-1343, Southern France - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-015, November 1997x	GHE-P-5389	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, R, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Italy - 1995 DowElanco Europe, Letcombe Regis, Oxon, UK R95-012, November 1997y	GHE-P-5388	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Barley and Soil at Harvest Following a Single Application of EF-1343, Spain - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK	GHE-P-6333	Yes	Unpublished Protected

Annex point(s) 91/414/EEC	Author, Title, Test institute, Report number/Study ID, Date of report For publications: reference	Dow AgroSciences Report No.	GLP GEP	Published Protected
	R96-006, November 1997z			
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Wheat at Intervals Following a Single or Double Application of EF-1343, Germany - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK RL96-013, December 1997aa	GHE-P-6347	Yes	Unpublished Protected
IIIA 8.2 (see IIA 6.3)	Gambie, A, Butler, RE, Residues of XDE-570 in Winter Barley at Intervals Following a Single or Double Application of EF-1343, Germany - 1996 DowElanco Europe, Letcombe Regis, Oxon, UK RL96-014, December 1997ab	GHE-P-6348	Yes	Unpublished Protected
IIIA 8.5 (see IIA 6.6)	MacDonald, A, The Uptake of XDE-570 into Four Succeeding Crops DowElanco Europe, Letcombe Regis, Oxon, UK 7U, December 1997	GHE-P-4889	Yes	Unpublished Protected
IIIA 8.1 (see IIA 6.1)	Pillar, F, The Metabolism of XDE-570 in Winter Wheat - Final Report DowElanco Europe, Letcombe Regis, Oxon, UK 5U, October 1997	GHE-P-5729	Yes	Unpublished Protected

ANNEX B

Florasulam

APPENDIX C : Metabolic pathways in animals and plants

Figure 1 : Metabolic pathway of Florasulam in rats

Figure 2 : Metabolic pathway of Florasulam in winter cereals

Figure 3 : Metabolic pathway in lactating goat and laying hen

ANNEX B

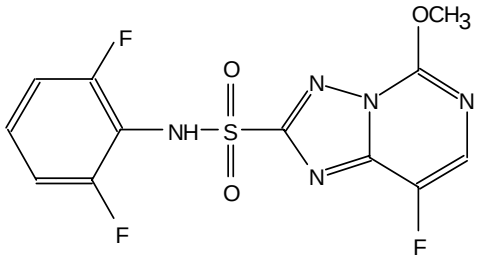
Florasulam

APPENDIX D :

Chemical names of synthetic reference compounds

Chemical names of synthetic reference compounds from Florasulam

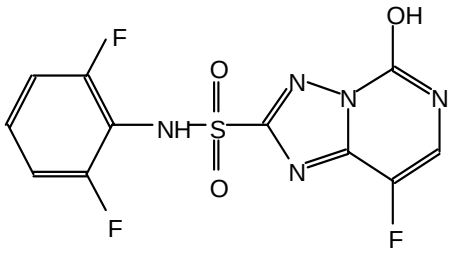
Registration number	Chemical names
Parent (DE-570)	N-(2,6-difluorophenyl)-8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide
4-OH-(phenyl)-Florasulam	N-(2,6-difluro-4-hydroxyphenyl)-8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide
5-OH-Florasulam	N-(2,6-difluorophenyl)-8-fluoro-5-hydroxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide



ASTP (2-sulphonamide)	8-fluoro-5-methoxy(1,2,4)triazolo(1,5-c)pyrimidine-2-sulphonamide

Florasulam (DE-570)

5-hydroxy-Florasulam



4-hydroxy-(phenyl)-Florasulam

ASTP (2-sulphonamide)

ANNEX B

Florasulam

APPENDIX E : Residue data from supervised trials

Residue data from supervised trials	
Crop	Pages
Winter wheat (soft and durum)	47 pages
Winter barley	40 pages