FLUENSULFONE (265)

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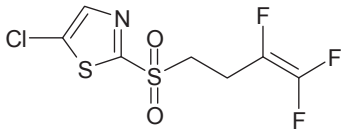
EXPLANATION

Fluensulfone is a non-fumigant, fluoroalkenyl nematicide used to control nematode pests in cucurbit vegetables, eggplant, peppers, and tomatoes. Fluensulfone shows activity in multiple nematode physiological systems; however, its specific nematicidal activity is not known at this time. Fluensulfone was considered for the first time for toxicology by the 2013 JMPR and for residues by the 2014 JMPR.

IDENTITY

ISO common name	Fluensulfone (provisionally approved)
Chemical Name	
IUPAC	5-chloro-1,3-thiazol-2-yl 3,4,4-trifluorobut-3-en-1-yl sulfone
CAS	5-chloro-2-[(3,4,4-trifluoro-3-buten-1-yl)sulfonyl]thiazole
CIPAC No.	Not Listed
CAS No.	318290-98-1
Synonyms	MCW-2
Structural Formula	
Molecular formula	$C_7H_5ClF_3NO_2S_2$
Molecular mass	291.7

Physical and chemical properties

Physical and chemical properties of fluensulfone

Property	Guideline and method	Test material specification and purity	Findings	Reference
Technical Grade Active Ingredient				
Melting point (Technical material)	EEC A1 OECD 102 OPPTS 830.7200	Batch No.: 36372130-291-PF1 96.75%	Mean of two determinations by DSC: 34.8 °C ± 0.5 °C (308.0 K ± 0.5 K)	Weissenfeld M., 2009 R-23310A
Boiling point (Technical material)	EEC A2 OECD 103 OPPTS 830.7220	Batch No.: 36372130-291-PF1 96.75%	No boiling point determined by DSC, as material decomposed without boiling. Atm. pressure = 99.6 kPa	Weissenfeld M., 2009a R-23310A
Decomposition temperature (Technical material)	EEC A2 OECD 103 OPPTS 830.7220	Batch No.: 36372130-291-PF1 96.75%	The test substance begins to decompose without boiling at 215 °C (capillary method). Atm. pressure = 99.6 kPa	Weissenfeld M., 2009a R-23310A

Property	Guideline and method	Test material specification and purity	Findings	Reference
Physical state and colour	OPPTS 830.6302 OPPTS 830.6303	Batch No.: 36372130-291-PF1 96.75%	Yellow, resin like solid.	Weissenfeld M., 2010 R-23307
Odour	OPPTS 830.6304	Batch No.: 36372130-291-PF1 96.75%	"Specific odour"	Weissenfeld M., 2010 R-23307
Solubility in organic solvents	EEC A6 OECD 105	Batch No.: 36372130-291-PF1 96.75%	Solubilities at 20 °C (shake flask method): Acetone 350.49 g/L Dichloromethane 306.14 g/L Ethyl acetate 350.76 g/L n-Heptane 19.01 g/L Methanol 359.29 g/L n-Octanol 90.42 g/L Xylene 356.18 g/L	Weissenfeld M., 2009d R-23317
Hydrolysis rate at pH 4, 7 and 9	OPPTS 835.2120 OECD Guideline 111.	[thiazole-4-^{14}C]fluensulfone Radiochemical Purity 97.2%	After 5 days at 50 °C and pH 4, 5 and 7, the concentration of [thiazole-^{14}C]fluensulfone comprised ≥ 96.8% of the applied dose in all samples.	Shepler, K 2010 R-23319
Pure Active Ingredient				
Melting, freezing or solidification point	EEC A1 OECD 102 OPPTS 830.7200	Batch No.: 381-022-02 99.1%	Mean of two determinations by DSC: 34.4 °C ± 0.2 °C (307.6 K ± 0.2 K)	Weissenfeld M., 2008a. R-23309
Boiling point	EEC A2 OECD 103 OPPTS 830.7220	Batch No.: 381-022-02 99.1%	Mean of two determinations by DSC: 282.5 °C ± 0.2 °C (555.7 K ± 0.2 K) Atm. pressure = 100.2 kPa	Weissenfeld M., 2008b R-23310
Temperature at which decomposition or sublimation occurs	EEC A2 OECD 103 OPPTS 830.7220	Batch No.: 381-022-02 99.1%	No decomposition or sublimation observed. Boiling point successfully determined.	Weissenfeld M., 2009a R-23310A
Relative density of purified active substance	EEC A3 OECD 109 OPPTS 830.7300	Batch No.: 381-022-02 99.1%	Relative density at 20 °C = 1.876 (Gas comparison pycnometer)	Weissenfeld M., 2008c R-23312
Vapour pressure of purified active substance	EEC A4 OECD 104	Batch No.: 381-022-02 99.1%	Vapour pressure results: 25 °C = 3.0×10^{-2} Pa 35 °C = 1.3×10^{-1} Pa 45 °C = 3.4×10^{-1} Pa (Gas saturation method) Vapour pressure extrapolated from vapour pressure curve was calculated to be 3.0×10^{-2} Pa at 25 °C	Weissenfeld M., 2008d R-23313
Henry's Law constant	Calculation	Batch No.: 381-022-02 99.1%	1.68×10^{-2} Pa m^3/mol	Weissenfeld M., 2009b R-23313A
Physical state and colour	OPPTS 830.6302 OPPTS 830.6303	Batch No.: 381-022-02 99.1%	White, fine crystalline powder	Weissenfeld M., 2010 R-23307

Property	Guideline and method	Test material specification and purity	Findings	Reference
Odour	OPPTS 830.6304	Batch No.: 381-022-02 99.1%	"Specific odour"	Weissenfeld M., 2010 R-23307
Solubility in water	EEC A6 OECD 105 OPPTS 830.7840	Batch No.: 381-022-02 99.1%	Water solubility at 20 °C = 545.3 mg/L (shake flask method)	Weissenfeld M., 2008e R-23316
n-octanol/water partition coefficient	EEC A8 OECD 117 OPPTS 830.7570	Batch No.: 381-022-02 99.1%	Log P_{ow} = 1.96 (HPLC method)	Weissenfeld M., 2008f R-23318
	Based on solubilities	Not Applicable	Log P_{ow} based on individual solubilities in n-octanol and water: n-Octanol solubility: 90.42 g/L Water solubility: 0.545 g/L Log P_{ow} = Log (90.42/0.545) = 2.2	
Direct phototransformation of purified active substance in water	OPPTS 835.2240 OECD Proposal for a New Guideline Phototransformation of Chemicals in Water (2007)	[thiazole-4-^{14}C]fluensulfone trifluorobutene-1,2-^{14}C]fluensulfone	Aqueous photolysis may contribute to the rapid degradation of fluensulfone in the environment. DT_{50} irr. = < 11 hours of continuous sun test irradiation, when extrapolated to environmental conditions results in a DT_{50} < 1 day for all latitudes.	Schick, M 2011 R-23322

Fluensulfone is registered as an emulsifiable concentrate (EC) formulation containing 480 g ai/L.

METABOLISM AND ENVIRONMENTAL FATE

Metabolism and environmental fate studies were conducted with [thiazole-4-^{14}C]fluensulfone and [trifluorobutene-1.2-^{14}C]fluensulfone (Figures 1 and 2).

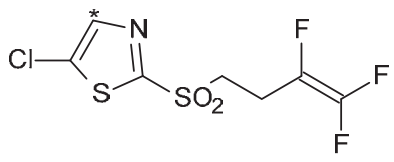


Figure 1 [thiazole-4-^{14}C]fluensulfone

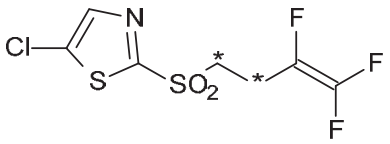
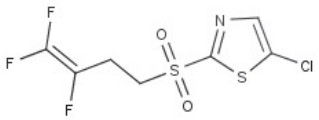
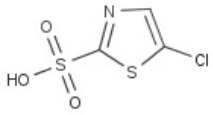
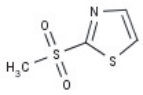
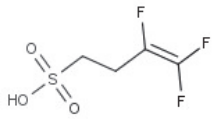
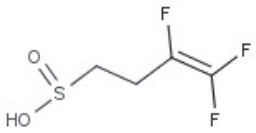
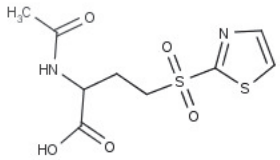
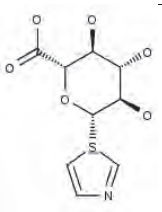


Figure 2 [trifluorobutene-1,2-^{14}C]fluensulfone

Chemical names, structures, and code names of metabolites and degradation products of fluensulfone are shown below.

Known metabolites and degradation products of fluensulfone

Code Names	Chemical name, molecular formula, molar mass	Structure	Where found
Fluensulfone (parent compound) MCW-2	CAS: 5-chloro-2-(3,4,4-trifluoro-but-3-ene-1-sulfonyl)-thiazole CAS No. 318290-98-1 IUPAC: 5-chloro-1,3-thiazol-2-yl 3,4,4-trifluorobut-3-en-1-yl sulfone $C_7H_5ClF_3NO_2S_2$ 291.70 g/mol		Soil, poultry, rotational crops (minor)
M-3625 Thiazole sulfonic acid TSA	IUPAC: 5-chloro-1,3-thiazole-2-sulfonic acid $C_3H_2ClNO_3S_2$ 199.64 g/mol		Soil, crops, rotational crops, rat (minor)
M-3626 Thiazole methyl sulfone MeS	IUPAC: 2-methylsulfonyl-1,3-thiazole $C_4H_5NO_2S_2$ 163.22 g/mol		Soil, ruminant, rat (minor)
M-3627 Butene sulfonic acid BSA	IUPAC: 3,4,4-trifluorobut-3-ene-1-sulfonic acid $C_4H_5F_3O_3S$ 190.14 g/mol		Soil, crops, rotational crops, rat (minor)
Butene sulfinic acid	IUPAC: 3,4,4-trifluorobut-3-ene-1-sulfinic acid $C_4H_5F_3O_2S$ 174.14 g/mol		Rat, ruminant
thiazole mercapturate	IUPAC: 2-acetamido-4-(1,3-thiazole-2-sulfonyl)butanoic acid $C_9H_{12}N_2O_5S_2$ 292.33		Rat
MW-327-I and MW-327-II Thiazole glucuronides (α and ß isomers)	Structure not specified $C_9H_{12}NO_6S$ 262.26		Rat

Animal Metabolism

The Meeting received metabolism studies on laboratory animals (2013 Meeting), lactating goats, and laying hens. Note that in the tables below, all data are reported to the level of precision specified in the study reports. All of the studies were conducted with fluensulfone which was radio-labelled,

separately, in the thiazole ring [Thiazole-4-^{14}C; Th-^{14}C] and the ethane bridge between the sulfonyl and trifluorobutene moieties [Trifluorobutene-1,2-^{14}C; Bu-^{14}C].

In animals, fluensulfone is cleaved at the sulfonyl bridge, apparently via glutathione conjugation, to yield products based on the thiazole and trifluorobutene halves of the parent molecule, with each half having the SO_x moiety. No parent fluensulfone was detected in any rat or lactating goat matrix, whereas parent fluensulfone was a major residue (> 10% of the total radioactive residue, TRR) in poultry fat. In both lactating goat and laying hen, radiolabel from fluensulfone was incorporated into natural products (lactose/glucose in the goat study; sugars, fatty acids, and proteins in the hen study).

Laboratory animals

Fluensulfone was rapidly absorbed at a dose level of 5 mg/kg bw, but the absorption phase was significantly longer at 500 mg/kg bw. The recovery of excreted radiolabel was 94–99% for individual rats. Radiolabel was found mainly in urine (71–83%), faeces (9–11%) and the cage wash (6–16%). One day after dosing with radiolabelled fluensulfone, an average of 0.6–0.8% of the administered radiolabel was in liver and 0.1% in kidney, with 1.7–2.1% in the carcass and 4.5–4.7% remaining in the gastrointestinal tract. By 7 days after treatment with radiolabelled fluensulfone, an average of 0.1–0.2% of the administered radiolabel remained in liver, and 0.03% in kidney.

The majority of the faecal radioactivity was not identified. It consisted of a number of peaks, each representing less than 2% of the administered dose; the only faecal metabolite representing more than 5% of the administered dose was thiazole sulfonic acid. In urine, there were no metabolites common to both radiolabels, which indicate that the initial step is cleavage at the sulfonyl bond. The initial reaction is probably with glutathione to release the trifluorobutene group and conjugation of the thiazole moiety.

Lactating goats

The metabolism of fluensulfone in lactating goats was investigated by LaMar and Quistad (2010, Study R-25458). For each radiolabel position, a single goat was dosed for five days at ca. 29 mg/day (equivalent to 10 ppm in the diet). Milk was collected twice daily and excreta were collected once daily throughout the study. Goats were sacrificed 20–22 hours after the final dosing, at which point tissues, bile, blood, and GI tract (with contents) were collected for analysis.

Total radioactive residues were determined by liquid scintillation counting (LSC) of solubilized tissues (liver, kidney, muscle, blood, bile, and fat), combusted samples (faeces, GI tract), or direct counting (urine). Samples of liver, kidney, and muscle were extracted with twice with acetonitrile:water (ACN:H_2O, 1:1, v/v) and once by ACN (neat) for extraction of residues for characterization and identification. Samples of flank muscle from the butene-label treated goat were additionally extracted with hexane:acetone (4:1, v/v) followed by acetone (neat) prior to alkaline

treatment of the post-extraction solids (PES). Residue analysis for these extracts was by high-performance liquid chromatography (HPLC) and, in some cases, thin-layer chromatography (TLC). For milk, the fat component was separated by centrifugation and extracted with acetone:hexane (1:4, v:v) and then once with acetone. The non-fat milk portion was extracted with acetone to precipitate milk proteins, which were then extracted with acetone:water (1:1, v:v). The resulting extract was added back to the skim milk for direct analysis by HPLC and TLC. Post-extraction solid fractions of all matrices except skim milk and poultry fat underwent further treatment, including alkaline digestion which was followed by acid digestion for liver and kidney (butene label only). Numerous HPLC systems with varying stationary and mobile phases were investigated to achieve satisfactory separation of the radiolabelled components, with detection by UV absorption or mass spectrometry (MS). Identification of metabolites was by co-chromatography with known standards and/or by mass spectral analysis.

The total recovery of radioactivity was 67 and 87% of the AD for the thiazole- and butene-labels, respectively. Low total recovery could be attributed to conversion of radiolabelled material to $^{14}CO_2$ and the fact that the entire carcass was not analysed for radioactivity. Most of the radioactivity was recovered in urine (38–70% of the AD). The thiazole label excretion in urine was only 53% that of the butene label. Faeces and the gastrointestinal tracts, at sacrifice, contained 14–19% of the AD. Radioactivity in tissues and body fluids accounted for 11% (thiazole-radiolabel) and 3.5% (butene-radiolabel) of the administered dose (Table 1). For both radiolabel positions, residues appeared to plateau in skim milk and reach a steady state of excretion by Day 2 or Day 3 (Tables 2 and 3). It is unclear whether or not residues in milk fat reached a plateau during the treatment phase of the study.

The TRR levels were highest in the liver (0.87–1.6% of AD), followed by kidney (0.1–0.2% of AD). TRR levels in thiazole-labelled muscle samples were about 4 times those found in the butene-labelled muscle samples (ca. 0.22–0.24 mg fluensulfone eq/kg vs. ca. 0.04–0.05 mg fluensulfone eq/kg). Muscle contained 4.2% of the AD for the thiazole label and ca. 1% of the AD for the butene label. Fat had low levels of radioactivity (ca. 0.07–0.13 mg fluensulfone eq/kg (thiazole label) and 0.04–0.07 mg fluensulfone eq/kg (butene label)). Milk contained 1.7% (thiazole label) and 1.1% (butene label) of the administered dose with the thiazole label being excreted at a higher rate than the butene label.

Fluensulfone and the known plant metabolites (i.e. methyl sulfone, thiazole sulfonic acid and butene sulfonic acid) were not identified in any of the goat milk or tissue samples. Thiazole methyl sulfone (25% TRR) and butene sulfinic acid (66% TRR) were identified in urine as major metabolites. No other fluensulfone-related ^{14}C-residues could be identified in any other matrix. Major radiolabelled residues were extensively broken down and appeared to be incorporated into natural products.

Lactose and glucose accounted for the majority of the radioactive residues in liver (ca. 8–9% of the TRR). The majority of the radioactivity, extractable by strong alkaline treatment (24% KOH), was assumed to be composed of a range of other sugars and natural products. Lactose was also the

major residue in skim milk (ca. 46–63% of the TRR). The majority of the remaining radioactivity (31–38% of the TRR) in both skim milk and liver was associated with proteins and amino acids. Radiolabelled glucose was also seen in kidney (13–17% of the TRR). Radioactivity associated with proteins in kidney accounted for 25–36% of the TRR.

Incorporation of radiolabelled residues into triglycerides was apparent in all fat matrices. In milk fat, radioactivity associated with fatty acids accounted for 8 and 31% of the TRR for the butene and thiazole labels, respectively. Fatty acid-radiolabel association in the remaining matrices was for subcutaneous fat (15 and 52% of the TRR), renal fat (24 and 21% of the TRR) and omental fat (13 and 43% of the TRR) for the thiazole and butene labels, respectively. Association of thiazole and butene labels with proteins was 5 and 34% of the TRR in milk fat and 5 and 15% of the TRR in subcutaneous fat.

Radiolabelled residues were also examined in blood with relation to bovine haemoglobin. It was apparent that radioactivity was associated with the globin-protein in haemoglobin in blood.

Table 1 Total radioactive residues (TRRs) of [^{14}C]fluensulfone in tissues, body fluids and excreta

Matrix	[Thiazole-4-^{14}C]Fluensulfone		[Trifluorobutene-1,2-^{14}C]Fluensulfone	
	mg eq/kg*	% of admin. dose	mg eq/kg*	% of admin. dose
Tissues and Body Fluids				
Liver	2.623	1.67	0.975	0.87
Kidney	1.402	0.20	0.671	0.10
Skim Milk	0.512	1.40	0.297	0.94
Milk Fat	1.977	0.31	0.531	0.12
Flank Muscle	0.217	Not Reported	0.054	Not Reported
Loin Muscle	0.239	4.2[a]	0.040	0.93 [a]
Subcutaneous Fat	0.131	0.01[b]	0.071	0.02 [b]
Omental Fat	0.071	0.04	0.070	0.03
Renal Fat	0.083	0.06	0.043	0.02
Bile	1.412	0.02	0.082	0.00
Blood	0.948	2.76[c]	0.146	0.47 [c]
Excreta				
Faeces	–	15.66	–	12.05
Gastrointestinal Tract	–	2.93	–	2.08
Urine	–	37.49	–	69.66
Cage Wash	–	0.04	–	0.10
Total Recovery	–	66.85	–	87.39

[a] Based on average ^{14}C content, muscle = 50% total goat weight (Luginbuhl, J.M.)

[b] Subcutaneous fat was subsampled and does not accurately represent %AD

[c] Based on blood = 1/12 total goat weight (Haenlein, G.F.W.)

*Values in mg eq/kg taken from extraction data (sum of fractions) except bile (solubilisation) and blood (combustion)

Table 2 Time course of total radioactive residues (TRRs) of [thiazole-4-^{14}C]fluensulfone in milk and excreta

		Skim milk		Milk fat		Urine	Faeces	Total
Sampling Time		mg eq/kg	% of AD	mg eq/kg	% of AD	% of AD	% of AD	% of AD
Day 1	AM	n.d.	–	n.d.	–	0	0	0.08
	PM	0.287	0.07	0.526	0.01			
Day 2	AM	0.29	0.11	0.725	0.06	4.73	2.97	7.99

		Skim milk		Milk fat		Urine	Faeces	Total
Sampling Time		mg eq/kg	% of AD	mg eq/kg	% of AD	% of AD	% of AD	% of AD
	PM	0.455	0.1	1.037	0.02			
Day 3	AM	0.397	0.17	1.179	0.05	7.47	3.73	11.58
	PM	0.546	0.13	1.57	0.03			
Day 4	AM	0.462	0.19	1.728	0.03	8.74	2.44	11.56
	PM	0.631	0.13	2.155	0.03			
Day 5	AM	0.436	0.18	1.863	0.03	8.72	3.03	12.05
	PM	0.323	0.07	1.427	0.02			
Day 6	AM	0.512	0.24	1.977	0.04	7.83	3.49	11.6
Total		1.71% (whole milk)				37.49	15.66	54.86

n.d. = not detected.

Table 3 Time course of total radioactive residues (TRRs) of [trifluorobutene-1,2-^{14}C]fluensulfone in milk and excreta

		Skim milk		Milk fat		Urine	Faeces	Total
Sampling time		mg eq/kg	% of AD	mg eq/kg	% of AD	% of AD	% of AD	% of AD
Day 1	AM	n.d.	–	n.d.	–	0	0	0.12
	PM	0.310	0.11	0.454	0.01			
Day 2	AM	0.122	0.07	0.390	0.01	12.65	2.95	15.80
	PM	0.384	0.11	0.655	0.01			
Day 3	AM	0.152	0.09	0.457	0.01	14.86	2.38	17.48
	PM	0.393	0.12	0.694	0.02			
Day 4	AM	0.145	0.08	0.458	0.01	13.69	1.99	15.91
	PM	0.369	0.12	0.748	0.02			
Day 5	AM	0.119	0.06	0.452	0.01	14.72	2.33	17.15
	PM	0.081	0.02	0.257	0.01			
Day 6	AM	0.297	0.16	0.531	0.02	13.74	2.40	16.32
Total		1.06% (whole milk)				69.66	12.05	82.78

n.d. = not detected.

Table 4 Summary of extraction of radioactive residues from the fluensulfone goat metabolism study

			% TRR					
	TRR (mg eq/kg)		ACN:H_2O or Acetone:Hexane		0.1 M KOH 24% KOH 6 N HCl		PES	
Matrix	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]
Muscle	0.22-0.24	0.04-0.05	36-37	43-53	54-56	26-30	7.8-9.2	16.7-17.5
Kidney	1.40	0.67	40	48	55	50	5.6	1.9
Liver	2.62	0.98	26	28	72	71	2.0	1.1
Skim milk [a]	0.41	0.26	54	64	37	33	9.0	3.5
Milk fat [a]	3.42	0.33	44	64	34	5	n.d.	n.d.
Subcutaneous fat	0.13	0.07	35	80	57	7	0.8	12.7
Renal fat	0.08	0.04	51	61	35	23	14.5	25.6
Omental fat	0.07	0.07	58	74	37	14	5.6	11.4

[a] Milk from Day 6, AM.

n.d. = not detected.

Table 5 Characterization of radioactive residues in kidney

	Kidney			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	1.402	100.0	0.671	100.0
Solvent Extractable (ACN:H_2O)	0.558	39.8	0.322	48.0
Glucose	0.236	16.8	0.090	13.4
Unknowns [a]	0.243	17.4	0.203	30.1
Digestion of PES				
0.1 M KOH	0.029	2.1	0.029	4.3
24% KOH	0.736	52.5	0.137	20.4
6 N HCl (Rinse & Reflux)	–	–	0.170	25.3
Combined Extracts [b] Acidified and Partitioned with EtAc				
Aqueous Phase	0.689	49.1	0.294	43.8
Unknowns [c]	0.689	49.1	0.294	43.8
EtAc Phase	0.076	5.4	0.042	6.3
Unknowns [d]	0.051	3.7	0.023	3.3
PES	0.079	5.6	0.01	1.9

[a] For the thiazole label, there were at least six unknowns which each accounted for 1.1–9.5% of the TRR. For the butene label, there were at least seven unknowns which each accounted for 1.8–9.8% of the TRR.

[b] For the thiazole label, combined extracts are 0.1 M KOH and 24% KOH extracts. For the butene label, combined extracts are 0.1 M KOH, 24% KOH and 6 N HCl.

[c] For the thiazole label, there were at least three unknowns which each accounted for 7.7–26.0% of the TRR. For the butene label, there were at least four unknowns which each accounted for 1.8–30.7% of the TRR. Further work indicates that these were likely to be natural components.

[d] For the thiazole label, there were at least five unknowns which each accounted for 0.2–2.4% of the TRR. For the butene label, there were at least five unknowns which each accounted for 0.3–1.8% of the TRR.

Table 6 Characterization of radioactive residues in liver

	Liver			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	2.623	100.0	0.975	100.0
Solvent Extractable	0.673	25.7	0.276	28.3
Glucose	0.232	8.8	0.039	4.0
Lactose	0.208	7.9	0.036	3.7
Unknowns [a]	0.164	6.2	0.123	12.6
Digestion of PES				
0.1M KOH Extract	0.028	1.1	0.042	4.3
24% KOH Extract	1.328	50.6	0.483	49.5
6 N HCl Extract	0.542	20.7	0.163	16.7
Acidification of Combined Extracts [b] & Partition with EtAc				
Aqueous Phase	1.733	66.1	0.636	65.2
Unknowns [c]	1.711	65.3	0.566	58.2
EtAc Phase	0.165	6.3	0.052	5.3
Unknowns [d]	0.122	4.6	0.032	3.2
PES	0.052	2.0	0.011	1.1

[a] For thiazole labelled liver, there were at least five unknowns which each accounted for 0.6–1.8% of the TRR. For butene labelled liver, there were at least four unknowns which each accounted for 0.8–5.0% of the TRR.

[b] Combined extracts are 0.1 M KOH, 24% KOH and 6 N HCl extracts.

[c] For thiazole labelled liver, there were at least six unknowns which each accounted for 1.1–33.1% of the TRR. For butene

labelled liver, there were at least five unknowns which each accounted for 2.1–36.5% of the TRR. Further work indicates that these were likely to be natural components.

[d] For thiazole labelled liver, there were at least four unknowns which each accounted for 0.3–2.4% of the TRR. For butene labelled liver, there were at least five unknowns which each accounted for 0.4–1.6% of the TRR.

Table 7 Characterization of radioactive residues in skim milk

	Skim Milk			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.409	100.0	0.260	100.0
Solvent extractable	0.221	54.0	0.166	63.8
Lactose	0.187	45.7	0.164	63.1
Unknowns [a]	0.022	5.4	0.002	0.8
Digestion of PES				
Protease	0.151	36.9	0.085	32.7
PES	0.037	9.0	0.009	3.5

[a] For the thiazole label, there were two unknowns which each accounted for 2.2–3.2% of the TRR. For the butene label, there was one unknown.

Table 8 Characterization of radioactive residues in milk fat

	Milk Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	3.416	100.0	0.330	100.0
Solvent extractable	1.489	43.6	0.212	64.2
Clean-up on Silica-Gel				
Hexane Fraction	0.004	0.1	0	0
EtAc:Hexane Fraction	1.446	42.3	0.206	62.4
EtAc Fraction	0.039	1.1	0.006	1.8
Saponification of EtAc:Hexane Fraction & Partition with Hexane:H_2O and Acidified DCM				
Hexane Phase	0.197	5.8	0.122	37.0
Aqueous Phase	0.181	5.3	0.059	17.9
DCM Phase	1.069	31.3	0.025	7.6
Digestion of PES				
Protease	1.165	34.1	0.015	4.5
24% KOH	0.219	6.4	0	0
Loss [a]	0.543	15.9	0.103	31.2
PES [b]	0	0	0	0

[a] Difference in TRR. Loss assumed to be due to conversion to volatile ^{14}C-residues.

[b] No PES remained following digestion with 24% KOH.

Table 9 Characterization of radioactive residues in omental fat

	Omental Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.071	100	0.070	100
Solvent extractable	0.041	57.7	0.052	74.3
Clean-up on Silica-Gel				
Hexane Fraction	0.009	12.7	0.044	62.9
EtAc:Hexane Fraction	0.006	8.5	0.005	7.1

	Omental Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
EtAc Fraction	0.026	36.6	0.004	5.7
Saponification of Hexane Fraction & Partition with (1) Hexane:H_2O and (2) acidified DCM				
Basic Hexane Phase	0	0	0	0
Aqueous Phase	0	0	0.014	20.0
DCM Phase	0.009	12.7	0.030	42.9
Digestion of PES				
0.1 M KOH	0.007	9.9	0.005	7.1
24% KOH	0.019	26.8	0.005	7.1
Combined Alkaline Extracts Acidified and Partitioned with EtAc				
Aqueous Phase	0.021	29.6	–	–
EtAc Phase	0.005	7.0	–	–
PES	0.004	5.6	0.008	11.4

Table 10 Characterization of radioactive residues in subcutaneous fat

	Subcutaneous Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.131	100.0	0.071	100.0
Solvent Extractable (Hexane:Acetone)	0.046	35.1	0.057	80.3
Aqueous Phase	0.010	7.6	0.004	5.6
Clean-up on Silica-Gel of Combined Organic Extracts				
Hexane Fraction	0.020	15.3	0.049	69.0
EtAc:Hexane Fraction	0.008	6.1	0.003	4.2
EtAc Fraction	0.018	13.7	0.005	7.0
Saponification of Hexane Fraction & Partition with (1) Hexane:H_2O and (2) Acidified DCM				
Basic Hexane Phase	0	0	0	0
Aqueous Phase	0	0	0.012	16.9
DCM Phase	0.020	15.3	0.037	52.1
Digestion of PES				
0.1 M KOH	0.019	14.5	0.005	7.0
24% KOH	0.055	42.0	–	–
Combined Alkaline Fractions Partitioned with EtAc				
Aqueous Phase	0.061	46.6	–	–
EtAc Phase	0.013	9.9	–	–
PES	0.001	0.8	0.009	12.7

Table 11 Characterization of radioactive residues in renal fat

	Renal Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR	0.083	100.0	0.043	100.0
Solvent Extractable	0.042	50.6	0.022	51.2
Clean-up on Silica-Gel				
Hexane Fraction	0.020	24.1	0.014	32.6
EtAc:Hexane Fraction	0.006	7.2	0.004	9.3
EtAc Fraction	0.016	19.3	0.004	9.3
Saponification of Hexane Fraction & Partition with (1) Hexane:H_2O and (2) Acidified DCM				
Basic Hexane Phase	0	0	0.002	4.7
Aqueous Phase	0	0	0.003	7.0
DCM Phase	0.020	24.1	0.009	20.9
Digestion of PES				
0.1 M KOH	0.008	9.6	0.004	9.3
24% KOH	0.021	25.3	0.006	14.0
PES	0.012	14.5	0.011	25.6

Table 12 Characterization of radioactive residues in muscle

	Flank Muscle				Loin Muscle			
	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.217	100.0	0.054	100	0.239	100.0	0.040	100.0
Solvent extractable								
ACN:H_2O Fraction	0.079	36.4	0.023	42.6	0.087	36.4	0.021	52.5
Unknowns [a]	0.073	33.6	0.018	33.4	0.078	32.7	0.023	57.5
Hexane:Acetone	–	–	0.008	14.8	–	–	–	–
Digestion of PES								
0.1 M KOH	0.007	3.2	0.003	5.6	0.009	3.8	0.002	5.0
24% KOH	0.114	52.5	0.011	20.4	0.121	50.6	0.010	25.0
Combined Alkaline Extracts Acidified and Partitioned with EtAc								
Aqueous Phase	0.111	51.2	0.012	22.2	0.119	49.8	0.010	25.0
Unknowns [b]	0.088	40.4	–	–	0.089	37.2	–	–
EtAc Phase	0.010	4.6	0.002	3.7	0.011	4.6	0.002	5.0
PES	0.017	7.8	0.009	16.7	0.02	9.2	0.007	17.5

[a] Flank muscle: thiazole = six unknowns, 3.2–12.4% TRR; butene = five unknowns, 3.7–13.0% TRR. Loin muscle: thiazole = six unknowns, 1.7–20.1% TRR; butene = eight unknowns, 2.5–40.0% TRR. Further work indicates that these were likely to be natural components.

[b] Flank muscle: thiazole = six unknowns, 1.8–23.0% TRR. Loin muscle: thiazole = six unknowns, 2.5–20.1% TRR.

In summary, fluensulfone was not a significant residue in goat tissues or milk. Initially the parent compound is cleaved, displacing butene sulfinic acid which is readily excreted in the urine. However, excretion of the butene half of the molecule is not fully effective and the butene moiety is likely broken down to carbon dioxide and enters the normal metabolic pathways. The thiazole half of the molecule is converted to the thiazole methyl sulfone for excretion, but is not excreted as quickly. Therefore, a much larger portion of the thiazole moiety is incorporated into natural products much in the same way as the butene label. Incorporation of radiolabelled residues into glucose and eventually into lactose takes place mainly in the liver, but is also seen in the kidneys. Lactose is then exported to be excreted in milk. Through the citric acid cycle (i.e. oxaloacetate) radiolabelled residues can also be converted and incorporated into fatty acids and a variety of amino acids (e.g. aspartate) then eventually into triglycerides and proteins.

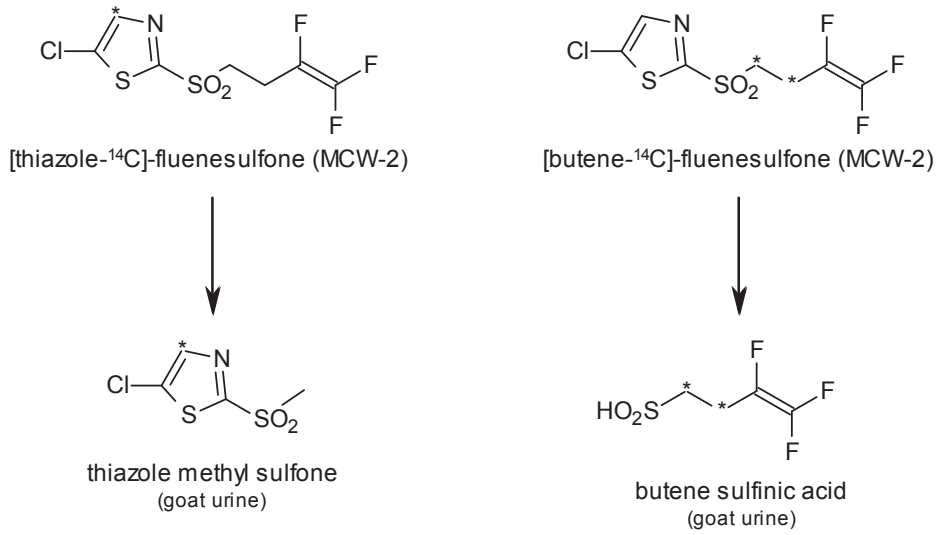


Figure 3 Proposed metabolic pathway of fluensulfone in lactating goat

Laying hens

The metabolism of fluensulfone in laying hens was investigated by LaMar and Quistad (2010, Study R-25454). For each radiolabel position, a group of ten hens was dosed for seven consecutive days at ca. 1.3 mg/bird/day (equivalent to 9.8 ppm in the diet). Eggs were collected twice daily and excreta were collected once daily throughout the study. Hens were sacrificed 20–22 hours after the final dosing, at which point tissues and GI tract (with contents) were collected for analysis.

Tissues, including GI tract with contents, were each homogenized in the presence of dry ice. Total radioactive residues were determined by LSC of solubilized tissues (liver, muscle, and fat) or following combustion (faeces, GI tract). Samples of liver, eggs, and muscle were extracted with twice with ACN:H_2O (1:1, v/v) and once by ACN (neat) for extraction of residues for characterization and identification. Samples of fat were extracted twice with hexane:acetone (4:1, v/v) followed by acetone (neat). Following the extraction procedures, all samples underwent alkaline treatment (KOH in MeOH/H_2O) of the post-extraction solids (PES). Residue analysis for the various extracts was by high-performance liquid chromatography (HPLC) and/or thin-layer chromatography (TLC). Numerous HPLC systems with varying stationary and mobile phases were investigated to achieve satisfactory separation of the radiolabelled components, with detection by UV absorption or refractive index. Identification of metabolites was by co-chromatography with known standards.

In the treated laying hens, 80% (thiazole label) and 79% (butene label) of the AD were recovered. Most of the administered dose was recovered in the excreta and gastrointestinal tracts (76–80%; Table 13). Butene radiolabelled matrices contained consistently higher ^{14}C-residues when compared to the thiazole radiolabel. For example, only 0.15% of the AD for the thiazole radiolabel was excreted in eggs compared to 1.7% for the butene radiolabel. Differences in the amount of total

radioactive residues between the two radiolabels can be attributed to increased incorporation into natural products for the butene label. Thiazole methyl sulfone and butene sulfonic acid were both identified in the excreta. For both radiolabel positions, residues in eggs steadily increased from Day 1 to Day 8 and did not plateau within the dosing period Table 14).

In fat samples, solvent extraction (acetone:hexane) released 81–95% of the TRR. Solvent extraction in liver, egg, and muscle was not as efficient, releasing approximately 13–34% of the total radioactivity from the matrix of interest. Use of basic and/or acidic conditions was required to accomplish more quantitative extraction (Table 15).

The TRRs were highest for liver (thiazole label: 0.64 mg eq/kg; butene label: 1.4 mg eq/kg) and egg (thiazole label: 0.29 mg eq/kg; butene label: 4.06 mg eq/kg). Thiazole-labelled omental and subcutaneous fats (0.04 mg eq/kg and 0.08 mg eq/kg, respectively), contained substantially lower radioactivity compared to butene radiolabelled fat (both 0.31 mg eq/kg). Breast and thigh muscle had the lowest amount of radiolabel in comparison to other tissues; however, butene radiolabelled muscle contained significantly higher residues (0.13 mg eq/kg for both thigh and breast muscles), compared to thiazole radiolabelled muscle (both 0.04 mg eq/kg). No tissues other than liver accounted for more than 0.1% of the AD.

Fluensulfone was detected in omental and subcutaneous fat, (0.009 mg/kg and 0.04 kg/kg for thiazole label, 0.02 mg/kg and 0.04 mg/kg for butene label). Trace amounts of fluensulfone may have been present in other matrices but could not be confirmed due to low levels. With the exception of thiazole sulfonic acid in liver (0.02 mg/kg), no other metabolites of fluensulfone were identified in eggs or tissues. Thiazole methyl sulfone and butene sulfonic acid were identified in faeces. The majority of the radioactivity appeared to be incorporated into natural products such as natural sugars (in liver) fatty acids (in eggs, fat and liver) and in proteins. Comparison of extraction of radioactivity from liver samples treated with and without protease enzyme indicates that ca. 0.16 mg/kg (24% TRR) is associated with proteins and/or amino acids. Incorporation of the radioactivity into triglycerides was noted in both fat matrices and in eggs, and accounted for 7% and 27% of the TRR for the thiazole and butene labels, respectively, in eggs and for 7–12% and 79–87% of the TRR for the thiazole and butene labels, respectively, in the fat matrices. In excreta, the identified residues were the methyl sulfone and BSA metabolites; parent fluensulfone was not observed. The tables below summarize the results of the poultry metabolism study.

Table 13 Total radioactive residues (TRRs) in tissues and excreta

Matrix	Thiazole-labelled Fluensulfone		Butene-labelled Fluensulfone	
	mg eq/kg	% of dose	mg eq/kg	% of dose
Tissues				
Liver	0.643	0.3	1.368	0.7
Eggs	0.286	0.15	4.064	1.71
Omental Fat	0.044	0.0	0.311	0.1
Subcutaneous Fat	0.075	0.0	0.311	0.0
Thigh Muscle	0.043	0.0	0.127	0.1

Matrix	Thiazole-labelled Fluensulfone		Butene-labelled Fluensulfone	
	mg eq/kg	% of dose	mg eq/kg	% of dose
Breast Muscle	0.043	0.0	0.117	0.1
Excreta				
Excreta	–	79.4	–	75.8
Gastrointestinal Tract	–	0.2	–	0.5
Total	–	80.1	–	79.0

Table 14 Total radioactive residues (TRRs) in eggs as function of time

Eggs		(Thiazole-^{14}C)-Label		(Butene-^{14}C)-Label	
		mg eq/kg	% of AD	mg eq/kg	% of AD
Day 1	AM [a]	not detected		not detected	
	PM	–		not detected	
Day 2	AM	0.009	0.00	0.006	0.00
	PM	–		0.050	0.00
Day 3	AM	0.019	0.01	0.218	0.11
	PM	–		0.294	0.01
Day 4	AM	0.029	0.02	0.342	0.17
	PM	–		0.661	0.03
Day 5	AM	0.041	0.02	0.486	0.24
	PM	–		–	
Day 6	AM	0.055	0.03	0.578	0.33
	PM	–		–	
Day 7	AM	0.061	0.03	0.684	0.37
	PM	–		–	
Day 8	AM	0.072	0.04	0.745	0.45
	PM	–		–	
Total		n.a.	0.15	n.a.	1.71

– = No egg production.

n.a. = Not applicable.

[a] Pre-dosing.

Table 15 Extractability of TRRs in tissues

			% TRR					
	TRR (mg eq/kg)		ACN:H_2O or Acetone:hexane		0.1 M KOH 24% KOH 6 N HCl MeOH		PES	
Matrix	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]	[Th-^{14}C]	[Bu-^{14}C]
Liver	0.60	1.17	13	15	73	84	14	0.4
Egg [a]	0.07	0.68	34	5.2	59	67	0	0
Omental fat	0.04	0.31	81	95	n.d.	n.d.	19	5
Subcutaneous fat	0.08	0.32	83	94	n.d.	n.d.	16	7
Thigh muscle	0.04	0.12	29	17	49	65	22	18
Breast muscle	0.04	0.11	22	20	53	65	25	15

[a] Day 8, morning collection

n.d. = No data

Table 16 Characterization of radioactive residues in liver

	Liver			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (by Sum of Fractions)	0.601	100.0	1.170	100.0
Solvent Extractable	0.078	13.0	0.180	15.4
Thiazole Sulfonic Acid	0.016	2.7	–	–
Unknowns [a]	0.030	5.0	0.164	14.1
Digestion of PES				
0.1 M KOH	0.045	7.5	0.059	5.0
24% KOH	0.334	55.6	0.703	60.1
6 N HCl	0.047	7.8	0.130	11.1
MeOH	0.012	2.0	0.093	7.9
Saponification of Combined Extracts [b] & Partition with (1) Hexane and (2) Acidic DCM				
Basic Hexane Phase	0	0	0	0
Acidic DCM Phase (Analysed by TLC)	0.064	10.6	0.068	5.8
Acidic Aqueous Phase	0.374	62.2	0.917	78.4
Unknowns [c]	0.264	43.9	0.801	68.4
Acidification of Combined Extracts & Partition with Ethyl Acetate				
EtAc Phase	0.203	33.8	0.248	21.2
Loss on Concentration	0.123	20.5	0.175	15.0
EtAc Phase (Analysed by HPLC)	0.080	13.3	0.073	6.2
Unknowns [d]	0.063	10.4	0.044	3.7
Acidic Aqueous Phase	0.235	39.1	0.737	63.0
PES	0.085	14.1	0.005	0.4

[a] For the thiazole label, there were at least four unknowns with two having retention times corresponding to the MCW-2 and methyl sulfone metabolite regions. Each unknown accounted for 0.5–2.7% of the TRR. For the butene label, there were at least five unknowns with one having a retention time corresponding to the MCW-2 region. Each unknown accounted for 0.3–11.5% of the TRR.

[b] Combined extracts are 0.1 M KOH, 24% KOH, 6 N HCl and MeOH Extracts.

[c] For the thiazole label, there were at least six unknowns which each accounted for 3.5–13.1% of the TRR. For the butene label, there were at least 10 unknowns which each accounted for 3.7–22.6% of the TRR.

[d] For the thiazole label, there were seven unknowns which each accounted for 0.7–3.2% of the TRR. For the butene label, there were at least seven unknowns which each accounted for 0.3–0.8% of the TRR.

Table 17 Characterization of radioactive residues in eggs

	Eggs (Day 8, AM)			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (by Sum of Fractions)	0.071	100.0	0.675	100.0
Solvent Extractable with ACN:H_2O	0.024	33.8	0.035	5.2
Hexane Phase (After Partition)	0.005	7.0	0	0
ACN:H_2O Phase	0.019	26.8	0.035	5.2
Unknowns [a]	0.014	19.7	0.034	4.9
Solvent Extractable with Hexane:Acetone	0.005	7.0	0.182	27.0
Hexane Phase	–	–	0	0
DCM Phase	–	–	0.164	24.3
Aqueous Phase	–	–	0.018	2.7
Digestion of PES				
0.1 M KOH Extract	0.005	7.0	0.058	8.6
24% KOH Extract	0.037	52.1	0.400	59.3
Acidification of Combined Extracts [b]& Partition with Ethyl Acetate				
EtAc Phase	0.020	28.2	0.202	29.9

	Eggs (Day 8, AM)			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
Unknowns [c]	0.009	12.6	–	–
Aqueous Phase	0.022	31.0	0.256	37.9
H_2O Rinse (Following C_{18} SPE)	0.011	15.5	0.081	12.0
MeOH Rinse (Following C_{18} SPE)	0.011	15.5	0.175	25.9
Unknowns [d]	–	–	0.172	25.4
PES [e]	0	0	0	0

[a] For the thiazole label, there were at least seven unknowns which each accounted for 1.4–8.5% of the TRR. For the butene label, there were at least six unknowns which accounted for 0.1–1.8% of the TRR.

[b] Combined extracts are the 0.1 M KOH and 24% KOH extracts.

[c] For the thiazole label, there were four unknowns which each accounted for 1.4–5.6% of the TRR.

[d] For the butene label, there were at least 10 unknowns which each accounted for 1.3–6.4% of the TRR.

[e] Following extraction with KOH, no PES remained.

Table 18 Characterization of radioactive residues in omental fat

	Omental Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR	0.043	100.0	0.312	100.0
Solvent Extractable	0.035	81.4	0.297	95.2
Silica-Gel SPE				
Hexane Rinses	0.005	11.6	0.272	87.2
Combined Hexane: EtAc Eluates and ACN Phases	0.030	69.8	0.025	8.0
HPLC Analysis of the Combined Hexane: EtAc:ACN Fractions				
Fluensulfone	0.009	20.9	0.016	5.1
Unknowns [a]	0.020	46.6	0.002	0.6
Saponification of SPE Hexane Fraction and Partitioning with Hexane:H_2O and DCM				
Alkaline Hexane Phase	–	–	0.011	3.5
Acid DCM Phase	–	–	0.237	76.0
Acid Aqueous Phase	–	–	0.024	7.7
PES	0.008	18.6	0.015	4.8

[a] For the thiazole label, there were at least two unknowns which each accounted for 4.7 or 41.9% of the TRR. For the butene label, there were at least two unknowns which each accounted for 0.3% of the TRR.

Table 19 Characterization of radioactive residues in subcutaneous fat

	Subcutaneous Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.075	100.0	0.324	100.0
Solvent Extractable	0.062	82.7	0.303	93.5
Clean-up on Silica-Gel				
Hexane Rinsing	0.006	8.0	0.257	79.3
Hexane: EtAc:ACN Combined	0.056	74.7	0.048	14.8
HPLC				
Fluensulfone	0.041	54.7	0.037	11.4
M1	–	–	0.010	3.1
Unknowns [a]	0.013	17.4	–	–
Saponification of Hexane Fraction and Partitioning				
Alkaline Hexane Phase	–	–	0.013	4.0
Acid DCM Phase	–	–	0.231	71.3

	Subcutaneous Fat			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR
Acid Aqueous Phase	–	–	0.014	4.3
Further Extraction of PES with ACN and ACN:H_2O	0.001	1.3	–	–
PES	0.012	16.0	0.021	6.5

[a] For the thiazole label, there were at least three unknowns which each accounted for 2.7–12.0% of the TRR. For the butene label, there were no unknowns.

Table 20 Characterization of radioactive residues in muscle

	Thigh Muscle				Breast Muscle			
	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	%TRR	mg eq/kg	%TRR	mg eq/kg	%TRR	mg eq/kg	%TRR
TRR (Sum of Fractions)	0.041	100.0	0.121	100	0.036	100.0	0.111	100
Solvent extractable	0.012	29.3	0.020	16.5	0.008	22.2	0.022	19.8
Unknowns [a]	0.008	19.3	0.020	16.5	0.006	16.7	0.015	13.5
Digestion of PES								
0.1 M KOH Extract	0.003	7.3	0.007	5.8	0.002	5.6	0.007	6.3
24% KOH Extract	0.017	41.5	0.072	59.5	0.017	47.2	0.065	58.6
Acidification of Combined Extracts [b] & Partition with EtAc								
EtAc Phase	0.010	24.4	0.015	12.4	0.005	13.9	0.009	8.1
Unknowns [c]	0.010	24.4	–	–	–	–	–	–
Aqueous Phase	0.011	26.8	0.064	52.9	0.014	38.9	0.063	56.8
H_2O Rinse (Following C_{18} SPE)	–	–	0.019	15.7	–	–	0.019	17.1
MeOH Rinse (Following C_{18} SPE)	–	–	0.045	37.2	–	–	0.044	39.6
Unknowns [d]	0.010	24.4	0.041	33.8	0.014	38.8	0.035	31.5
PES	0.009	22.0	0.022	18.2	0.009	25.0	0.017	15.3

[a] For the thiazole labelled thigh muscle, there were at least six unknowns with one having a retention time in the region of MCW-2. Each unknown accounted for 2.4–7.3% of the TRR. For the butene labelled thigh muscle, there were at least three unknowns which accounted each for 5.0–5.8% of the TRR. For the thiazole labelled breast muscle, there were at least six unknowns with one having a retention time in the region of MCW-2. Each unknown accounted for 0–11.1% of the TRR. For the butene labelled breast muscle, there were at least three unknowns which each accounted for 1.8–8.1% of the TRR.

[b] Combined extracts are the 0.1 M KOH and 24% KOH extracts.

[c] For the thiazole labelled thigh muscle, there was only one peak in the fraction.

[d] For the thiazole labelled thigh muscle, there were at least four unknowns which each accounted for 2.4–9.8% of the TRR. For the thiazole labelled breast muscle, there were two unknowns each accounting for 19.4% of the TRR.

In summary, the poultry metabolism study indicates that the parent compound is cleaved displacing butene sulfinic acid, while the thiazole moiety is converted to the thiazole methyl sulfone and thiazole sulfonic acid. Both are eliminated in the excreta. Fluensulfone is broken down to carbon dioxide and subsequently enters normal metabolic pathways. Through the citric acid cycle, radiolabelled residues are converted and incorporated into fatty acids and a variety of amino acids, then eventually into triglycerides and proteins (as seen in fat and liver). The thiazole portion of fluensulfone is excreted at a slightly higher rate. The higher levels of butene radiolabel incorporation

into natural products can be mostly attributed to association with fatty acids, which is not as apparent with thiazole radiolabelled tissues.

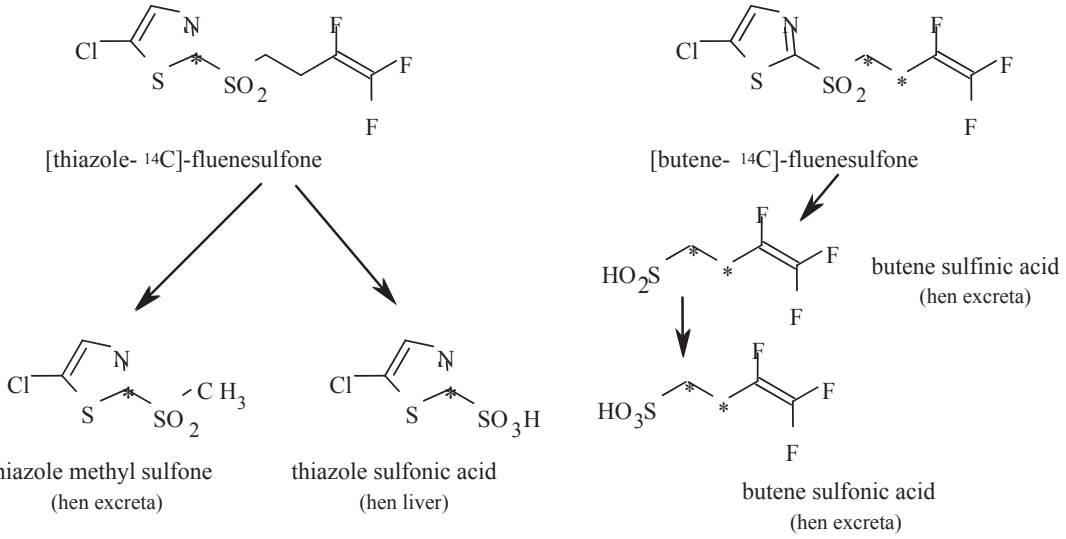


Figure 4 Proposed metabolic pathway of fluensulfone in laying hens

Plant metabolism

The Meeting received studies depicting the metabolism of fluensulfone in tomato, lettuce and potato. All of the studies were conducted with fluensulfone which was radiolabelled, separately, in the thiazole ring and the ethane bridge between the sulfonyl and trifluorobutene moieties.

Fluensulfone was extensively metabolised in all of the studies, with the only major residues being the BSA and TSA metabolites. A few chromatographic fractions had radioactivity in excess of 10% TRR. Investigation of these fractions indicated that the residues were associated with the BSA or TSA metabolites, as salts or other forms of the compounds.

Tomato

The metabolism of fluensulfone was investigated in tomato by Quistad and Bautista (2011, Report OR-25456). For each radiolabel position, an application of fluensulfone, formulated as an emulsifiable concentrate (48% ai), was made to soil at a rate of 4.1 kg ai/ha. Later that same day, tomato seedlings were planted into the treated soil.

Mature tomato fruits were harvested 87 days after treatment. Total radioactive residues were determined by combustion and LSC. Samples were extracted with ACN and ACN:H_2O followed by strong basic hydrolysis for residue characterization and analysis by TLC and/or HPLC. Residue identification was by co-chromatography of the available reference standards. Presence of the known metabolites BSA, MeS, and TSA was confirmed by HPLC-UV, HPLC-MS, and TLC. For unknown

metabolites, the extracts were cleaned up by solid-phase extraction (SPE) with silica-gel columns followed by analytical and semi-preparative HPLC followed by HPLC-MS. No storage stability determination was required as storage time after harvest did not exceed 18 days. Nevertheless a tomato sample containing thiazole labelled residues was reanalysed after 178 days of frozen storage. Fruit was extracted with ACN:H_2O in the same way as the initial fruit sample. HPLC analysis of the combined ACN:H_2O extracts confirmed the stability of the extracts under storage conditions.

Total radioactive residues were higher in samples from the [Bu-^{14}C]fluensulfone treatment than from the [Th-^{14}C]fluensulfone treatment (Table 21). Residues were < 0.001 mg eq/kg in the control sample. There was good agreement between total residues based on the sum of extracted fractions and total residues based on the combustion analysis.

Residues were readily extracted with ACN + ACN:H_2O (Table 22), with the follow-up alkaline extraction releasing only an additional 7–8% of the TRR. No fluensulfone was detected in the tomato samples. The identified residues were predominantly the BSA (42% TRR) and TSA (45% TRR) metabolites from the [Bu-^{14}C] and [Th-^{14}C] treatments, respectively (Table 23). From the [Th-^{14}C] treatment, M3, the most abundant unknown metabolite, was considered to be due to the non-retention of TSA, which is a known phenomenon for sulfonic acids. This was confirmed by analysis with and without the presence of matrix which had an effect on peak shape and also by assessing the effects of column loading. Some inter-conversion between M1 and M3 was also noted during these experiments. Further investigation of M1 and M2 suggests that these compounds were salts of TSA. Unresolved radioactivity accounted for 22% of the TRR. From the [Bu-^{14}C] treatment, Fraction F1-F2 in the combined ACN:H_2O extracts accounted for 27% of the TRR and was found to be mainly due to unretained BSA. Fractions F4 and F5 (2–5% of the TRR) were salts of BSA or related compounds. Unresolved radioactivity accounted for 14% of the TRR.

Table 21 Total radioactive residues (TRRs) in tomato following pre-plant application of [^{14}C]fluensulfone

	TRR (mg eq/kg) [a]				
	[Th-^{14}C]		[Bu-^{14}C]		
Matrix	sum of fractions	by combustion	sum of fractions	by combustion	Untreated Control
Tomato Fruits	0.256	0.266	0.517	0.516	< 0.001

[a] Values determined as sum of extracted and unextracted radiocarbon, except for untreated controls which were determined by combustion

Table 22 Extraction summary for tomato fruits after treatment with [^{14}C]fluensulfone

	Radioactive Distribution			
	[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR
ACN:H_2O	0.227	88.67	0.472	91.30
KOH (0.1 M)	0.009	3.52	0.016	3.09
KOH (24%)	0.011	4.30	0.020	3.87
PES	0.009	3.52	0.009	1.74

Total	0.256	100.0	0.517	100.0

Table 23 Radiocarbon detected in tomato fruit following treatment with [^{14}C]fluensulfone

	Tomato Fruit			
	[Th-^{14}C]		[Bu-^{14}C]	
Metabolite/Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.256 (0.266) [a]	100.0	0.517 (0.516)	100.0
Solvent Extractable	0.227	88.7	0.472	91.3
Fluensulfone	–	–	–	–
TSA	0.116	45.4	–	–
M1—Form of TSA	0.009	3.5	–	–
M2—Form of TSA	0.007	2.7	–	–
M3—Form of TSA	0.037	14.5	–	–
M4	0.001	0.4	–	–
M8	< 0.001	0.1	–	–
BSA	–	–	0.215	41.6
F1-F2—Form of BSA	–	–	0.137	26.5
F4—Form of BSA	–	–	0.027	5.2
F5—Form of BSA	–	–	0.011	2.1
Unresolved	0.056	21.9	0.074	14.3

[a] Values in parentheses determined by combustion

Lettuce

The metabolism of fluensulfone was investigated in lettuce by Quistad and Bautista (2011, Report R-25455). For each radiolabel position, an application of fluensulfone, formulated as an emulsifiable concentrate (48% ai), was made to soil at a rate of 4.1 kg ai/ha. Lettuce seeds were planted prior to application.

Samples of lettuce foliage were collected 49 days (immature) and 64 days (mature) after treatment. Within 23 days of harvest, the harvested lettuce samples were homogenized and the TRRs in each sample were determined by combustion analysis and LSC. Samples were extracted with ACN:H_2O and ACN, followed by strong basic hydrolysis. For thiazole-labelled samples, the extract was analysed by HPLC and TLC. For butene-labelled samples, the extract was filtered and the individual residues were then purified by two different HPLC methods. Purified metabolite (butene sulfonic acid) was then analysed via TLC and LC-MS.

Total radioactive residues were higher in samples from the [Th-^{14}C]fluensulfone treatment than from the [Bu-^{14}C]fluensulfone treatment (Table 24). Residues were < 0.001 mg eq/kg in the control sample. There was good agreement between total residues based on the sum of extracted fractions and total residues based on the combustion analysis, although the total by sum of fractions was consistently ca. 87% of that determined by combustion.

Residues were readily extracted with ACN + ACN:H2O (Table 25), with the follow-up alkaline extraction releasing an additional 5–20% of the TRR. Trace levels of fluensulfone were found in the immature lettuce samples from both radiolabel positions. Major residues were the BSA (24%

TRR/38% TRR, immature/mature) and TSA (68% TRR/71% TRR, immature/mature) metabolites from the [Bu-^{14}C] and [Th-^{14}C] treatments, respectively (Table 26). From the [Th-14C] treatment, the sum of all other fractions (including unresolved) accounted for 24% of the TRR. Further analysis showed that the separated fractions were salts of TSA and/or other forms of TSA. M3 was found to be polar and due to unretained TSA. M1 was found to be a TSA salt or artifact due to chromatography. Metabolites M4, M5 and M6 were also chromatographic artefacts. Unresolved radioactivity accounted for 6–17% of the TRR. From the [Bu-^{14}C] treatment, the sum of all other fractions (including unresolved) accounted for 46–52% of the TRR. Unresolved radioactivity accounted for 14–24% of the TRR. Further investigation of unidentified fractions showed that most of the fractions were salts or other forms of BSA and/or BSA bound to matrix compounds. Therefore, only BSA is present as a major metabolite with minor amounts of conjugated parent.

Table 24 Total radioactive residues (TRRs) in lettuce following one application of [^{14}C]fluensulfone

	TRR (mg eq/kg) [a]				
	[Th-^{14}C]		[Bu-^{14}C]		
Matrix	sum of fractions	by combustion	sum of fractions	by combustion	Untreated Control
Immature Lettuce (49 DAT)	5.302	6.092	2.071	2.436	< 0.001
Mature Lettuce (69 DAT)	6.145	7.098	1.290	1.548	< 0.001

[a] Values determined as sum of extracted and unextracted radiocarbon, except for untreated controls which were determined by combustion

Table 25Extraction summary for lettuce after treatment with [^{14}C]fluensulfone

	Radioactive Distribution							
	Immature Lettuce (49 DAT)				Mature Lettuce (69 DAT)			
	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
ACN:H_2O	4.867	91.8	1.582	76.4	5.831	94.9	1.078	83.6
0.1 N KOH	0.201	3.8	0.156	7.5	0.153	2.5	0.095	7.4
24% KOH	0.209	3.9	0.273	13.2	0.145	2.4	0.103	8.0
PES	0.025	0.5	0.060	2.9	0.016	0.3	0.014	1.1
Total	5.302	100.0	2.071	100.0	6.145	100.0	1.290	100.0

Table 26 Metabolites detected in lettuce following treatment with [^{14}C]fluensulfone

		Immature Lettuce				Mature Lettuce			
		[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Metabolite		mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	Sum of Fractions	5.30	100.0	2.071	100.0	6.15	100.0	1.29	100.0
	Combustion	6.09		2.436		7.10		1.55	
Solvent Extractable		4.867	91.8	1.582	76.4	5.831	94.9	1.078	83.6
Fluensulfone		0.009	0.2	0.008	0.4	–	–	–	–
TSA		3.572	67.5	–	–	4.34	70.6	–	–
M1—Form of TSA		0.390	7.4	–	–	0.138	2.2	–	–
M2—Form of TSA		0.372	7.0	–	–	0.191	3.1	–	–
M3—Form of TSA		0.091	1.7	–	–	0.024	0.4	–	–
M4		0.041	0.8	–	–	0.057	0.9	–	–

M5	0.050	0.9	–	–	–	–	–	–
M6	–	–	–	–	0.014	0.2	–	–
BSA	–	–	0.492	23.8	–	–	0.485	37.6
F1-F2—Form of BSA	–	–	0.161	7.7	–	–	0.094	7.3
F4—Form of BSA	–	–	0.104	5.0	–	–	0.019	1.5
F5	–	–	0.183	8.9	–	–	0.072	5.5
F6	–	–	0.227	11.0	–	–	0.054	4.2
F7	–	–	0.032	1.5	–	–	0.007	0.5
F11	–	–	0.035	1.7	–	–	0.008	0.6
F12	–	–	0.005	0.2	–	–	0.032	2.5
Unresolved	0.336	6.3	0.293	14.1	1.067	17.4	0.307	23.8

Potato

The metabolism of fluensulfone was investigated in potato by Quistad and Bautista (2011, Report R-25459). For each radiolabel position, an application of fluensulfone, formulated as an emulsifiable concentrate (48% ai), was made to soil at a rate of 4.0 kg ai/ha ([Th-^{14}C]label) or 4.1 kg ai/ha ([Bu-^{14}C]label). Potato seed pieces were planted prior to application.

Samples of potato tuber were collected 70 days (immature) and 106 days (mature) after treatment. Within 35 days of harvest, the harvested potato tuber samples were homogenized and the TRRs in each sample were determined by combustion analysis and LSC. Samples were extracted with ACN:H_2O and ACN, followed by strong basic hydrolysis ([Bu-^{14}C] treatment only) and strong acid extraction (mature samples only). The initial organic extract was analysed by HPLC and TLC.

Total radioactive residues were higher in samples from the [Th-^{14}C]fluensulfone treatment than from the [Bu-^{14}C]fluensulfone treatment (Table 27). Residues were < 0.001 mg eq/kg in the control sample. There was good agreement between total residues based on the sum of extracted fractions and total residues based on the combustion analysis.

Residues were readily extracted with ACN + ACN:H_2O (Table 28), with the follow-up alkaline extraction releasing an additional 12–22% of the TRR from the [Bu-^{14}C] treated samples. For the mature [Bu-^{14}C] treated sample, the acid extraction released ca. 8% of the TRR. Trace levels of fluensulfone were found in the mature tuber samples from both radiolabel positions (however, this was not confirmed by TLC analysis). Major residues were the BSA (31% TRR/26% TRR, immature/mature) and TSA (63% TRR/65% TRR, immature/mature) metabolites from the [Bu-^{14}C] and [Th-^{14}C] treatments, respectively (Table 29). From the [Th-^{14}C] treatment, the sum of all other fractions (including unresolved) accounted for 25–29% of the TRR. The most abundant unidentified fraction in the combined ACN:H_2O extracts was M3 and accounted for 3–7% of the TRR. Further examination showed this was a polar fraction which was considered to be an artifact resulting from the non-retention of TSA. A small amount of M1 was detected (< 2% of the TRR) which may attributable to methyl sulfone, but this was not confirmed by TLC analysis. Unresolved radioactivity accounted for 20–21% of the TRR and was attributed to matrix-bound radioactivity causing smearing within the HPLC column or remaining in the pre-column. Further extraction of the PES (8% of the TRR) was not performed due to the low levels of radioactivity compared the amounts that had been

identified. From the [Bu-^{14}C] treatment, the sum of all other fractions (including unresolved) accounted for 46–50% of the TRR. The most abundant unidentified fraction was the composed fraction F1-F2 in the combined ACN:H_2O extracts which accounted for 16–18% of the TRR. It was found to be mainly due to unretained BSA. Unresolved radioactivity (due to chromatographic artefacts) accounted for 28% of the TRR. Three other fractions F4, F5 and F9, containing < 1% of the TRR, were also resolved but no identification work was carried out due to the very low levels of radioactivity.

Table 27 Total radioactive residues (TRRs) in potato tubers following application of [^{14}C]fluensulfone

	TRR (mg eq/kg) [a]				
	Thiazole Label		Butene Label		
Matrix	sum of fractions	by combustion	sum of fractions	by combustion	Untreated Control
Immature Potato Tubers (70 DAT)	0.335	0.324	0.225	0.222	< 0.001
Mature Potato Tubers (106 DAT)	0.467	0.436	0.163	0.168	< 0.001

[a] Values determined as sum of extracted and unextracted radiocarbon, except for untreated controls which were determined by combustion

Table 28 Extraction summary for potato tubers after treatment with [^{14}C]fluensulfone

	Radioactive Distribution (mg eq/kg)							
	Immature Potato Tubers (70 DAT)				Mature Potato Tubers (106 DAT)			
	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
ACN:H_2O	0.308	91.94	0.173	76.89	0.428	91.65	0.129	79.14
0.1 N KOH	–	–	0.014	6.22	–	–	0.010	6.13
24% KOH	—	—	0.036	16.00	—	—	0.010	6.13
72% H_2SO_4	—	—	—	—	—	—	0.013	7.98
PES	0.027	8.06	0.002	0.9	0.039	8.35	0.001	0.61
Total	0.335	100.0	0.225	100.0	0.467	100.0	0.163	100.0

Table 29 Radiocarbon detected in potato tubers treated with [^{14}C]fluensulfone

		Immature Potato Tubers (70 DAT)				Mature Potato Tubers (106 DAT)			
		[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Metabolite/Fraction		mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
TRR	Sum of fractions	0.335	100.0	0.225	100.0	0.467	100.0	0.163	100.0
	Combustion	0.324		0.222		0.436		0.168	
Solvent Extractable		0.308	91.9	0.173	76.9	0.428	91.7	0.129	79.1
Fluensulfone		–	–	–	–	0.005	1.1	0.005	3.1
TSA		0.211	63.0	–	–	0.305	65.3	–	–
M1—Form of TSA		0.005	1.5	–	–	0.009	1.9	–	–
M3—Form of TSA		0.023	6.9	–	–	0.016	3.4	–	–
BSA		–	–	0.069	30.7	–	–	0.042	25.8
F1-F2—Form of BSA		–	–	0.037	16.4	–	–	0.029	17.8
F4—Form of BSA		–	–	< 0.001	< 0.1	–	–	0.002	1.2
F5		–	–	0.001	0.4	–	–	0.002	1.2
F9		–	–	0.002	0.9	–	–	0.002	1.2
Unresolved		0.069	20.6	0.064	28.4	0.093	19.9	0.046	28.2

Overall, the metabolism of fluensulfone in tomato, lettuce, and potato is similar and corresponds well with that observed in rotational crop (see below). An overall summary of the metabolic residue profile from the target crops studies is shown in Table 30, followed by the proposed pathway in Figure 5.

Table 30 Summary of results from metabolism studies with fluensulfone in tomato, lettuce, and potato

	Lettuce				Potato					
	Immature		Mature		Immature		Mature		Tomato	
Fraction/ Compound	% TRR	mg equiv./kg	% TRR	mg equiv./kg	% TRR	mg equiv./kg	% TRR	mg equiv./kg	% TRR	mg equiv./kg
[^{14}C-Butene] Fluensulfone										
TRR, mg/kg	2.4		1.6		0.22		0.17		0.52	
Extract	76	1.6	84	1.1	77	0.17	79	0.13	91	0.47
Parent	0.2	0.009	–	–	–	–	3.1	0.005	–	–
BSA [a]	60 (36)	1.2 (0.75)	60 (22)	0.77 (0.29)	47 (18)	0.11 (0.041)	44 (21)	0.071 (0.035)	68 (21)	0.35 (0.06)
TSA [b]	–	–	–	–	–	–	–	–	–	–
Other	14	0.29	24	0.31	30	0.068	32	0.052	22	0.11
Digest	21	0.43	15	0.20	22	0.05	20	0.033	7.0	0.036
PES [c]	2.9	0.06	1.1	0.014	0.9	0.002	0.61	0.001	1.7	0.009
[^{14}C-Thiazole] Fluensulfone										
TRR, mg/kg	6.1		7.1		0.32		0.44		0.27	
Extract	92	4.9	95	5.8	92	0.31	92	0.43	89	0.23
Parent	0.4	0.008	–	–	–	–	1.1	0.005	–	–
BSA [a]	–	–	–	–	–	–	–	–	–	–
TSA [b]	85 (18)	4.5 (1.4)	77 (6.6)	4.8 (0.41)	71 (8.4)	0.24 (0.028)	71 (5.3)	0.33 (0.025)	67 (21)	0.17 (0.06)
Other	6.3	0.34	17	1.1	21	0.069	20	0.096	22	0.056
Digest	7.7	0.41	4.9	0.30	–	–	–	–	7.8	0.02
PES	0.5	0.025	0.3	0.016	8.1	0.027	8.4	0.039	3.5	0.009

[a] Includes fractions shown to be salts and/or chromatographic artefacts of BSA, which are shown parenthetically.

[b] Includes fractions shown to be salts and/or chromatographic artefacts of TSA, which are shown parenthetically.

[c] Post-extraction solids

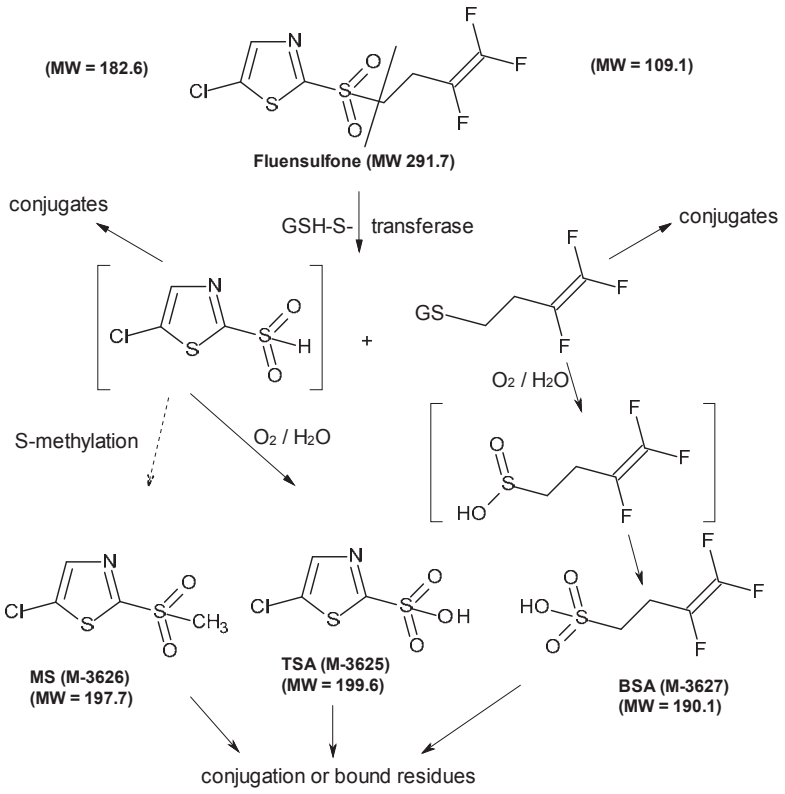


Figure 5 Proposed metabolic pathway of fluensulfone in target and rotational crops

Environmental fate in soil

The Meeting received studies depicting the photodegradation of fluensulfone on soil; aerobic soil metabolism of fluensulfone, TSA, and MeS; and a confined rotational crop study with radish, lettuce, and wheat.

Photolysis

Photolysis of fluensulfone on the surface of soil was investigated by Ponte (2012, Report R-23320) in a study consisting of a preliminary test phase and a definitive test phase. In both phases, [Bu-^{14}C] or [Th-^{14}C] labelled fluensulfone was applied to a medium textured sandy loam soil (Table 31) at a rate of 4 kg/ha. The soil was irradiated with artificial sunlight, continuously, for 14 days, corresponding to 32 days of natural sunlight at 38°N. Soils were maintained at 75% of field moisture capacity (at 1/3 bar) and sampled at various time points throughout the irradiation period. The experimental design included a trapping system to capture volatile organic compounds as well as CO_2. Volatilized radiocarbon was released from foam trap plugs by extraction with ACN. Soils were extracted with acetone:water (4:1, v/v). For each sample matrix, TRRs were determined by LSC of trap solution or extract. For determination of residues, soil extracts were analysed by HPLC-UV and co-chromatographed with known standards; confirmation of metabolites was by TLC.

Table 31 Characteristics of the Soil (Northwood, US) Used

Parameter (units)	Value
Source	Northwood, North Dakota, USA
pH in water	6.8
Cation Exchange Capacity (CEC, meq/100 g)	17
Organic Carbon (%)	2
% Moisture at 1/3 bar	21.9
% Moisture at 15 bar	14
% Moisture at 1/10 bar (pF 2.0)	29.3
Bulk Density (disturbed) (gm/cc)	1.02
Sand (%)	63
Silt (%)	16
Clay (%)	21
USDA Textural Classification	Sandy Loam
FAO Textural Class	Medium
Olsen Phosphorus (ppm)	11
Total Nitrogen (Analyser) (%)	0.16
Soluble Salts (mmhos/cm)	0.17
Base Saturation Data	
Cation	Percent / ppm
Calcium	63.2 / 2152
Magnesium	20.4 / 417
Sodium	0.3 / 13
Potassium	3.8 / 253
Hydrogen	12.2 / 21

In irradiated samples, fluensulfone levels decreased from their initial levels to 52% ([Bu-^{14}C]) or 34% ([Bu-^{14}C]) of the AR (Tables 32-34).

Table 32 Material balance and metabolism of [Th- and Bu-^{14}C]fluensulfone soil photolysis (preliminary test)

	[Th-^{14}C] (% AR)				[Bu-^{14}C] (%AR)			
	Incubation Time In Days							
	0	3	6	6	0	3	6	6
Fraction/Identity		(Light)	(light)	(Dark)		(Light)	(Light)	(Dark)
Fluensulfone	92.1	78.4	59.5	84.6	92.8	70.5	62.3	88.3
Other HPLC peaks	0.0	0.4	0.9	0.0	0.6	0.6	0.1	0.4
Other volatiles in EG [a]	NA	1.5	3.5	0.8	NA	1.3	2.2	0.4
$^{14}CO_2$	NA	6.5	12.3	2.6	NA	1.7	6.9	2.2
Non-extractables	3.2	10.3	16.8	4.9	6.2	21.1	20.1	6.1
Total	95.3	97.1	93.0	92.9	99.6	95.2	91.6	97.4
Mean total ± SD	94.6 ± 2				96 ± 3.4			

[a] Ethylene glycol

Table 33 Material balance and metabolism of [Bu-^{14}C]fluensulfone soil photolysis (definitive test)

	[Bu-^{14}C] (%AR)					
	Incubation Time In Days					
Fraction/Identity	0	2	5	7	9	13
Fluensulfone	91.8	82.9	71.5	74.6	56.2	52.2
Others [a]	0.3	0.2	1.8	1.0	3.9	4.9
Non-extractables	3.7	12.2	20.2	16.0	16.5	19.4

EG Trap	NS	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
NaOH Trap	NS	1.1	< 1.8	3.1	8.2	8.4
ACN Trap	NS	0.6	< 0.9	0.7	2.5	2.6
Total	95.8	96.9	95.9	95.2	87.5	87.4
Mean total ± SD	93.1 ± 4.4					

NS = Not Sampled

[a] Corresponds to at least six fractions.

Table 34 Material balance and metabolism of [Th-^{14}C]fluensulfone soil photolysis (definitive test)

	[Th-^{14}C] (%AR)		
	Incubation Time in Days		
Fraction/Identity	0	4	14
Fluensulfone	83.5	78.4	34.4
TSA	0.2	0.3	8.6
Others	0.7	0.8	1.1
Non-extractables	6.2	10.0	16.4
Foam plug trap	1.0	0.4	3.8
2 N H_2SO_4 trap	0.5	0.1	2.7
NaOH trap	4.3	1.3	19.9
Total	96.3	91.3	86.9
Mean total ± SD	91.5 ± 4.7		

Aerobic soil metabolism (Fluensulfone)

The metabolism and degradation kinetics of fluensulfone in aerobic soils was investigated by Moser (2011, Report R-27436). In that study, [Bu-^{14}C] or [Th-^{14}C] labelled fluensulfone was applied at a rate of 4 kg/ha to six different soils (Table 35). The soils were incubated under dark, aerobic conditions at 20 °C for 120 days. Samples were collected at various time points throughout the study, extracted first with $CaCl_2$ and then with ACN:H_2O and analysed for residues by LSC, HPLC, and/or TLC. In addition, the Fislis soil underwent Soxhlet extraction and analysis by LSC and TLC.

Table 35 Characteristics of the soils used in the aerobic metabolism study for fluensulfone

Parameter	Value					
Name	Fislis	Hagenthal	Horn	Montesquieu	Senozan	Sevelen
pH ($CaCl_2$)	6.75	7.13	7.23	7.36	7.54	7.36
Organic carbon %	2.13	1.65	2.36	1.5	0.61	1.61
CEC (meq/100 g soil)	22.99	18.79	21.72	21.09	13.63	9.09
Soil type	silt loam	silt loam	loam	clay loam	loam	sandy loam
Bulk density [kg/dm^3]	1.08	1.22	0.99	1.18	1.21	1.18
Particle size analyses (mm):						
0.002 (clay) [%]	26.42	24.42	25.11	38.70	20.58	9.51
0.002–0.05 (silt) [%]	65.57	53.51	36.22	31.84	35.25	36.96
0.05–2.0 (sand) [%]	8.01	22.07	38.67	29.46	44.17	53.53
Water holding capacity (g water/100 g soil):						
at pF 1.0	75.62	56.80	73.15	59.76	48.77	58.94
at pF 2.0	39.65	36.88	33.52	33.52	29.97	31.48
at pF 2.5	30.98	25.83	28.47	25.91	19.52	21.45
Biomass determination as mg C/100 g soil (%)						
pre-study	26.9 (1.3)	22.5 (1.4)	15.1 (0.6)	26.9 (1.8)	26.9 (4.4)	18.1 (1.1)
test initiation	28.0 (1.3)	22.5 (1.4)	39.1 (1.7)	22.5 (1.5)	17.0 (2.8)	22.5 (1.4)
mid-study	22.5 (1.1)	22.5 (1.4)	22.5 (1.0)	28.1 (1.9)	17.0 (2.8)	17.0 (1.1)
test end	18.1 (0.8)	28.0 (1.7)	33.6 (1.4)	17.0 (1.1)	17.0 (2.8)	22.5 (1.4)

Table 36 Distribution of applied radioactivity following application of [^{14}C]fluensulfone to six soils

		Percent of applied radioactivity, [Bu-^{14}C]/ [Th-^{14}C]						
Soil	Day	$CaCl_2$ extract	Organic extract	Total extractable	Soil bound	$^{14}CO_2$	VOC	Total recovered
Fislis	0	18.8/24.1	68.8/68.5	87.6/92.6	9.8/4.6	NA/NA	NA/NA	97.4/97.2
	2	18.8/22.8	59.7/66.4	78.5/89.2	15.5/8.0	4.6/0.7	< 0.1/< 0.1	98.6/97.9
	7	15.6/27.2	51.5/59.9	67.1/87.1	19.0/12.3	0.6 [a]/1.9	< 0.1/< 0.1	86.7 [a]/101.4
	14	13.2/29.4	33.8/53.9	47.1/83.3	31.5/10.3	39.1/4.3	0.1/< 0.1	117.8 [b]/97.9
	21	11.3/30.5	31.8/50.9	43.1/81.4	29.9/11.3	1.1/5.3	< 0.1/< 0.1	74.1 [a]/98.1
	28	9.6/27.3	27.5/53.0	37.1/80.3	33.4/9.8	29.6/5.1	< 0.1/< 0.1	100.1/95.2
	50	6.8/33.0	12.8/45.3	19.7/78.2	37.8/12.7	44.3/7.4	< 0.1/< 0.1	101.8/98.3
	77	2.6/NS	3.2/NS	5.8/NS	43.9/NS	55.7/NS	< 0.1/NS	105.5/NS
	90	1.9/NS	3.0/NS	4.8/NS	38.8/NS	55.5/NS	< 0.1/NS	99.1/NS
	120	0.5/33.1	1.7/39.6	2.2/72.7	40.1/6.0	11.2/16.8	< 0.1/< 0.1	53.6 [a]/95.5
Hagenthal	0	28.4/30.2	61.8/64.6	90.2/94.9	6.5/3.9	NA/NA	NA/NA	96.7/98.7
	2	22.6/28.6	57.9/60.7	80.5/89.3	12.7/5.9	5.5/0.5	< 0.1/< 0.1	98.7/95.7
	7	18.4/32.8	43.2/55.3	61.5/88.1	23.7/10.4	12.5/1.7	< 0.1/< 0.1	97.8/100.2
	14	12.6/35.9	24.7/47.4	37.3/83.4	31.7/11.3	23.0/3.7	< 0.1/< 0.1	92.0/98.4
	21	15.2/35.4	25.9/45.2	41.0/80.6	26.7/10.5	28.2/5.8	0.1/< 0.1	96.0/96.9
	28	11.5/32.5	21.0/48.2	32.5/80.6	28.4/11.7	39.8/6.3	< 0.1/< 0.1	100.7/98.6
	50	9.2/38.9	10.8/36.3	20.0/75.2	30.1/12.0	36.5/7.1	< 0.1/< 0.1	86.6 [a]/94.3
	77	1.0/NS	1.7/NS	2.7/NS	38.5/NS	36.8/NS	< 0.1/NS	78.0 [a]/NS
	90	0.6/NS	1.2/NS	1.9/NS	37.7/NS	29.7/NS	< 0.1/NS	69.2 [a]/NS
	120	0.6/32.1	1.4/29.2	2.0/61.3	34.7/12.3	52.2/20.3	< 0.1/< 0.1	88.9 [a]/93.9
Horn	0	20.8/23.4	65.8/68.7	86.6/92.1	8.8/5.8	NA/NA	NA/NA	95.5/97.9
	2	17.1/22.7	57.5/66.0	74.6/88.7	18.0/10.9	5.1/0.1	< 0.1/< 0.1	97.7/99.6
	7	14.7/25.7	40.5/58.8	55.2/84.5	27.8/13.4	16.0/0.2	< 0.1/< 0.1	99.0/98.2
	14	10.8/29.9	40.5/50.7	51.4/80.6	28.1/14.4	15.0/0.3	< 0.1/< 0.1	94.6/95.3
	21	10.5/35.9	22.0/47.4	32.5/83.3	30.9/12.9	31.8/10.5	< 0.1/< 0.1	95.2/106.8
	28	7.3/27.4	21.0/51.0	28.3/78.4	34.9/13.3	36.9/8.4	< 0.1/< 0.1	100.2/100.2
	50	3.5/33.4	4.3/43.2	7.8/76.6	41.9/12.4	50.7/9.8	< 0.1/< 0.1	100.4/98.9
	77	0.4/NS	1.6/NS	2.0/NS	37.9/NS	40.9/NS	< 0.1/NS	80.8 [a]/NS
	90	1.3/NS	2.2/NS	3.5/NS	42.2/NS	51.7/NS	0.3/NS	97.6/NS
	120	0.4/27.7	1.6/38.3	2.0/66.0	32.7/14.4	54.6/20.6	< 0.1/< 0.1	89.3 [a]/101.0
Montesquieu	0	28.1/25.5	63.6/66.4	91.7/91.9	6.9/3.8	NA/NA	NA/NA	98.6/95.7
	2	23.5/27.5	59.0/63.4	82.5/90.8	11.8/6.9	2.3/0.4	< 0.1/< 0.1	96.6/98.1
	7	17.9/29.8	47.0/56.9	64.9/86.8	22.5/9.6	8.2/1.2	< 0.1/< 0.1	95.7/97.7
	14	18.2/32.8	36.4/51.4	54.6/84.1	28.3/11.6	15.7/3.4	< 0.1/< 0.1	98.6/99.2
	21	16.3/34.7	33.0/48.6	49.3/83.3	28.9/9.3	23.0/5.0	< 0.1/< 0.1	101.2/97.6
	28	12.4/30.9	28.4/49.5	40.9/80.4	29.4/13.1	27.4/5.1	< 0.1/< 0.1	97.6/98.7
	50	8.8/35.6	13.5/40.3	22.3/75.9	38.6/14.0	36.8/6.5	0.1/< 0.1	97.9/96.5
	77	3.2/NS	3.7/NS	7.0/NS	49.4/NS	45.8/NS	< 0.1/NS	102.1/NS
	90	1.2/NS	2.1/NS	3.2/NS	43.5/NS	46.0/NS	< 0.1/NS	92.7/NS
	120	0.4/35.4	1.5/34.9	1.9/70.3	36.1/11.9	43.8/13.4	0.5/< 0.1	82.3 [a]/95.6
Senozan	0	40.2/40.3	57.4/57.3	97.6/97.6	4.5/2.7	NA/NA	NA/NA	102.0/100.3
	2	33.8/36.2	55.5/57.4	89.3/93.6	8.0/4.4	2.1/0.6	< 0.1/0.2	99.4/98.8
	7	25.9/36.0	45.4/53.3	71.3/89.3	18.9/6.9	8.1/1.6	< 0.1/< 0.1	98.3/97.9
	14	22.9/37.5	35.5/51.8	58.4/89.3	21.5/6.7	31.8/2.6	0.1/< 0.1	111.9 [b]/98.7
	21	17.4/39.7	27.4/48.7	44.8/88.4	32.7/9.1	15.7/0.8	< 0.1/< 0.1	93.2/98.4
	28	15.9/30.3	33.7/54.1	49.6/84.4	25.3/8.7	11.5 [a]/5.5	< 0.1/< 0.1	86.4/98.7
	50	18.6/37.7	27.6/45.6	46.2/83.3	28.8/8.5	23.6/6.0	< 0.1/< 0.1	98.7/97.8
	77	15.0/NS	19.8/NS	34.9/NS	29.3/NS	26.9/NS	< 0.1/NS	91.1/NS
	90	16.7/NS	21.9/NS	38.6/NS	25.0/NS	28.9/NS	< 0.1/NS	92.5/NS
	120	12.7/36.0	13.2/37.8	25.9/73.8	25.9/11.4	28.1 [a]/11.7	0.4/0.1	80.3 [a]/97.0
Sevelen	0	29.1/30.3	63.3/64.3	92.4/94.6	8.0/5.0	NA/NA	NA/NA	100.4/99.6
	2	25.6/29.1	54.1/60.1	79.7/89.3	12.5/7.6	3.7/0.1	< 0.1/< 0.1	95.9/97.0
	7	20.7/30.1	45.0/55.3	65.7/85.4	20.7/10.5	16.1/4.4	< 0.1/< 0.1	102.4/100.3
	14	18.1/32.7	33.6/48.8	51.7/81.5	25.8/12.5	17.6/5.3	< 0.1/< 0.1	95.1/99.3
	21	16.5/33.3	28.0/44.7	44.5/77.9	24.3/12.0	25.0/4.1	< 0.1/< 0.1	93.8/94.0

		Percent of applied radioactivity, [Bu-^{14}C]/ [Th-^{14}C]						
Soil	Day	$CaCl_2$ extract	Organic extract	Total extractable	Soil bound	$^{14}CO_2$	VOC	Total recovered
	28	12.7/32.8	22.0/41.8	34.6/74.6	29.7/15.2	30.6/7.3	< 0.1/< 0.1	94.9/97.2
	50	8.2/31.8	9.2/34.9	17.4/66.7	33.1/12.9	35.1/16.5	< 0.1/< 0.1	85.6 [a]/96.0
	77	3.4/NS	3.0/NS	6.4/NS	33.7/NS	50.4/NS	< 0.1/NS	90.5/NS
	90	1.8/NS	2.3/NS	4.1/NS	36.9/NS	53.3/NS	< 0.1/NS	94.3/NS
	120	1.0/25.4	1.4/23.2	2.5/48.5	32.6/14.6	52.0/30.3	< 0.1/< 0.1	87.1 [a]/93.5

[a] Due to losses of $^{14}CO_2$

[b] The KOH trap was probably mistakenly exchanged for another sample (cf. day 21).

NS = No Sample

Table 37 Formation of major soil metabolites of fluensulfone in six aerobic soils

		Percent of applied radioactivity			
Soil	Day	Fluensulfone ([Bu-^{14}C]/ [Th-^{14}C])	BSA	TSA	MeS
Filsis	0	86.4/83.2	1.2	9.4	0.0
	2	77.1/74.5	1.4	14.7	0.0
	7	48.6/45.6	18.5	41.5	0.0
	14	35.4/27.1	11.6	53.8	2.4
	21	30.4/23.8	12.7	53.1	4.6
	28	23.2/17.6	13.9	59.3	3.4
	50	7.9/5.6	11.8	68.5	4.2
	77	2.1/NS	3.7	NS	NS
	90	1.9/NS	2.9	NS	NS
	120	1.0/0.0	1.2	72.7	0.0
Hagenthal	0	90.2/87.6	0.0	7.3	0.0
	2	76.2/73.1	4.4	16.2	0.0
	7	47.0/47.3	14.6	40.8	0.0
	14	26.0/20.0	11.1	61.0	2.4
	21	22.3/11.7	18.7	64.4	4.5
	28	15.9/10.5	16.7	64.6	5.5
	50	5.5/2.3	14.5	69.7	3.2
	77	0.9/NS	1.8	NS	NS
	90	0.6/NS	1.2	NS	NS
	120	0.7/0.0	1.3	61.3	0.0
Horn	0	81.9/81.8	4.7	10.3	0.0
	2	70.0/70.6	4.6	18.0	0.0
	7	47.1/37.9	8.1	46.6	0.0
	14	37.1/16.3	14.3	58.8	5.5
	21	16.3/9.8	16.2	68.7	4.9
	28	8.9/5.8	19.4	68.8	3.8
	50	1.3/0.0	5.7	76.6	0.0
	77	0.5/NS	1.2	NS	NS
	90	0.7/NS	2.4	NS	NS
	120	0.5/0.0	1.2	66.0	0.0
Montesquieu	0	90.0/86.8	1.7	5.2	0.0
	2	79.6/86.0	2.9	4.8	0.0
	7	50.1/56.7	14.9	30.0	0.0
	14	40.1/30.9	14.5	53.2	0.0
	21	32.0/33.4	17.3	49.9	0.0
	28	12.7/19.0	28.1	57.2	4.2
	50	8.3/5.5	14.1	65.0	5.4
	77	2.4/NS	4.6	NS	NS
	90	1.2/NS	2.0	NS	NS
	120	0.9/0.0	1.0	70.3	0.0
Senozan	0	97.6/93.4	0.0	4.2	0.0
	2	89.3/90.0	0.0	3.6	0.0

		Percent of applied radioactivity			
Soil	Day	Fluensulfone ([Bu-^{14}C]/ [Th-^{14}C])	BSA	TSA	MeS
	7	62.6/59.8	8.7	29.6	0.0
	14	48.8/55.0	9.7	34.3	0.0
	21	31.0/36.1	13.8	48.4	3.9
	28	32.9/32.4	16.7	48.4	3.6
	50	21.1/19.8	25.1	59.7	3.8
	77	8.7/NS	26.2	NS	NS
	90	7.6/NS	31.0	NS	NS
	120	2.2/0.0	23.8	73.8	0.0
Sevelen	0	92.4/89.8	0.0	4.8	0.0
	2	75.0/82.4	4.7	6.9	0.0
	7	48.3/37.1	17.4	48.3	0.0
	14	34.4/21.2	17.3	57.8	2.5
	21	NS/NS	NS	NS	NS
	28	15.1/8.7	19.5	58.5	7.5
	50	2.5/2.1	14.9	58.4	6.2
	77	0.8/NS	5.6	NS	NS
	90	0.6/NS	3.5	NS	NS
	120	0.4/0.0	2.1	48.5	0.0

NS = No Sample

Table 38 Summary of half-life estimates for fluensulfone and BSA in six soils

Soil	Fislis	Hagenthal	Horn	Montesquieu	Senozan	Sevelen
Type	Silt loam	Silt loam	Loam	Clay loam	Loam	Sandy loam
Model	SFO [a]	SFO	SFO	SFO	SFO	SFO
Residue	Half-life (days)					
Fluensulfone	10.5	7.6	7.2	11.1	16.5	7.1
BSA	19.7	22.6	21.9	17.8	[b]	26.3

[a] SFO = Single First-Order

[b] Degradation rate of BSA could not be calculated due to insufficient data points

Aerobic soil degradation rate (TSA)

The degradation rate of TSA metabolite of fluensulfone in three aerobic soils was investigated by Brands (2011, R-28470). In that study, Fislis, Horn, and Sevelen soils (see fluensulfone aerobic soil metabolism section above) were treated with the test substance at a nominal concentration of 3.2 mg/kg dry soil and incubated, in the dark, for 150 days. Duplicate samples were collected at nine time points throughout the study, extracted with ACN:H_2O (50:50, v/v), and analysed by HPLC-MS/MS.

Overall procedural recoveries from freshly fortified soils ranged from 95–112% of the applied amount (Table 39) and levels of TSA showed a slow decline over the incubation period (Table 40). Single first-order half-life estimates for TSA were 560 days for Fislis soil, 450 days for Horn soil, and 230 days for Sevelen soil.

Table 39 Procedural recovery of TSA from soils fortified at 3.2 mg/kg

	Fislis		Horn		Sevelen	
Sample time ID	TSA (mg/kg)	Recovery (% of nominal)	TSA (mg/kg)	Recovery (% of nominal)	TSA (mg/kg)	Recovery (% of nominal)
7	3.25	101	3.39	105	3.48	108
15	3.4	106	3.29	102	3.43	107
28	3.4	106	3.33	104	3.48	108
42	3.59	112	3.55	110	3.13	97
60	3.18	100	3.03	95	3.13	98
91	3.14	98	3.26	102	3.14	98
120	3.32	104	3.12	98	3.45	108
150	3.45	107	3.36	105	3.17	99

Table 40 Levels of TSA in three soils incubated for 150 days, normalized to Time 0

Time (days)	Fislis	Horn	Sevelen
0	100, 100	100, 100	100, 100
7	109, 106	98, 101	88, 105
15	101, 96	95, 108	87, 97
28	93, 94	92, 100	83, 96
42	90, 96	90, 94	86, 89
60	85, 82	76, 83	74, 77
91	93, 94	82, 90	64, 81
120	88, 86	88, 90	67, 74
150	83, 88	163 [a], 0 [a]	57, 70

[a] Unexpected results were not used for calculation of DT_{50} and DT_{90}

Aerobic soil degradation rate (MeS)

The degradation rate of MeS metabolite of fluensulfone in three aerobic soils was investigated by Brands (2011, R-28472). In that study, Fislis, Horn, and Sevelen soils (see fluensulfone aerobic soil metabolism section above) were treated with the test substance at a nominal concentration of 0.4 or 0.04 mg/kg dry soil and incubated, in the dark, for 120 days. Duplicate samples were collected at eight time points throughout the study, extracted with ACN:H_2O (50:50, v/v), and analysed by HPLC-MS/MS.

Overall procedural recoveries from freshly fortified soils ranged from 95–112% of the applied amount (Table 41) and levels of MeS showed a slow decline over the incubation period (Table 42). Single first-order half-life estimates for MeS were 41 days for Fislis soil, 28 days for Horn soil, and 30 days for Sevelen soil.

Table 41 Procedural recovery of MeS from soils fortified at 0.4 or 0.04 mg/kg

	Fislis		Horn		Sevelen	
Sample time ID	MeS (mg/kg)	Recovery (% of nominal)	MeS (mg/kg)	Recovery (% of nominal)	MeS (mg/kg)	Recovery (% of nominal)
7	0.393	98	0.338	85	0.357	89
15	0.406	102	0.361	90	0.366	92
28	0.469	117	0.408	102	0.349	87
42	0.0418	104	0.0435	108	0.0369	92
60	0.0395	98	0.0403	100	0.0418	104

	Fislis		Horn		Sevelen	
Sample time ID	MeS (mg/kg)	Recovery (% of nominal)	MeS (mg/kg)	Recovery (% of nominal)	MeS (mg/kg)	Recovery (% of nominal)
91	0.0391	97	0.0395	99	0.0378	94
120	0.0441	110	0.0393	100	0.0415	103

Table 42 Levels of MeS in three soils incubated for 150 days, normalized to Time 0

Time (days)	Fislis	Horn	Sevelen
0	100, 100	100, 100	100, 100
7	95, 111	85, 78	78, 83
15	84, 89	57, 67	62, 60
28	61, 67	47, 42	37, 44
42	48, 54	36, 34	39, 35
60	38, 41	23, 24	26, 30
91	22, 23	14, 14	17, 17
120	14, 16	8, 7	10, 10

Anaerobic soil metabolism

No anaerobic soil metabolism studies were provided.

Confined rotational crop studies

The fate of fluensulfone as relates to rotational crops was investigated by Quistad *et al*. (2011, Report OR-25457). In that study, radish, lettuce and wheat were planted into test boxes that had been treated with [Bu-^{14}C] or [Th-^{14}C] labelled fluensulfone at a rate of ca. 4 kg/ha. The crops were planted into the test boxes at 30, 120, and 360 days after treatment (390 days for lettuce due to crop failure at the 360-day plant-back interval). At each plant-back interval (PBI), samples consisted of radish roots and radish tops; lettuce leaves; and wheat forage, grain, hay, and straw.

After harvest, the samples were homogenized and an aliquot was taken for TRR determination by combustion and LSC. In addition, samples were extracted initially with ACN:H_2O (1:1, v/v) and ACN, followed by strong basic and, in some cases, acidic hydrolysis. Extracted residues were analysed by TLC and/or HPLC (UV and radio-chromatography via fraction collection and LSC) for residue determination. Multiple TLC systems and HPLC conditions were used to obtain adequate separation and analysis.

Total radioactive residues in the rotational crops are shown in Table 43. There was generally good agreement between TRR by combustion and TRR by sum of fractions. The TRR levels from the [Th-^{14}C] treatments were higher from than those from the [Bu-^{14}C] treatments and tended to show a plateau between the 120-day and 360/390-day PBIs that was not seen with the [Bu-^{14}C] treatments.

The ACN:H_2O solution was able to extract the majority of the TRR from all of the rotational crop matrices (Tables 44–47). Analysis of the extracts showed levels of fluensulfone in radish (Tables 48–51), lettuce (Tables 52–55), and wheat (Table 56–63) samples from at least one PBI/radiolabel position/sample matrix combination. In all cases, the occurrence of fluensulfone was ≤ 5.1% TRR and

was higher in samples from the [Bu-^{14}C] treatments. The major residues in all matrices were TSA and BSA from the [Bu-^{14}C] and [Th-^{14}C] treatments, respectively. Across PBIs, levels of BSA generally declined in terms of both absolute concentration and in terms of %TRR. Absolute levels of TSA generally declined with increasing PBI, especially between the 30-day and 120-day PBIs, but increased in terms of %TRR over the course of the study. Numerous minor metabolites and/or fractions were observed. Most of these were attributed to salts or chromatographic artifacts of TSA or BSA.

Table 43 Summary of TRRs in rotational crops at each plant-back interval

	TRRs [a] (mg eq/kg)					
Crop	[Th-^{14}C]			[Bu-^{14}C]		
PBI	30 DAT	120 DAT	360 DAT	30 DAT	120 DAT	360 DAT
Radish (foliage)	5.26 (5.76)	1.76 (1.90)	2.86 (3.58)	0.48 (0.54)	0.47 (0.51)	0.04 (0.04)
Radish (roots)	0.79 (0.83)	0.44 (0.45)	0.38 (0.39)	0.15 (0.19)	0.10 (0.08)	0.01 (0.01)
Lettuce (immature)	0.65 (0.58)	0.71 (0.81)	0.13 (0.13) [b]	0.31 (0.33)	0.05 (0.04)	0.05 (0.05) [b]
Lettuce (mature)	0.57 (0.60)	0.33 (0.34)	0.34 (0.33)	0.20 (0.21)	0.05 (0.04)	0.02 (0.01)
Wheat (forage)	16.6 (19.2)	2.96 (3.42)	3.33 (3.19)	2.53 (3.17)	0.71 (0.84)	0.06 (0.07)
Wheat (straw)	18.6 (18.5)	3.52 (3.85)	6.64 (7.26)	1.94 (1.99)	0.30 (0.31)	0.17 (0.16)
Wheat (grain)	0.36 (0.36)	0.30 (0.32)	0.34 (0.35)	0.17 (0.17)	0.06 (0.07)	0.04 (0.04)
Wheat (hay)	27.0 (26.4)	9.40 (9.29)	10.8 (11.3)	4.50 (4.35)	0.37 (0.36)	0.13 (0.14)

[a] Values in parenthesis obtained by direct combustion

[b] 390 day lettuce samples since 360-day lettuce was replanted because of crop failure

DAT = Days after treatment.

Table 44 Extraction summary for radish foliage and roots after soil treatment with [^{14}C]fluensulfone

Crop	Radish							
Matrix	Foliage				Roots			
^{14}C Label	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
PBI	30 DAYS							
ACN:H_2O Extract	5.166	98.2	0.452	94.4	0.723	91.2	0.126	86.3
0.1 N KOH Extract	0.053	1.0	0.010	2.1	0.011	1.4	0.008	5.5
24% KOH Extract	0.033	0.6	0.013	2.7	0.023	2.9	0.008	5.5
PES	0.011	0.2	0.004	0.8	0.036	4.5	0.004	2.7
Total	5.263		0.479		0.793		0.146	
PBI	120 DAYS							
ACN:H_2O Extract	1.709	97.3	0.436	93.4	0.382	87.4	0.079	76.0
0.1 N KOH Extract	0.021	1.2	0.006	1.3	0.009	2.1	0.006	5.8
24% KOH Extract	0.020	1.1	0.023	4.9	0.026	5.9	0.015	14.4
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	–	–	–	–	0.002	1.9
Aqueous Phase	–	–	–	–	–	–	0.019	18.3
PES	0.006	0.3	0.002	0.4	0.020	4.6	0.004	3.8
Total	1.756		0.467		0.437		0.104	
PBI	360 DAYS							
ACN:H_2O Extract	2.842	99.4	0.031	81.6	0.365	96.3	0.006	50.0
0.1 N KOH Extract	0.007	0.2	0.001	2.6	0.001	0.3	< 0.001	0.0
24% KOH Extract	0.010	0.4	0.005	13.2	0.009	2.4	0.005	41.7
PES	0.001	0.0	0.001	2.6	0.004	1.1	0.001	8.3
Total	2.860		0.038		0.379		0.012	

Table 45 Extraction summary for immature and mature lettuce after soil treatment with [^{14}C]fluensulfone

Crop	Lettuce							
Matrix	Immature				Mature			
^{14}C Label	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
PBI	30 DAYS							
ACN:H_2O Extract	0.495	76.5	0.221	71.1	0.494	87.4	0.137	67.2
Acidification with HCl & Partition with EtAc								
EtAc Phase	0.196	30.3	–	–	–	–	–	–
Aqueous Phase	0.299	46.2	–	–	–	–	–	–
0.1 N KOH Extract	0.038	5.9	0.030	9.6	0.023	4.1	0.017	8.3
24% KOH Extract	0.099	15.3	0.055	17.7	0.043	7.6	0.041	20.1
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	0.018	5.8	0.016	2.8	0.010	4.9
Aqueous Phase	–	–	0.067	21.5	0.050	8.8	0.048	23.5
PES	0.015	2.3	0.005	1.6	0.005	0.9	0.009	4.4
Total	0.647		0.311		0.565		0.204	
PBI	120 DAYS							
ACN:H_2O Extract	0.622	87.6	0.021	46.7	0.299	90.3	0.021	46.7
0.1 N KOH Extract	0.031	4.4	0.004	8.9	0.012	3.6	0.004	8.9
24% KOH Extract	0.045	6.3	0.014	31.1	0.018	5.4	0.014	31.1
72% H_2SO_4 Extract	0.007	1.0						
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	0	0.0	–	–	0.000	0.0
Aqueous Phase	–	–	0.018	40.0	–	–	0.016	35.6
PES	0.005	0.7	0.006	13.3	0.002	0.6	0.006	13.3
Total	0.710		0.045		0.331	99.9	0.045	
PBI	390 DAYS [a]							
ACN:H_2O Extract	0.119	89.5	0.030	60.0	0.331	97.6	0.030	60.0
0.1 N KOH Extract	0.004	3.0	0.004	8.0	0.002	0.6	0.004	8.0
24% KOH Extract	0.009	6.8	0.013	26.0	0.005	1.5	0.013	26.0
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	0.002	1.5	0.003	6.0	–	–	–	–
Aqueous Phase	0.011	8.3	0.014	28.0	–	–	–	–
PES	0.001	0.8	0.003	6.0	0.001	0.3	0.003	6.0
Total	0.133		0.050		0.339		0.050	

[a] 390-day lettuce samples because of crop failure of 360-day lettuce samples.

Table 46 Extraction summary for wheat forage and straw after soil treatment with [^{14}C]fluensulfone

Crop	Wheat							
Matrix	Forage				Straw			
^{14}C Label	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
PBI	30 DAYS							
ACN:H_2O Extract	15.594	94.1	2.240	88.5	15.626	84.2	1.035	53.5
0.1 N KOH Extract	0.300	1.8	0.073	2.9	0.906	4.9	0.195	10.1
24% KOH Extract	0.538	3.2	0.184	7.3	1.443	7.8	0.350	18.1
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	–	–	0.507	2.7	0.079	4.1
Aqueous Phase	–	–	–	–	1.842	9.9	0.466	24.1
72% H_2SO_4 Extract	–	–	–	–	0.441	2.4	0.283	14.6
PES	0.147	0.9	0.033	1.3	0.153	0.8	0.072	3.7
Total	16.579		2.530		18.569		1.935	
PBI	120 DAYS							
ACN:H_2O Extract	2.809	94.8	0.642	90.0	2.966	84.3	0.195	64.4
0.1 N KOH Extract	0.079	2.7	0.024	3.4	0.094	2.7	0.041	13.5

Crop	Wheat							
Matrix	Forage				Straw			
^{14}C Label	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
24% KOH Extract	0.058	2.0	0.038	5.3	0.331	9.4	0.042	13.9
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	0.005	0.7	0.081	NR	0.013	NR
Aqueous Phase	–	–	0.057	8.0	0.344	NR	0.070	NR
72% H_2SO_4 Extract	0.012	0.4	0.007	1.0	0.126	3.6	0.025	8.3
PES	0.005	0.2	0.002	0.3	0.126	3.6	0.025	8.3
Total	2.963		0.713		3.517		0.303	
PBI	360 DAYS							
ACN:H_2O Extract	3.157	94.9	0.039	65.0	6.051	91.2	0.102	61.8
0.1 N KOH Extract	–	–	0.003	5.0	0.259	3.9	0.011	6.7
24% KOH Extract	–	–	0.014	23.3	0.229	3.5	0.032	19.4
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	–	–	–	–	0.094	1.4	0.010	6.1
Aqueous Phase	–	–	–	–	0.394	5.9	0.033	20.0
PES	0.169	5.1	0.004	6.7	0.097	1.5	0.020	12.1
Total	3.326		0.060		6.636		0.165	

Table 47 Extraction summary for wheat hay and grain after soil treatment with [^{14}C]fluensulfone

Crop	Wheat							
Matrix	Hay				Grain			
^{14}C Label	[Th-^{14}C]		[Bu-^{14}C]		[Th-^{14}C]		[Bu-^{14}C]	
Fraction	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
PBI	30 DAYS							
ACN:H_2O Extract	18.891	70.0	2.127	47.3	0.263	73.3	0.109	63.7
0.1 N KOH Extract	5.321	19.7	1.478	32.8	0.034	9.6	–	–
24% KOH Extract	2.224	8.2	0.741	16.5	–	–	–	–
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	1.177	4.4	0.249	5.5	0.003	0.8	–	–
Aqueous Phase	6.368	23.6	1.970	43.8	0.059	16.6	–	–
72% H_2SO_4 Extract	0.479	1.8	–	–	–	–	–	–
PES	0.089	0.3	0.154	3.4	–	–		
Total	27.004		4.500		0.359		0.173	
PBI	120 DAYS							
ACN:H_2O Extract	7.185	76.5	0.225	60.3	0.247	83.4	0.023	39.0
0.1 N KOH Extract	1.288	13.7	0.060	16.1	0.017	5.7	0.006	10.2
24% KOH Extract	0.715	7.6	0.068	18.2	0.003	1.0	0.001	1.7
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	0.282	3.0	0.009	2.4	–	–	–	–
Aqueous Phase	1.721	18.3	0.119	31.9	–	–	–	–
72% H_2SO_4 Extract	0.209	2.2	0.020	5.4	–	–	–	–
PES	0.209	2.2	0.020	5.4	0.029	9.8	0.029	49.2
Total	9.397		0.373		0.296		0.059	
PBI	360 DAYS							
ACN:H_2O Extract	7.768	71.7	0.070	54.7	0.260	76.0	0.013	34.2
0.1 N KOH Extract	1.166	10.8	0.011	8.6	0.022	6.4	0.006	15.8
24% KOH Extract	1.230	11.4	0.026	20.3	–	–	–	–
Combined 0.1 N KOH & 24% KOH Extracts, Acidified and Partitioned with EtAc								
EtAc Phase	0.594	5.5	0.001	8.6	0.008	2.3	–	–
Aqueous Phase	1.802	16.6	0.026	20.3	0.014	4.1	–	–
PES	0.671	6.2	0.021	16.4	0.060	17.5	0.019	50.0
Total	10.835		0.128		0.342		0.038	

Table 48 Summary of [Th-^{14}C]fluensulfone labelled residues in radish foliage

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	5.263	100.0	1.756	100.0	2.860	100.0
Solvent Extractable	5.166	98.2	1.709	97.3	2.842	99.4
Fluensulfone	0.010	0.2	–	–	–	–
Thiazole Sulfonic Acid	4.726	89.8	1.624	92.5	2.558	89.4
M1—Form of TSA	0.113	2.2	0.073	4.2	–	–
M3—Form of TSA	0.034	0.6	–	–	–	–
Unresolved	0.258	4.9	0.012	0.7	0.283	9.9

Table 49 Summary of [Th-^{14}C]fluensulfone labelled residues in radish roots

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.793	100.0	0.437	100.0	0.379	100.0
Solvent Extractable	0.723	91.2	0.382	87.4	0.365	96.3
Thiazole Sulfonic Acid	0.687	86.6	0.355	81.2	0.341	90.0
M1—Form of TSA	–	–	0.004	0.9	–	–
M3—Form of TSA	0.004	0.5	0.001	0.2	0.004	1.1
Unresolved	0.020	2.5	0.016	4.2	0.019	5.0

M1: This fraction consists of two compounds with the major part of this identified a salt of TSA.

M3: This polar radioactive fraction was always observed as a possible artifact due to the non-retention of TSA.

Alkaline and acid digestion released additional small amounts of radiolabelled compounds.

Table 50 Summary of [Bu-^{14}C]fluensulfone labelled residues in radish foliage

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.479	100.0	0.467	100.0	0.038	100.0
Solvent Extractable	0.452	94.4	0.436	93.4	0.031	81.6
Fluensulfone	0.015	3.1	0.024	5.1	0.001	3.0
Butene Sulfonic Acid	0.315	65.8	0.328	70.2	–	–
F1-F2—Form of BSA	0.016	3.4	0.002	0.4	0.002	5.1
F4—Form of BSA	0.017	3.5	–	–	–	–
F5	0.005	1.0	0.015	3.2	0.001	3.6
F6	0.001	0.2	–	–	0.002	5.3
F7	–	–	–	–	0.005	13.2
F9	–	–	–	–	0.001	3.2
Unresolved	0.059	12.3	0.068	14.6	0.013	34.2

Table 51 Summary of [Bu-^{14}C]fluensulfone labelled residues in radish roots

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.146	100.0	0.104	100.0	0.012	100.0
Solvent Extractable	0.126	86.3	0.079	76.0	0.006	50.0
Fluensulfone	0.002	1.5	–	–	–	–
Butene Sulfonic Acid	0.058	40.0	0.041	39.4	–	–
F1 - F2—Form of BSA	0.009	6.2	0.002	2.3	0.001	8.3
F5	0.007	4.8	0.005	4.5	–	–
F7	0.006	3.8	–	–	–	–
Unresolved	0.034	23.3	0.025	24.0	0.005	41.7

Table 52 Summary of [Th-^{14}C]fluensulfone labelled residues in immature lettuce

	30-Day PBI		120-Day PBI		390-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.647	100.0	0.710	100.0	0.133	100.0
Solvent Extractable	0.495	76.5	0.622	87.6	0.119	89.5
Fluensulfone	0.005	0.8	0.004	0.6	–	–
Thiazole Sulfonic Acid	0.183	28.3	0.401	56.5	0.086	64.7
M1—Form of TSA	0.122	18.9	0.113	15.9	0.013	9.8
M2—Form of TSA	–	–	0.009	1.3	–	–
M3—Form of TSA	0.007	1.1	0.004	0.6	0.003	2.3
Unresolved	0.179	27.7	0.091	12.8	0.016	12.0

Table 53 Summary of [Th-^{14}C]fluensulfone labelled residues in mature lettuce

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.565	100.0	0.331	100.0	0.339	100.0
Solvent Extractable	0.494	87.4	0.299	90.3	0.331	97.6
Fluensulfone	0.006	1.1	–	–	–	–
Thiazole Sulfonic Acid	0.237	41.9	0.184	55.6	0.279	82.3
M1—Form of TSA	0.113	20.0	0.086	26.0	0.004	1.2
M3—Form of TSA	0.002	0.4	0.004	1.2	–	–
Unresolved	0.134	23.7	0.025	7.6	0.046	13.6

M1: This fraction consists of two compounds with the major part of this identified as a salt of TSA.

M3: This polar radioactive fraction was always observed as a possible artifact due to the non-retention of TSA.

Alkaline & acid digestion: Unresolved metabolites were released especially with 24% KOH. A major component appeared to be TSA.

Table 54 Summary of [Bu-^{14}C]fluensulfone labelled residues in immature lettuce

	30-Day PBI		120-Day PBI		390-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.311	100.0	0.045	100.0	0.050	100.0
Solvent Extractable	0.221	71.1	0.021	46.7	0.030	60.0
Fluensulfone	0.016	5.1	–	–	0.002	4.0
Butene Sulfonic Acid	0.004	1.2	0.001	2.2	–	–
F1-F2—Form of BSA	0.006	1.9	0.006	13.3	0.005	10.0
F4—Form of BSA	< 0.001	0.1	0.002	4.4	–	–
F5	0.002	0.5	–	–	–	–
F6	0.003	1.2	–	–	–	–
F7	0.002	0.6	0.001	1.3	0.001	2.0
F9	0.010	3.2	0.001	2.2	–	–
F10	< 0.001	0.1	–	–	–	–
Unresolved	0.176	56.6	0.009	20.0	0.019	38.0

Table 55 Summary of [Bu-^{14}C]fluensulfone labelled residues in mature lettuce

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.204	100.0	0.045	100.0	0.017	100.0
Solvent Extractable	0.137	67.2	0.027	60.0	0.008	47.1
Fluensulfone	0.004	2.0	–	–	–	–
Butene Sulfonic Acid	0.018	8.8	–	–	–	–
F1-F2—Form of BSA	0.011	5.4	0.016	35.6	0.002	11.8

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
F5	0.001	0.6	–	–	–	–
Unresolved	0.100	49.0	0.010	21.9	0.006	35.3

Table 56 Summary of [Th-^{14}C]fluensulfone labelled residues in wheat forage

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	16.579	100.0	2.963	100.0	3.326	100.0
Solvent Extractable	15.594	94.1	2.809	94.8	3.157	94.9
Thiazole Sulfonic Acid	12.241	73.8	2.254	76.0	2.737	82.3
M1—Form of TSA	0.521	3.1	0.104	3.5	0.011	0.3
M3—Form of TSA	0.147	0.9	–	–	0.036	1.1
Unresolved	2.237	13.5	0.449	15.2	0.376	11.3

Table 57 Summary of [Th-^{14}C]fluensulfone labelled residues in wheat hay

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	27.004	100.0	9.397	100.0	10.835	100.0
Solvent Extractable	18.891	70.0	7.185	76.5	7.768	71.7
Thiazole Sulfonic Acid	15.571	57.7	6.221	66.2	5.771	53.3
M1—Form of TSA	0.496	1.8	0.227	2.4	0.084	0.8
M3—Form of TSA	0.413	1.5	0.167	1.8	0.542	5.0
Unresolved	2.348	8.7	0.498	5.3	1.313	12.1

Table 58 Summary of [Th-^{14}C]fluensulfone labelled residues in wheat grain

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.359	100.0	0.296	100.0	0.342	100.0
Solvent Extractable	0.263	73.9	0.247	83.4	0.260	76.0
Thiazole Sulfonic Acid	0.120	33.4	0.171	57.8	0.195	57.0
M1—Form of TSA	0.047	13.1	0.011	3.7	0.029	8.5
M3—Form of TSA	0.018	5.0	0.009	3.0	0.009	2.6
Unresolved	0.078	21.7	0.056	18.9	0.027	7.9

Table 59 Summary of [Th-^{14}C]fluensulfone labelled residues in wheat straw

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	18.569	100.0	3.517	100.0	6.636	100.0
Solvent Extractable	15.626	84.2	2.966	84.3	6.051	91.2
Thiazole Sulfonic Acid	10.712	57.7	2.196	62.4	5.060	76.3
M1—Form of TSA	0.364	2.0	0.031	0.9	0.056	0.8
M3—Form of TSA	0.273	1.5	–	–	0.401	6.0
Unresolved	4.268	23.0	0.727	20.7	0.484	7.3

M1 & M3: Fraction not confirmed by TLC analysis leading to the suggestion to be a chromatographic artifact of TSA. Alkaline and acid digestion, especially with 24% KOH, liberated several, unresolved metabolites that could not be identified. A major component appeared to be TSA.

Table 60 Summary of [Bu-^{14}C]fluensulfone labelled residues in wheat forage

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	2.530	100.0	0.713	100.0	0.060	100.0
Solvent Extractable	2.240	88.5	0.642	90.0	0.039	65.0
Fluensulfone	0.028	1.1	0.021	2.9	–	–
Butene Sulfonic Acid	1.377	54.4	0.427	59.9	0.002	3.2
F1-F2—Form of BSA	0.090	3.6	0.026	3.6	0.009	15.0
F4—Form of BSA	0.020	7.9	0.016	2.2	–	–
F5	0.069	2.7	0.038	5.3	0.001	1.7
F6	0.035	1.4	–	–	–	–
F7	0.004	0.1	–	–	–	–
F9	0.041	1.6	0.015	2.1	–	–
F10	0.019	0.8	–	–	–	–
Unresolved	0.374	14.8	0.066	9.3	0.024	40.0

Table 61 Summary of [Bu-^{14}C]fluensulfone labelled residues in wheat hay

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	4.500	100.0	0.373	100.0	0.128	100.0
Solvent Extractable	2.127	47.3	0.225	60.3	0.070	54.7
Fluensulfone	0.016	0.4	0.004	1.1	–	–
Butene Sulfonic Acid	1.223	27.2	0.095	25.5	–	–
F1-F2—Form of BSA	0.059	1.3	0.033	8.8	0.021	16.4
F4—Form of BSA	0.050	1.1	0.006	1.7	0.001	0.8
F5	0.077	1.7	0.006	1.6	0.002	1.4
F6	–	–	–	–	0.001	0.6
F7	–	–	–	–	0.001	0.8
F9	–	–	0.003	0.8	0.002	1.6
F10	–	–	–	–	–	–
Unresolved	0.700	15.6	0.064	17.2	0.037	28.9

Table 62 Summary of [Bu-^{14}C]fluensulfone labelled residues in wheat grain

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	0.173	100.0	0.059	100.0	0.038	100.0
Solvent extractable	0.109	63.0	0.023	39.0	0.013	34.2
F1-F2—Form of BSA	0.007	4.0	0.011	18.6	0.004	10.5
unresolved	0.102	59.0	0.012	20.3	0.009	23.7

Table 63 Summary of [Bu-^{14}C]fluensulfone labelled residues in wheat straw

	30-Day PBI		120-Day PBI		360-Day PBI	
Fraction/residue	mg eq/kg	% TRR	mg eq/kg	% TRR	mg eq/kg	% TRR
TRR	1.935	100.0	0.303	100.0	0.165	100.0
Solvent Extractable	1.035	53.5	0.195	64.4	0.102	61.8
Fluensulfone	0.004	0.2	–	–	–	–
Butene Sulfonic Acid	0.272	14.1	0.031	10.2	0.012	7.0
F1-F2—Form of BSA	0.189	9.8	0.095	31.4	0.016	9.7
F5	0.007	0.4	–	–	0.002	1.0
F9	0.007	0.3	–	–	0.002	1.0
Unresolved	0.546	28.2	0.068	22.4	0.069	41.8

F3: Suggested to be BSA. Due to matrix effects the retention time of BSA is changing considerably leading to chromatographic artefacts.

F4 & F5: The HPLC-MS analysis of these fractions gave a high molecular weight which suggests that it is possibly a natural product.

Field rotational crop studies

No field rotational crop studies were provided.

Field dissipation studies

No field dissipation studies were provided.

RESIDUE ANALYSIS

Summary of analytical methods

Methods for the analysis of fluensulfone and its breakdown products BSA, MeS, and TSA are generally the same for plant, animal, and soil matrices, though there are some differences in the extraction of BSA and TSA in eggs and milk and in the clean-up steps for fatty samples. The methods are summarized in Table 64.

Table 64 Overview of the analytical methods submitted for fluensulfone and its major metabolites

Method ID (Report)	Matrix	Analyte	Extraction	Clean-up	Separation/ Analysis/LOQ
1997W (R-23334 and R-28495) Equivalent to 2061W	Plant commodities	Fluensulfone + MeS	ACN+H_2O (1+1, v/v)	Filtration	LC-MS/MS Fluensulfone m/z 292 $[M+H]^+ \rightarrow$ 166 (q) m/z 292 → 89 (c) m/z 292 → 59 (c) LOQ: 0.01 mg/kg MeS m/z 198 $[M+H]^+ \rightarrow$ 120 (q) m/z 198 → 122 (q) LOQ: 0.01 mg/kg
		BSA + TSA	ACN+H_2O (1+1, v/v)	C_{-18} SPE + filtration	LC-MS/MS BSA m/z 189 $[M-H]^- \rightarrow$ 81 (q) m/z 189 → 80 (c) LOQ: 0.01 mg/kg TSA m/z 198 $[M-H]^- \rightarrow$ 82 (q) m/z 198 → 118 (c) LOQ: 0.01 mg/kg
10M04006-01-VMPL (R-28495)	Plant commodities	MeS	ACN+H_2O (1+1, v/v)	Filtration	LC-MS/MS m/z 198 $[M+H]^+ \rightarrow$ 120 (q) m/z 198 → 122 (q) LOQ: 0.01 mg/kg
11M03036-01-VMPL (R-23489)	Plant commodities	Fluensulfone	ACN+H_2O (1+1, v/v)	Filtration	LC-MS/MS m/z 292 $[M+H]^+ \rightarrow$ 166 (q) m/z 292 → 89 (c) m/z 292 → 59 (c) LOQ: 0.01 mg/kg
		MeS	ACN+H_2O (1+1, v/v)	Orange: filtration Wheat grain and peanut:	LC-MS/MS m/z 198 $[M+H]^+ \rightarrow$ 120 (q) m/z 198 → 122 (q) LOQ: 0.01 mg/kg

Method ID (Report)	Matrix	Analyte	Extraction	Clean-up	Separation/ Analysis/LOQ
				partition against hexane + filtration	
		BSA + TSA	ACN+H_2O (1+1, v/v)	C_{-18} SPE + filtration	LC-MS/MS BSA m/z 189 $[M-H]^-$ → 81 (q) m/z 189 → 80 (c) LOQ: 0.01 mg/kg TSA m/z 198 $[M-H]^-$ → 82 (q) m/z 198 → 118 (c) LOQ: 0.01 mg/kg
11M03036-01-VMAT (R-28512)	Animal commodities	Fluensulfone + MeS	ACN+H_2O (1+1, v/v)	Fat: filtration All others: partition against hexane	LC-MS/MS Fluensulfone m/z 292 $[M+H]^+$ → 166 (q) m/z 292 → 89 (c) LOQ: 0.01 mg/kg MeS m/z 198 $[M+H]^+$ → 120 (q) m/z 198 → 125 (c) LOQ: 0.01 mg/kg
		BSA + TSA	Liver, kidney, meat, fat: ACN+H_2O (1+1, v/v) Eggs, milk: ACN	C_{-18} SPE + filtration	LC-MS/MS BSA m/z 189 $[M-H]^-$ → 81 (q) m/z 189 → 80 (c) LOQ: 0.01 mg/kg TSA m/z 198 $[M-H]^-$ → 82 (q) m/z 198 → 118 (c) LOQ: 0.01 mg/kg
2049W (R-23339)	Soils	Fluensulfone + MeS	ACN+H_2O (1+1, v/v)	Filtration	LC-MS/MS Fluensulfone m/z 292 $[M+H]^+$ → 166 (q) m/z 292 → 89 (c) LOQ: 0.01 mg/kg MeS m/z 198 $[M+H]^+$ → 135 (q) m/z 198 → 93 (c) LOQ: 0.01 mg/kg
		BSA + TSA	ACN+H_2O (1+1, v/v)	C_{-18} SPE + filtration	LC-MS/MS BSA m/z 189 $[M-H]^-$ → 81 (q) m/z 189 → 80 (c) LOQ: 0.01 mg/kg TSA m/z 198 $[M-H]^-$ → 82 (q) m/z 198 → 118 (c) LOQ: 0.01 mg/kg

Plant materials

For plant matrices, Method 1997W (equivalent to Method 2061W) has been developed as a suitable enforcement method by J. Marin (2010, Report R-23334) for fluensulfone, BSA, and TSA, and expanded by A. Witte (2011, Report R-28495) to include MeS. The method underwent independent validation for all four analytes by R. Bacher (2011, Report R-27478).

Residues are extracted from 10 g of sample matrix using ACN:H_2O (1:1, v/v, 50 mL) by shaking for five minutes followed by centrifugation. The extract is then split, with one aliquot for

analysis of fluensulfone/MeS and a second aliquot for analysis of BSA/TSA. Quantification of all residues is by comparison with external, matrix-matched standards.

For fluensulfone (all matrices) and MeS (non-grain/non-oily matrices), an aliquot of the extract is filtered (0.45 µm) and analysed, without further clean-up, by LC-MS/MS in positive ion spray mode. For MeS in grain and oily matrices, the extract is salted out with NaCl; the separated ACN phase is dried with $MgSO_4$ and an aliquot is partitioned against hexane to remove co-extracted material. The ACN phase is collected, evaporated to dryness, and the residues are reconstituted in ACN:H_2O (1:1, v/v). The resulting extract is filtered (0.45 µm) and analysed by LC-MS/MS in positive ion spray mode. Chromatography for all extracts is done on a reverse-phase C_{-18} column maintained at 45 °C using a gradient mobile phase that transitions from 0.1% formic acid in ACN (95%) + 0.1% formic acid in H_2O (5%) to 0.1% formic acid in H_2O (100%). Ion transitions $[M+H]^+$ for fluensulfone are *m/z* 292 → 166 for quantitation (q), *m/z* 292 → 89 for confirmation (c), and *m/z* 292 → 59 (c). Ion transitions for MeS are *m/z* 198 → 120 (q) and the corresponding chlorine isotope transition (*m/z* 200 → 122).

For BSA and TSA (all matrices), a 6 mL aliquot of the initial extract is concentrated to 3 mL and cleaned-up on a C_{-18} SPE cartridge. Eluate from the cartridge is brought to volume and analysed by LC-MS/MS in negative ion mode. Chromatography is by reverse-phase C_{-18} column maintained at 45 °C using a gradient mobile phase that transitions from 0.05% formic acid in ACN (95%) + 0.05% formic acid in H_2O (5%) to 0.05% formic acid in H_2O (100%). Ion transitions $[M-H]^-$ for BSA are *m/z* 189 → 81 (q) and *m/z* 189 → 80 (c). Ion transitions for TSA are *m/z* 198 → 89 (q) and *m/z* 198 → 118).

Linearity data were provided and showed linear responses ($R^2 \geq 0.992$ and generally > 0.998) from 0.2–20 ng/mL. In a few studies, linearity was demonstrated over a broader range, including up to 100 ng/mL. Accuracy and precision data, in the form of spike and recovery studies, were provided for cucumber, lemon, melon, orange flesh, peanut, pepper, tomato and wheat grain. Samples were spiked at either 0.01 or 1 mg/kg of fluensulfone, BSA, MeS, or TSA (separately). Mean recoveries for each analyte at each spiking level and for each matrix were within the generally accepted range of 70–120%. Of the 860 method validation analyses, ten had recoveries outside of the generally accepted range of 70–120%: 53% and 54% for TSA in peanut, 174% for BSA in wheat grain, and seven recoveries ranging from 121% to 170% for fluensulfone, MeS, or TSA in orange flesh or lemon. In all cases, relative standard deviations were ≤ 20%.

Testing of fluensulfone and the two sulfonic acid metabolites, BSA and TSA, through the FDA PAM multiresidue method protocols was conducted by T. Ballard (2012, Report R-29565) for non-fatty foods. The compounds showed poor sensitivity, poor recovery, and/or poor chromatography. Overall, the results indicate that the FDA PAM multiresidue protocols are not suitable for the detection or enforcement of fluensulfone, BSA, or TSA residues in non-fatty foods.

Animal materials

A residue analytical method for the analysis of fluensulfone and its BSA, MeS, and TSA metabolites in animal matrices has been developed by Witte (2011, Report R-28512). It is identical to the method for those analytes in plant matrices described above, with the exception of the extraction of BSA and TSA from eggs and milk. For those matrices, extraction is accomplished with ACN (neat). The method was successfully validated by R. Bacher (2012, Report R-29562).

As with the plant method, extracts (except eggs and milk) are split for separate analysis of fluensulfone and MeS or BSA and TSA. For fluensulfone/MeS, the only clean-up is filtration whereas for BSA and TSA, there is clean-up by C_{-18} SPE and filtration. The LC-MS/MS conditions and ions are the same as described above for plants. The method showed linear response from 0.2–20 ng/mL for fluensulfone and MeS, and from 0.2–15 ng/mL for BSA and TSA. Recoveries from 900 spike-and-recovery analyses for all three analytes ranged from 71–109%, with the exception of four analyses, all for fluensulfone: 122% in pork meat, 154% in kidney, and 164% for liver, and egg.

Soil

A residue analytical method for the analysis of fluensulfone and its BSA, MeS, and TSA metabolites in animal matrices has been developed by Marin (2010, Report R-23339, Method 2049W). It is identical to the method for those analytes in plant matrices described above. The method was successfully validated by R. Barker (2012, Report R-29564).

As with the plant method, extracts are split for separate analysis of fluensulfone and MeS or BSA and TSA. For fluensulfone/MeS, the only clean-up is filtration whereas for BSA and TSA, there is clean-up by C_{-18} SPE and filtration. The LC-MS/MS conditions and ions are the same as described above for plants.

Mean recoveries ranged from 78 to 114% for all analyses, with relative standard deviations of < 12%.

Stability of residues in stored samples

The stability of fluensulfone, BSA, and TSA in frozen storage has been investigated in tomato, pepper (Korpalski, S. 2011, 09-01858), cucumber and melon (Korpalski, S. 2011, 09-01859). In addition, the stability of those analytes and MeS was investigated in frozen, stored tomato puree and paste (Jones, G.L. 2011, R-23487). No dissipation of any analyte was observed during the storage periods for the various matrices. Stability was demonstrated in tomato raw agricultural commodity (RAC) for at least 469 days (ca. 15 months) and in tomato processed commodities for at least 181 days (ca. 6 months). For pepper, cucumber, and melon, residues were stable for at least 488 days (ca. 16 months).

Table 65 Storage Stability of fluensulfone, TSA and BSA in cucumber

Analyte	Storage Interval days / months	Spiking Level (mg/kg)	Percent of Nominal Spiking Level	
			Procedural Recovery	Stored (% Remaining)
Fluensulfone	0 / 0	0.10	102, 90, 112	–
	91 / 3		100, 106	104, 97, 101
	266 / 9		84, 82	92, 104, 98
	488 / 16		79, 74	88, 86, 92
TSA	0 / 0	0.10	99, 97, 90	–
	91 / 3		101, 97	104, 105, 105
	267 / 9		110, 110	109, 110, 115
	488 / 16		94, 98	97, 100, 102
BSA	0 / 0	0.10	95, 104, 93	–
	91 / 3		100, 97	97, 95, 96
	267 / 9		110, 108	115, 118, 119
	488 / 16		98, 96	96, 105, 105

Table 66 Storage stability of fluensulfone, TSA and BSA in melon

Analyte	Storage Interval days / months	Spiking Level (mg/kg)	Percent of Nominal Spiking Level	
			Procedural Recovery	Stored (% Remaining)
Fluensulfone	0 / 0	0.10	79, 96, 77	–
	91 / 3		100, 103	101, 91, 106
	266 / 9		84, 76	74, 96, 95
	488 / 16		77, 79	91, 98, 98
TSA	0 / 0	0.10	85, 92, 89	–
	91 / 3		93, 97	90, 95, 97
	267 / 9		103, 103	110, 108, 113
	488 / 16		95, 94	89, 93, 89
BSA	0 / 0	0.10	83, 99, 93	–
	91 / 3		81, 90	79, 85, 89
	267 / 9		100, 103	115, 117, 116
	488 / 16		89, 93	93, 99, 94

Table 67 Storage stability of fluensulfone, TSA and BSA in pepper

Analyte	Storage Interval days / months	Spiking Level (mg/kg)	Percent of Nominal Spiking Level	
			Procedural Recovery	Stored (% Remaining)
Fluensulfone	0 / 0	0.10	91, 80, 89	–
	95 / 3		116, 117	113, 116, 119
	263 / 8.5		103, 107	102, 108, 109
	488 / 16		90, 94	96, 98, 106
TSA	0 / 0	0.10	85, 77, 81	–
	95 / 3		103, 101	105, 88, 95
	263 / 8.5		95, 100	94, 108, 101
	488 / 16		92, 89	85, 94, 98
BSA	0 / 0	0.10	76, 74, 78	–
	95 / 3		98, 110	97, 87, 99
	263 / 8.5		94, 102	102, 103, 102
	488 / 16		89, 94	102, 106, 107

Table 68 Storage stability of fluensulfone, TSA and BSA in tomato

Analyte	Storage Interval	Spiking	Percent of Nominal Spiking Level

	days / months	Level (mg/kg)	Procedural Recovery	Stored (% Remaining)
Fluensulfone	0 / 0	0.10	85, 117, 105	–
	92 / 3		97, 94	97, 87, 98
	244 / 8		112, 108	109, 108, 108
	469 / 15		78,98	96, 99, 100
TSA	0 / 0	0.10	101, 89, 97	–
	92 / 3		88, 84	91, 90, 91
	244 / 8		114, 95	102, 92, 108
	469 / 15		90, 89	94, 95, 93
BSA	0 / 0	0.10	96, 95, 99	–
	92 / 3		88, 89	87, 81, 84
	244 / 8		105, 95	96, 86, 104
	469 / 15		93, 97	96, 106, 98

Table 69 Storage stability of fluensulfone, TSA, MES and BSA in tomato puree

Analyte	Storage Interval days / months	Spiking Level (mg/kg)	Percent of Nominal Spiking Level	
			Procedural Recovery	Stored (% Remaining)
Fluensulfone	27 / 1	0.10	104, 107	103, 108
	89 / 3		101, 100	98, 86
	181 / 6		80, 84	73, 75
TSA	27 / 1	0.10	80, 74	80, 78
	89 / 3		81, 81	81, 88
	181 / 6		72, 73	79, 81
MES	27 / 1	0.10	88, 88	85, 90
	89 / 3		93, 98	100, 82
	181 / 6		89, 86	88, 87
BSA	27 / 1	0.10	89, 98	93, 98
	89 / 3		93, 95	93, 94
	181 / 6		92, 95	98, 99

Table 70 Storage stability of fluensulfone, TSA, MES and BSA in tomato paste

Analyte	Storage Interval days / months	Spiked Level (mg/kg)	Percent of Nominal Spiking Level	
			Procedural Recovery	Stored (% Remaining)
Fluensulfone	90 / 3	0.10	97, 87	79, 74
	181 / 6		94, 92	83, 73
TSA	90 / 3	0.10	62, 63	65, 65
	181 / 6		63, 63	67, 69
MES	90 / 3	0.10	92, 88	89, 86
	181 / 6		82, 88	89, 88
BSA	90 / 3	0.10	73, 80	87, 85
	181 / 6		85, 84	89, 93

USE PATTERN

Table 71 Good agricultural practices (GAPs) proposed for fluensulfone [a]

Crop and/ or Situation	Pests or Group of Pests Controlled	Application Method Kind	Growth Stage & Season	No.	Interval Between Applications (min)	Rate (kg ai/ha, min–max)	PHI (days)
U.S.A Registration							
Cucurbit	Root-knot,	Drip irrigation,	Pre-planting	1	N/A	1.92–2.8	N/A

Crop and/ or Situation	Pests or Group of Pests Controlled	Application Method Kind	Growth Stage & Season	No.	Interval Between Applications (min)	Rate (kg ai/ha, min–max)	PHI (days)
vegetables & fruiting vegetables	root-lesion and cyst nematodes	Band application, Broadcast spray	(minimum of 7 days before transplanting) [b]				

[a] Representative formulation is an EC containing 480 g/L (4 lb/gal) of fluensulfone.

[b] Only outdoor uses are permitted.

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

The Meeting received data from supervised residue trials conducted on cucumber, summer squash, cantaloupe, tomato, and pepper conducted in the USA and Canada. For all samples, analyses were conducted for fluensulfone, BSA, and TSA, and analysis of MeS was conducted for at least some samples from each crop. The reports included method validation data, as recoveries from spiked samples at levels reflecting those observed in the field trial samples; dates from critical events during the study, including application, harvest, storage, and analysis; as well as detailed information on the field site and treatment parameters. Analytical reports were sufficiently detailed and included example chromatograms and example calculations. Samples were analysed by Method 1997W (equivalent to Method 2061W) described above. The results are supported by concurrent recoveries ranging, on average for each analyte and crop, from 81–120% for all commodity × analyte combinations except for fluensulfone in dry tomato pomace, which averaged 131% in one study. Samples were stored, frozen, for the following durations: cucumber = 10 months, squash = 10 months, melons = 9 months, pepper = 7 months, and tomato = 7 months. The storage durations are less than or equal to those for which residues have been demonstrated to be stable.

The field trial study designs included control plots. All measured residues from control plots were < 0.01 mg/kg (i.e., < LOQ) and are not included in the summary tables in this evaluation.

Supervised trials for fluensulfone:

Commodity	Crop	Table
Fruiting vegetable, cucurbit	Cucumber (VC 0424)	Table 72
Fruiting vegetable, cucurbit	Summer squash (VC 0431)	Table 73
Fruiting vegetable, cucurbit	Cantaloupe/muskmelon (VC 4199/VC 4239)	Table 74, 75
Fruiting vegetable, other than cucurbit	Pepper (VO 0051	Table 76
Fruiting vegetable, other than cucurbit	Tomato (VO 0448)	Table 77

Fruiting Vegetables, Cucurbits

Cucumber

Table 72 Residues of fluensulfone, BSA, MeS, and TSA in cucumber following pre-plant treatment.

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
cGAP - USA	3.84		7 days pre-plantin g	drip irrig., band applic., broadcast spray	–				
Montezuma, Georgia, USA 2010 [Speedway]	4.01	2087	3 days pre-plantin g	drip irrigation	46	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.039, 0.058 (0.049)
(09-01859)					49	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.056, 0.065 (0.061)
					53	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.052, 0.049 (0.051)
					56	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.050, 0.085 (0.068)
					60	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.039, 0.035 (0.037)
Clermont, Florida, USA 2009 [Marketmore 76]	4.00	2083	3 days pre-plantin g	drip irrigation	70	< 0.01, < 0.01 (< 0.01)	0.012, 0.019 (0.016)	n.a.	0.020, 0.035 (0.028)
(09-01859)					73	< 0.01, < 0.01 (< 0.01)	0.013, < 0.01 (0.011)	n.a.	0.029, 0.014 (0.022)
					77	< 0.01, < 0.01 (< 0.01)	0.012, < 0.01 (0.011)	n.a.	0.028, 0.014 (0.021)
					80	< 0.01, < 0.01 (< 0.01)	< 0.01, 0.012 (0.011)	n.a.	0.013, 0.026 (0.020)
					84	< 0.01, < 0.01 (< 0.01)	< 0.01, 0.022 (0.016)	n.a.	0.020, 0.037 (0.029)
Fresno, California, USA 2009 [Straight Eight]	4.00	2083	3 days pre-plantin g	drip irrigation	78	< 0.01, < 0.01 (< 0.01)	0.048, 0.071 (0.060)	n.a.	0.063, 0.090 (0.077)
(09-01859)					81	< 0.01, < 0.01 (< 0.01)	0.030, 0.032 (0.031)	n.a.	0.050, 0.038 (0.044)
					85	< 0.01, < 0.01 (< 0.01)	0.033, 0.032 (0.033)	n.a.	0.056, 0.046 (0.051)
					88	< 0.01, < 0.01 (< 0.01)	0.035, 0.028 (0.032)	n.a.	0.040, 0.040 (0.040)
					92	< 0.01,	0.034, 0.018	n.a.	0.052, 0.044

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
						< 0.01 (< 0.01)	(0.026)		(0.048)
Visalia, California, USA 2010 [Poinsett 76] (AA100708)	4.09	379	7 d pre-planting	BCS	70	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
	4.00	9000	7 d pre-planting	drip irrigation	70	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Hobe Sound, Florida, USA 2010 [Impact] (AA100708)	3.87	222	7 d pre-planting	BCS	45	< 0.01, < 0.01 (< 0.01)	0.076, 0.064 (0.070)	0.028, 0.029 (0.029)	0.048, 0.040 (0.044)
Athens, Georgia, USA 2010 [Burpless Hybrid] (AA100708)	4.05	361	7 d pre-planting	BCS	71	< 0.01, < 0.01 (< 0.01)	0.010, 0.010 (0.010)	0.011, 0.011 (0.011)	0.081, 0.084 (0.083)
Seven Springs, North Carolina, USA 2010 [Ashley] (AA100708)	4.10	358	7 d pre-planting	BCS	41	< 0.01, < 0.01 (< 0.01)	0.085, 0.215 (0.150)	0.021, 0.024 (0.023)	0.408, 0.524 (0.47)
	4.00	9000	7 d pre-planting	drip irrigation	41	< 0.01, < 0.01 (< 0.01)	**0.353**, 0.084 (0.22)	0.035, 0.042 (0.039)	0.718, 0.500 (0.61)
Raymondville, Texas, USA 2010 [Sweet Slice] (AA100708)	3.72	261	7 d pre-planting	BCS	46	< 0.01, < 0.01 (< 0.01)	0.176, 0.164 (0.17)	0.079, 0.071 (0.075)	0.522, 0.507 (0.52)
Thorndale, Ontario, Canada 2010 [Cross Country] (AA100708)	3.81	381	8 d pre-planting	BCS	50	< 0.01, < 0.01 (< 0.01)	0.045, 0.081 (0.063)	0.061, 0.075 (0.068)	0.198, 0.258 (0.23)
Portage la Prairie, Manitoba, Canada 2010 [Slicing] (AA100708)	4.11	359	7 d pre-planting	BCS	73	< 0.01, < 0.01 (< 0.01)	< 0.01, 0.011 (0.010)	< 0.01, < 0.01 (< 0.01)	0.058, 0.070 (0.064)

Applic. Type BCS = broadcast spray

Residue n.a. = Not analysed

Summer squash

Table 73 Residues of fluensulfone, BSA, MeS, and TSA in summer squash following pre-plant treatment

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
cGAP - USA	3.84		7 days pre-plantin g	drip irrig., band applic., broadcast spray	–				
Porterville, California, USA 2010 [Dark Green Zucchini] (AA100708)	3.82	286	7 d pre-plantin g	BCS	49	< 0.01, < 0.01 (< 0.01)	0.014, 0.010 (0.012)	< 0.01, < 0.01 (< 0.01)	0.040, 0.028 (0.034)
	4.00	9000	7 d pre-plantin g	drip irrigation	49	< 0.01, < 0.01 (< 0.01)	0.062, 0.058 (0.060)	< 0.01, < 0.01 (< 0.01)	0.127, 0.079 (0.10)
Dover, Florida, USA 2010 [Enterprise] (AA100708)	4.01	250	7 d pre-plantin g	BCS	36	< 0.01, < 0.01 (< 0.01)	0.086, 0.078 (0.082)	< 0.01, < 0.01 (< 0.01)	0.117, 0.106 (0.11)
Seven Springs, North Carolina, USA 2010 [Early Prolific Straight neck] (AA100708)	4.02	352	7 d pre-plantin g	BCS	41	< 0.01, < 0.01 (< 0.01)	0.206, 0.165 (0.19)	0.033, 0.037 (0.035)	0.715, 0.701 (0.71)
Hinton, Oklahoma, USA 2010 [Enterprise] (AA100708)	4.02	256	6 d pre-plantin g	BCS	61	< 0.01, < 0.01 (< 0.01)	0.196, 0.231 (0.21)	0.023, 0.018 (0.021)	0.366, 0.563 (0.46)
Ephrata, Washington, USA 2010 [Aristocrat] (AA100708)	4.14	389	7 d pre-plantin g	BCS	62	< 0.01, < 0.01 (< 0.01)	**0.256**, 0.237 (0.25)	0.050, 0.045 (0.048)	0.267, 0.237 (0.25)
Berwick, Nova Scotia, Canada 2010 [Payroll] (AA100708)	4.07	363	7 d pre-plantin g	BCS	38	< 0.01, < 0.01 (< 0.01)	0.222, 0.169 (0.20)	0.016, 0.011 (0.014)	0.292, 0.253 (0.27)
Branchton, Ontario, Canada 2010 [Senator] (AA100708)	3.89	241	6 d pre-plantin g	BCS	45	< 0.01, 0.017 (< 0.013)	0.065, 0.035 (0.00)	0.013, 0.010 (0.012)	0.063, 0.051 (0.057)
	4.00	9000	6 d pre-plantin g	drip irrigation	45	< 0.01, < 0.01 (< 0.01)	0.029, 0.060 (0.045)	< 0.01, < 0.01 (< 0.01)	0.038, 0.061 (0.050)
Elm Creek, Manitoba,	3.80	286	7 d pre-plantin	BCS	71	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01	< 0.01, < 0.01	0.036, 0.034 (0.035)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
Canada 2010 [Zucchini] (AA100708)			g				(< 0.01)	(< 0.01)	

Applic. Type BCS = broadcast spray

Melons

Table 74 Residues of fluensulfone, BSA, MeS, and TSA in melons following pre-plant treatment

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
cGAP - USA	3.84		7 days pre-plantin g	drip irrig., band applic., broadcast spray	–				
Montezuma, Georgia, USA 2009 [Ambrosia Hybrid] (09-01859)	4.00	2087	3 days pre-plantin g	drip irrigation	70	< 0.01, < 0.01 (< 0.01)	0.010, < 0.01 (< 0.01)	n.a.	0.067, 0.053 (0.060)
					73	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.045, 0.037 (0.041)
					77	< 0.01, < 0.01 (< 0.01)	< 0.01, 0.010 (< 0.01)	n.a.	0.046, 0.057 (0.052)
					80	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.031, 0.031 (0.031)
Fresno, California, USA 2009 [Yuma Grande F1] (09-01859)	4.00	2083	3 days pre-plantin g	drip irrigation	77	< 0.01, < 0.01 (< 0.01)	0.091, 0.089 (0.090)	n.a.	0.144, 0.177 (0.16)
					80	< 0.01, < 0.01 (< 0.01)	0.117, 0.101 (0.11)	n.a.	0.197, 0.215 (0.21)
					84	< 0.01, < 0.01 (< 0.01)	0.070, 0.074 (0.072)	n.a.	0.146, 0.156 (0.15)
					87	< 0.01, < 0.01 (< 0.01)	0.060, 0.060 (0.060)	n.a.	0.128, 0.128 (0.13)
					91	< 0.01, < 0.01 (< 0.01)	0.050, 0.042 (0.046)	n.a.	0.090, 0.109 (0.10)
King City, California, USA 2010 [Hale's Best	3.93	383	7 d pre-plantin g	BCS	133	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	0.016, 0.018 (0.017)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
Jumbo] (AA100708)									
Arroyo Grande, California, USA 2010 [Top Mark] (AA100708)	3.85	365	7 d pre-plantin g	BCS	97	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Seven Springs, North Carolina, USA 2010 [Hales Best] (AA100708)	4.10	359	7 d pre-plantin g	BCS	66	< 0.01, < 0.01 (< 0.01)	0.061, 0.036 (0.049)	< 0.01, < 0.01 (< 0.01)	0.673, 0.437 (0.56)
Hinton, Oklahoma, USA 2010 [Caravelle] (AA100708)	3.98	253	6 d pre-plantin g	BCS	82	< 0.01, < 0.01 (< 0.01)	**0.065**, 0.062 (0.064)	< 0.01, < 0.01 (< 0.01)	0.303, 0.294 (0.30)
Branchton, Ontario, Canada 2010 [Primo] (AA100708)	4.04	253	6 d pre-plantin g	BCS	80	< 0.01, < 0.01 (< 0.01)	0.015, 0.027 (0.021)	< 0.01, < 0.01 (< 0.01)	0.032, 0.050 (0.041)
Portage la Prairie, Manitoba, Canada 2010 [Athena] (AA100708)	4.11	359	7 d pre-plantin g	BCS	91	< 0.01, < 0.01 (< 0.01)	0.034, 0.030 (0.032)	< 0.01, < 0.01 (< 0.01)	0.172, 0.154 (0.16)
Branchton, Ontario, Canada 2010 [Early sweet] (AA100708)	4.02	251	6 d pre-plantin g	BCS	83	< 0.01, < 0.01 (< 0.01)	0.030, 0.020 (0.025)	< 0.01, < 0.01 (< 0.01)	0.102, 0.091 (0.097)
Corning, California, USA 2010 [ACR 215] (AA100708)	4.02	233	7 d pre-plantin g	BCS	92	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)

Applic. Type BCS = broadcast spray

Residue n.a. = Not analysed

In a magnitude-of-the-residue study by Chevalier (2011, Report R-23486), muskmelon were grown under protected conditions in Southern Europe (Greece, Italy, and Spain) in soil that had been treated with fluensulfone by drip irrigation, at a rate of ca. 4.0 kg ai/ha, 7 days prior to transplanting. The melons were harvested at maturity, 62–79 days after application as well as for residue decline (up to 98 days after application), and stored frozen until preparation for analysis. Preparation consisted of separating the melon samples into their pulp and peel components, homogenizing the fractions, and

then storing them frozen prior to analysis. Analysis was by Method 1977W and the equivalent Method 2061W.

Table 75 Residues of fluensulfone, BSA, MeS, and TSA in melon pulp, peel, and whole fruit following treatment by drip irrigation seven days pre-transplant

Location (Region) Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	DAT, days	Fraction	Residue, mg/kg				Reference
					Fluen.	BSA	MeS	TSA	
cGAP - USA	3.84		–						
La Palma, Murcia, Spain (Southern Europe—Indoor) 2010 [Cantasapo]	3.94	9000	77	peel	< 0.01	0.01	n.a.	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	< 0.01	
				whole fruit	< 0.01	0.01	n.a.	< 0.01	
Ramonete, Murcia, Spain (Southern Europe—Indoor) 2010 [Gabriel]	3.94	18000	64	peel	< 0.01	< 0.01	n.a.	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	< 0.01	
				whole fruit	< 0.01	< 0.01	n.a.	< 0.01	
La Puebla, Murcia, Spain (Southern Europe—Indoor) 2010 [Sancho]	3.94	18000	63	peel	< 0.01	< 0.01	< 0.01	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	< 0.01	< 0.01	
				whole fruit	< 0.01	< 0.01	< 0.01	< 0.01	
La Puebla, Murcia, Spain (Southern Europe—Indoor) 2010 [Sancho]	3.94	18000	66	peel	< 0.01	< 0.01	n.a.	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	< 0.01	
				whole fruit	< 0.01	< 0.01	–	< 0.01	
La Puebla, Murcia, Spain (Southern Europe—Indoor) 2010 [Sancho]	3.94	18000	70	peel	< 0.01	< 0.01	n.a.	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	< 0.01	
				whole fruit	< 0.01	< 0.01	–	< 0.01	
La Puebla, Murcia, Spain (Southern Europe—Indoor) 2010 [Sancho]	3.94	18000	73	peel	< 0.01	0.02	n.a.	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	< 0.01	
				whole fruit	< 0.01	0.01	–	< 0.01	
La Puebla, Murcia, Spain (Southern Europe—Indoor) 2010 [Sancho]	3.94	18000	78	peel	< 0.01	< 0.01	< 0.01	< 0.01	BPL10/237/CL
				pulp	< 0.01	< 0.01	< 0.01	< 0.01	
				whole fruit	< 0.01	< 0.01	< 0.01	< 0.01	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Giusto]	3.94	9000	70	peel	< 0.01	0.20	n.a.	0.15	BPL10/237/CL
				pulp	< 0.01	0.09	n.a.	0.04	
				whole fruit	< 0.01	0.13	n.a.	0.08	
Salizzole, Verona, Italy (Southern Europe—Indoor)	3.94	9000	62	peel	< 0.01	0.25	n.a.	0.46	BPL10/237/CL

Location (Region) Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	DAT, days	Fraction	Residue, mg/kg				Reference
					Fluen.	BSA	MeS	TSA	
2010 [Macigno]									
				pulp	< 0.01	0.17	n.a.	0.20	
				whole fruit	< 0.01	0.20	n.a.	0.31	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Macigno]	3.94	9000	67	peel	< 0.01	0.03	< 0.01	0.02	BPL10/237/CL
				pulp	< 0.01	0.02	< 0.01	< 0.01	
				whole fruit	< 0.01	0.02	< 0.01	0.01	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Macigno]	3.94	9000	70	peel	< 0.01	0.04	n.a.	0.04	BPL10/237/CL
				pulp	< 0.01	0.02	n.a.	< 0.01	
				whole fruit	< 0.01	0.03	–	0.02	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Macigno]	3.94	9000	74	peel	< 0.01	0.06	n.a.	0.04	BPL10/237/CL
				pulp	< 0.01	0.02	n.a.	< 0.01	
				whole fruit	< 0.01	0.03	–	0.02	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Macigno]	3.94	9000	77	peel	< 0.01	0.11	n.a.	0.08	BPL10/237/CL
				pulp	< 0.01	0.03	n.a.	0.01	
				whole fruit	< 0.01	0.06	–	0.03	
Camacici di Sangiovanni Lupatoto, Verona, Italy (Southern Europe—Indoor) 2010 [Macigno]	3.94	9000	81	peel	< 0.01	0.07	< 0.01	0.05	BPL10/237/CL
				pulp	< 0.01	0.01	< 0.01	0.01	
				whole fruit	< 0.01	0.03	< 0.01	0.02	
Chalkidona, Macedonia, Greece (Southern Europe—Indoor) 2010 [Lavigal]	3.94	9000	79	peel	< 0.01	0.01	n.a.	0.07	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	0.02	
				whole fruit	< 0.01	0.01	n.a.	0.05	
Nea Magnisia, Macedonia, Greece (Southern Europe—Indoor) 2010 [Galia]	3.94	9000	84	peel	< 0.01	0.03	< 0.01	0.15	BPL10/237/CL
				pulp	< 0.01	0.01	< 0.01	0.05	
				whole fruit	< 0.01	0.02	< 0.01	0.10	
Nea Magnisia, Macedonia, Greece (Southern Europe—Indoor) 2010 [Galia]	3.94	9000	87	peel	< 0.01	0.02	n.a.	0.16	BPL10/237/CL
				pulp	< 0.01	< 0.01	n.a.	0.05	
				whole fruit	< 0.01	0.02	–	0.11	
Nea Magnisia, Macedonia,	3.94	9000	91	peel	< 0.01	0.04	n.a.	0.19	BPL10/237/CL

Location (Region) Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	DAT, days	Fraction	Residue, mg/kg				Reference
					Fluen.	BSA	MeS	TSA	
Greece (Southern Europe—Indoor) 2010 [Galia]									
				pulp	< 0.01	0.02	n.a.	0.09	
				whole fruit	< 0.01	0.03	–	0.14	
Nea Magnisia, Macedonia, Greece (Southern Europe—Indoor) 2010 [Galia]	3.94	9000	94	peel	< 0.01	0.05	n.a.	0.30	BPL10/237/CL
				pulp	< 0.01	0.01	n.a.	0.09	
				whole fruit	< 0.01	0.03	–	0.19	
Nea Magnisia, Macedonia, Greece (Southern Europe—Indoor) 2010 [Galia]	3.94	9000	98	peel	< 0.01	0.03	< 0.01	0.14	BPL10/237/CL
				pulp	< 0.01	< 0.01	< 0.01	0.05	
				whole fruit	< 0.01	0.02	< 0.01	0.09	
Average Ratio				peel/fruit	–	1.52	–	1.80	–
				pulp/fruit	–	0.62	–	0.50	–

n.a. = not analysed

Fruiting vegetables, other than Cucurbits

Peppers

Table 76 Residues of fluensulfone, BSA, MeS, and TSA in pepper following pre-plant treatment

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
cGAP - USA	3.84		7 days pre-plantin g	drip irrig., band applic., broadcast spray	–				
Chili Pepper									
Montezuma, Georgia, USA 2009 [Aristotle X3R] (09-01858)	4.01	2087	3 days pre-plantin g	drip irrigation	53	< 0.01, < 0.01 (< 0.01)	0.019, 0.018 (0.019)	n.a.	0.064, 0.069 (0.067)
					56	< 0.01, < 0.01 (< 0.01)	0.022, 0.020 (0.021)	n.a.	0.073, 0.064 (0.069)
					60	< 0.01, < 0.01 (< 0.01)	0.015, 0.015 (0.015)	n.a.	0.074, 0.069 (0.072)
					63	< 0.01, < 0.01 (< 0.01)	0.016, 0.016 (0.016)	n.a.	0.065, 0.070 (0.068)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
					67	< 0.01, < 0.01 (< 0.01)	0.014, 0.016 (0.015)	n.a.	0.052, 0.058 (0.055)
	4.01	2087	30 days post-plantin g	drip irrigation	20	< 0.01, < 0.01 (< 0.01)	0.230, 0.207 (0.22)	n.a.	0.140, 0.108 (0.12)
					23	< 0.01, < 0.01 (< 0.01)	0.219, 0.202 (0.21)	n.a.	0.125, 0.125 (0.12)
					27	< 0.01, < 0.01 (< 0.01)	0.181, 0.227 (0.20)	n.a.	0.118, 0.147 (0.13)
					30	< 0.01, < 0.01 (< 0.01)	0.184, 0.185 (0.18)	n.a.	0.117, 0.110 (0.11)
					34	< 0.01, < 0.01 (< 0.01)	0.165, 0.206 (0.186)	n.a.	0.090, 0.099 (0.095)
Clermont, Florida, USA 2009 [Patriot] (09-01858)	4.02	2088	3 days pre-plantin g	drip irrigation	65	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					68	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					72	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					75	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					79	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.011, < 0.01 (0.010)
	4.02	2088	36 days post-plantin g	drip irrigation	26	< 0.01, < 0.01 (< 0.01)	0.032, 0.030 (0.031)	n.a.	< 0.01, < 0.01 (< 0.01)
					29	< 0.01, < 0.01 (< 0.01)	0.027, 0.033 (0.030)	n.a.	< 0.01, < 0.01 (< 0.01)
					33	< 0.01, < 0.01 (< 0.01)	0.027, 0.021 (0.024)	n.a.	< 0.01, < 0.01 (< 0.01)
					36	< 0.01, < 0.01 (< 0.01)	0.019, 0.018 (0.019)	n.a.	< 0.01, < 0.01 (< 0.01)
					40	< 0.01, < 0.01 (< 0.01)	0.020, 0.021 (0.021)	n.a.	< 0.01, < 0.01 (< 0.01)
Porterville, California, USA 2010 [Fresno] (AA100707)	3.98	301	7 d pre-plantin g	BCS	83	< 0.01, < 0.01 (< 0.01)	0.049, 0.031 (0.040)	< 0.01, < 0.01 (< 0.01)	0.037, 0.033 (0.035)
	3.93 + 2.0	297 + 9000	7 d pre-plantin g + 40	BCS + drip irrigation	43	< 0.01, < 0.01 (< 0.01)	0.360, 0.392 (0.38)	< 0.01, < 0.01 (< 0.01)	0.137, 0.156 (0.15)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
			d post plant.						
					46	< 0.01, < 0.01 (< 0.01)	0.301, 0.252 (0.28)	< 0.01, < 0.01 (< 0.01)	0.147, 0.139 (0.14)
					51	< 0.01, < 0.01 (< 0.01)	0.282, 0.363 (0.32)	0.011, < 0.01 (0.010)	0.180, 0.155 (0.17)
					53	< 0.01, < 0.01 (< 0.01)	0.265, 0.318 (0.29)	0.010, < 0.01 (< 0.01)	0.118, 0.166 (0.14)
					56	< 0.01, < 0.01 (< 0.01)	0.226, 0.155 (0.19)	< 0.01, < 0.01 (< 0.01)	0.174, 0.145 (0.16)
Oviedo, Florida, USA 2010 [Sweet Banana] (AA100707)	3.90	279	7 d pre-plantin g	BCS	50	< 0.01, < 0.01 (< 0.01)	**0.201**, 0.167 (0.18)	< 0.01, < 0.01 (< 0.01)	0.092, 0.086 (0.089)
	3.92 + 2.0	280 + 9000	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	3	< 0.01, < 0.01 (< 0.01)	0.250, 0.223 (0.24)	< 0.01, < 0.01 (< 0.01)	0.092, 0.076 (0.084)
Hinton, Oklahoma, USA 2010 [Tam Jalapeno] (AA100707)	4.03	539	7 d pre-plantin g	BCS	101	< 0.01, < 0.01 (< 0.01)	0.044, 0.037 (0.041)	< 0.01, < 0.01 (< 0.01)	0.224, 0.274 (0.25)
	4.08 + 2.0	546 + 9006	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	53	< 0.01, < 0.01 (< 0.01)	0.092, 0.084 (0.088)	0.011, < 0.01 (0.010)	0.389, 0.367 (0.38)
Sweet Pepper									
Fresno, California, USA 2009 [Baron] (09-01858)	4.00	2088	3 days pre-plantin g	drip irrigation	102	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, 0.010 (< 0.01)
					105	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					109	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					112	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					116	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
	4.00	2088	38 days post-plantin g	drip irrigation	61	< 0.01, < 0.01 (< 0.01)	0.041, 0.040 (0.041)	n.a.	0.021, 0.016 (0.019)
					64	< 0.01,	0.025, 0.032	n.a.	0.013, 0.017

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
						< 0.01 (< 0.01)	(0.029)		(0.015)
					68	< 0.01, < 0.01 (< 0.01)	0.029, 0.026 (0.028)	n.a.	0.013, 0.015 (0.014)
					71	< 0.01, < 0.01 (< 0.01)	0.027, 0.021 (0.024)	n.a.	0.015, 0.014 (0.015)
					75	< 0.01, < 0.01 (< 0.01)	0.019, 0.018 (0.019)	n.a.	0.010, 0.011 (0.011)
Porterville, California, USA 2010 [California Wonder] (AA100707)	3.87	342	7 d pre-planting	BCS	104	< 0.01, < 0.01 (< 0.01)	0.067, 0.072 (0.070)	< 0.01, < 0.01 (< 0.01)	0.027, 0.027 (0.027)
	4.01	9000	7 d pre-planting	drip irrigation	104	< 0.01, < 0.01 (< 0.01)	0.073, 0.062 (0.068)	< 0.01, < 0.01 (< 0.01)	0.080, 0.067 (0.074)
	3.9 + 2.0	345 + 9000	7 d pre-planting + 40 d post plant.	BCS + drip irrigation	63	< 0.01, < 0.01 (< 0.01)	0.063, 0.055 (0.059)	< 0.01, < 0.01 (< 0.01)	0.031, 0.027 (0.029)
Oviedo, Florida, USA 2010 [Green Bell] (AA100707)	3.97	284	7 d pre-planting	BCS	63	< 0.01, < 0.01 (< 0.01)	0.225, **0.239** (0.23)	0.014, 0.012 (0.013)	0.150, 0.188 (0.17)
	3.94 + 2.0	282 + 9108	7 d pre-planting + 40 d post plant.	BCS + drip irrigation	16	< 0.01, < 0.01 (< 0.01)	0.379, 0.372 (0.38)	0.012, 0.010 (0.011)	0.169, 0.170 (0.17)
Seven Springs, North Carolina, USA 2010 [Jupiter] (AA100707)	4.02	351	7 d pre-planting	BCS	73	< 0.01, < 0.01 (< 0.01)	0.055, 0.054 (0.055)	< 0.01, < 0.01 (< 0.01)	0.438, 0.483 (0.46)
	3.99 + 2.00	349 + 6279	7 d pre-planting + 40 d post plant.	BCS + drip irrigation	26	< 0.01, < 0.01 (< 0.01)	0.116, 0.141 (0.13)	< 0.01, < 0.01 (< 0.01)	1.056, 1.285 (1.2)
					29	< 0.01, < 0.01 (< 0.01)	0.109, 0.129 (0.12)	< 0.01, < 0.01 (< 0.01)	0.915, 1.030 (0.97)
					33	< 0.01, < 0.01 (< 0.01)	0.166, 0.115 (0.14)	< 0.01, < 0.01 (< 0.01)	1.144, 0.853 (1.0)
					35	< 0.01, < 0.01 (< 0.01)	0.131, 0.052 (0.092)	< 0.01, < 0.01 (< 0.01)	1.012, 0.515 (0.76)
					40	< 0.01, < 0.01 (< 0.01)	0.099, 0.092 (0.096)	< 0.01, < 0.01 (< 0.01)	0.898, 0.933 (0.92)
Hinton, Oklahoma,	4.10	534	7 d pre-plantin	BCS	108	< 0.01, < 0.01	0.086, 0.078 (0.082)	< 0.01, < 0.01	0.341, 0.349 (0.34)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
USA 2010 [XR3 Camelot Sweet Bell] (AA100707)			g			(< 0.01)		(< 0.01)	
	4.11 + 2.00	535 + 9002	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	64	< 0.01, < 0.01 (< 0.01)	0.150, 0.160 (0.16)	< 0.01, < 0.01 (< 0.01)	0.507, 0.424 (0.47)
Thorndale, Ontario, Canada 2010 [Revolution] (AA100707)	3.84	384	7 d pre-plantin g	BCS	63	< 0.01, < 0.01 (< 0.01)	0.065, 0.060 (0.063)	< 0.01, < 0.01 (< 0.01)	0.286, 0.274 (0.28)
	3.85+ 2.00	385 + 900	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	46	< 0.01, < 0.01 (< 0.01)	0.268, 0.244 (0.26)	0.016, 0.017 (0.017)	0.313, 0.348 (0.33)
Portage la Prairie, Manitoba, Canada 2010 [California Wonder] (AA100707)	4.07	355	7 d pre-plantin g	BCS	102	< 0.01, < 0.01 (< 0.01)	0.049, 0.047 (0.048)	< 0.01, < 0.01 (< 0.01)	0.169, 0.162 (0.17)
	4.14+ 2.00	362 + 9000	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	46	< 0.01, < 0.01 (< 0.01)	0.151, 0.166 (0.16)	< 0.01, < 0.01 (< 0.01)	0.172, 0.162 (0.17)
Branchton, Ontario, Canada 2010 [Aristotle] (AA100707)	3.82	239	7 d pre-plantin g	BCS	76	< 0.01, < 0.01 (< 0.01)	0.027, 0.036 (0.032)	< 0.01, < 0.01 (< 0.01)	0.059, 0.073 (0.066)
	4.00	9000	7 d pre-plantin g	drip irrigation	76	< 0.01, < 0.01 (< 0.01)	0.068, 0.077 (0.073)	< 0.01, < 0.01 (< 0.01)	0.114, 0.118 (0.12)
	4.07 + 4.00	254 + 9000	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	27	< 0.01, < 0.01 (< 0.01)	0.128, 0.164 (0.15)	< 0.01, < 0.01 (< 0.01)	0.077, 0.075 (0.076)
Portage la Prairie, Manitoba, Canada 2010 [Hungarian Yellow Wax] (AA100707)	4.07	356	7 d pre-plantin g	BCS	102	< 0.01, < 0.01 (< 0.01)	0.141, 0.130 (0.14)	0.012, 0.012 (0.012)	0.198, 0.181 (0.19)
	3.93+ 2.00	344 + 9000	7 d pre-plantin g + 40 d post plant.	BCS + drip irrigation	56	< 0.01, < 0.01 (< 0.01)	0.297, 0.275 (0.29)	0.024, 0.019 (0.022)	0.162, 0.143 (0.15)

Applic. Type BCS = broadcast spray

Residue n.a. = not analysed

Tomatoes

Table 77 Residues of fluensulfone, BSA, MeS, and TSA in tomato following pre-plant treatment

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
cGAP - USA	3.84		7 days pre-planting	drip irrig., band applic., broadcast spray	–				
Clermont, Florida, USA 2010 [Celebrity] (09-01858)	4.01	2083	3 days pre-planting	drip irrigation	73	< 0.01, < 0.01 (< 0.01)	0.044, 0.044 (0.044)	n.a.	0.042, 0.037 (0.040)
					77	< 0.01, < 0.01 (< 0.01)	0.021, 0.014 (0.018)	n.a.	0.014, 0.010 (0.012)
					80	< 0.01, < 0.01 (< 0.01)	0.017, 0.014 (0.016)	n.a.	0.016, 0.012 (0.014)
					84	< 0.01, < 0.01 (< 0.01)	0.012, 0.011 (0.012)	n.a.	0.010, 0.010 (0.010)
					87	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	< 0.01, < 0.01 (< 0.01)
					115	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.016, 0.018 (0.017)
Fresno, California, USA 2009 [H 8004 Processing] (09-01858)	4.00	2088	3 days pre-planting	drip irrigation	118	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.024, 0.030 (0.027)
					122	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.023, 0.023 (0.023)
					125	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.026, 0.025 (0.026)
					129	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	n.a.	0.022, 0.029 (0.026)
Madera, California, USA 2009 [H 8004 Processing] (09-01858)	3.99	2086	3 days pre-planting	drip irrigation	122	< 0.01, < 0.01 (< 0.01)	0.016, 0.018 (0.017)	n.a.	0.029, 0.023 (0.026)
					125	< 0.01, < 0.01 (< 0.01)	0.012, 0.016 (0.014)	n.a.	0.036, 0.043 (0.040)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
					129	< 0.01, < 0.01 (< 0.01)	0.010, 0.012 (0.011)	n.a.	0.034, 0.024 (0.029)
					132	< 0.01, < 0.01 (< 0.01)	0.018, 0.014 (0.016)	n.a.	0.034, 0.025 (0.030)
					136	< 0.01, < 0.01 (< 0.01)	0.019, 0.014 (0.017)	n.a.	0.028, 0.020 (0.024)
Corning, California, USA 2010 [AB-3] (AA100707)	4.02	233	7 d pre-plantin g	BCS	114	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
	8.02	232	7 d pre-plantin g	BCS	114	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Porterville, California, USA 2010 [Rio Grande] (AA100707)	3.92	296	7 d pre-plantin g	BCS	112	< 0.01, < 0.01 (< 0.01)	0.059, 0.114 (0.087)	< 0.01, < 0.01 (< 0.01)	0.036, 0.053 (0.045)
Porterville, California, USA 2010 [Champion] (AA100707)	3.92	344	7 d pre-plantin g	BCS	146	< 0.01, < 0.01 (< 0.01)	0.014, 0.020 (0.017)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
	4.00	9000	7 d pre-plantin g	drip irrigation	146	< 0.01, < 0.01 (< 0.01)	0.024, 0.033 (0.029)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Livingston, California, USA 2010 [Champion] (AA100707)	3.99	357	7 d pre-plantin g	BCS	126	< 0.01, < 0.01 (< 0.01)	0.035, 0.033 (0.034)	< 0.01, < 0.01 (< 0.01)	0.026, 0.028 (0.027)
King City, California, USA 2010 [Rio Grande] (AA100707)	4.04	395	7 d pre-plantin g	BCS	150	< 0.01, < 0.01 (< 0.01)	0.024, 0.022 (0.023)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Visalia, California, USA 2010 [Champion] (AA100707)	3.94	357	7 d pre-plantin g	BCS	123	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Chico, California, USA 2010 [AB-3] (AA100707)	4.02	232	7 d pre-plantin g	BCS	143	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01 (< 0.01)
Arroyo Grande, California, USA 2010	3.64	345	7 d pre-plantin g	BCS	113	< 0.01, < 0.01 (< 0.01)	0.015, 0.010 (0.013)	< 0.01, < 0.01 (< 0.01)	0.018, 0.013 (0.016)

Location Year [Variety] (Reference)	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
						Fluensulfone	BSA	MeS	TSA
[Shady Lady] (AA100707)									
Hobe Sound, Florida, USA 2010 [Florida 47] (AA100707)	3.97	228	7 d pre-planting	BCS	102	< 0.01, < 0.01 (< 0.01)	0.271, 0.267 (0.27)	< 0.01, < 0.01 (< 0.01)	0.081, 0.100 (0.091)
Dover, Florida, USA 2010 [Tigris] (AA100707)	4.04	215	7 d pre-planting	BCS	78	< 0.01, < 0.01 (< 0.01)	**0.275**, 0.270 (0.27)	< 0.01, < 0.01 (< 0.01)	0.086, 0.075 (0.081)
Seven Springs, North Carolina, USA 2010 [Homestead] (AA100707)	4.11	359	7 d pre-planting	BCS	94	< 0.01, < 0.01 (< 0.01)	0.027, 0.024 (0.026)	< 0.01, < 0.01 (< 0.01)	0.202, 0.141 (0.17)
North Rose, New York, USA 2010 [Mountain Spring] (AA100707)	4.02	329	7 d pre-planting	BCS	93	< 0.01, < 0.01 (< 0.01)	0.058, 0.090 (0.074)	< 0.01, < 0.01 (< 0.01)	0.080, 0.115 (0.098)
Thorndale, Ontario, Canada 2010 [Mariana] (AA100707)	3.81	381	7 d pre-planting	BCS	101	< 0.01, < 0.01 (< 0.01)	0.085, 0.102 (0.094)	< 0.01, < 0.01 (< 0.01)	0.222, 0.234 (0.23)
Thorndale, Ontario, Canada 2010 [Heinz 3478] (AA100707)	3.75	375	7 d pre-planting	BCS	88	< 0.01, < 0.01 (< 0.01)	0.185, 0.211 (0.20)	< 0.01, < 0.01 (< 0.01)	0.281, 0.247 (0.26)
Portage la Prairie, Manitoba, Canada 2010 [Fantastic] (AA100707)	4.07	356	7 d pre-planting	BCS	91	< 0.01, < 0.01 (< 0.01)	0.081, 0.095 (0.088)	< 0.01, < 0.01 (< 0.01)	0.067, 0.088 (0.078)
Elm Creek, Manitoba, Canada 2010 [Fantastic] (AA100707)	4.12	360	7 d pre-planting	BCS	79	< 0.01, < 0.01 (< 0.01)	0.260, 0.201 (0.23)	< 0.01, < 0.01 (< 0.01)	0.374, 0.290 (0.33)
Branchton, Ontario, Canada 2010 [TSH 18] (AA100707)	3.98	249	7 d pre-planting	BCS	83	< 0.01, < 0.01 (< 0.01)	0.076, 0.067 (0.072)	< 0.01, < 0.01 (< 0.01)	0.128, 0.113 (0.12)
Branchton, Ontario, Canada 2010 [TSH 28] (AA100707)	3.86	241	7 d pre-planting	BCS	85	< 0.01, < 0.01 (< 0.01)	0.077, 0.055 (0.066)	< 0.01, < 0.01 (< 0.01)	0.082, 0.067 (0.075)

Location Year [Variety]	Applic. rate, kg ai/ha	Applic. volume, L/ha	Applic. timing	Applic. type	DAT	Residue, mg/kg			
(Reference)						Fluensulfone	BSA	MeS	TSA
	4.00	9000	7 d pre-plantin g	drip irrigation	85	< 0.01, < 0.01 (< 0.01)	0.069, 0.087 (0.078)	< 0.01, < 0.01 (< 0.01)	0.085, 0.106 (0.096)
Branchton, Ontario, Canada 2010 [TSH 25] (AA100707)	4.01	251	7 d pre-plantin g	BCS	83	< 0.01, < 0.01 (< 0.01)	0.180, 0.165 (0.17)	< 0.01, < 0.01 (< 0.01)	0.161, 0.174 (0.17)
Elm Creek, Manitoba, Canada 2010 [Bush Beefsteak] (AA100707)	3.92	296	7 d pre-plantin g	BCS	85	< 0.01, < 0.01 (< 0.01)	0.044, 0.039 (0.042)	< 0.01, < 0.01 (< 0.01)	0.060, 0.050 (0.055)

Applic. Type BCS = broadcast spray

Residue n.a. = not analysed

FATE OF RESIDUES IN STORAGE AND PROCESSING

Nature of the residue during processing

High-temperature hydrolysis

High-temperature hydrolysis of fluensulfone, BSA, MeS, and TSA was investigated by G. Morlock (2011, R-28467). In the study, fluensulfone, BSA, MeS, and TSA were spiked into buffered solutions, in duplicate, at a target concentration of 1 mg/L. The spiked solutions were put into conditions, in the dark, simulating pasteurisation (90 °C, pH 4, 20 min.); baking, brewing, boiling (100 °C, pH 5, 60 min); and sterilisation (120 °C, pH 6, 20 min.). Prior to and after processing, an aliquot from each sample was collected and preserved with acetonitrile. Samples were stored for not more than 17 days, refrigerated (ca. 4 °C) prior to analysis. Analysis consisted of diluting an aliquot of sample with water (fluensulfone, MeS) or acetonitrile/water (BSA, TSA) followed by HPLC-MS/MS determination. Procedural recoveries from samples spiked at 0.1 or 1.0 mg/L ranged from 88 to 102% with standard deviations of not more than 11% across all four compounds and at both spiking levels.

Table 78 Results of high-temperature hydrolysis studies with fluensulfone, BSA, MeS, and TSA (G. Morlock, 2011, R-28467)

	pH		Mass, g		
Analyte	Start	End	Start	End	Recovery
50 mM Citric Acid Buffer, 90 °C, 20 min.					
Fluensulfone	4.03	4.01	224.9	224.9	100.0
	4.03	4.00	225.7	225.7	100.0
TSA	4.02	4.00	224.5	224.4	100.0
	4.02	3.99	223.3	223.1	99.9

MeS	4.02	4.00	224.9	223.9	99.5
	4.02	4.00	225.9	225.9	100.0
BSA	4.02	4.00	226.2	226.2	100.0
	4.02	4.00	225.9	225.8	100.0
50 mM Acetic Acid Buffer, 100 °C, 60 min.					
Fluensulfone	5.04	5.04	221.6	221.5	99.9
	5.04	5.04	225.0	224.8	99.9
TSA	5.05	5.04	224.5	224.2	99.99
	5.04	5.03	224.3	224.2	100.0
MeS	5.05	5.04	224.8	224.8	100.0
	5.05	5.04	223.6	223.6	100.0
BSA	5.05	5.04	223.8	223.6	99.9
	5.05	5.03	226.2	225.9	99.9
50 mM Citric Acid Buffer, 120 °C, 20 min.					
Fluensulfone	6.02	6.01	226.4	226.1	99.9
	6.01	6.01	224.8	224.4	99.8
TSA	6.01	6.01	222.5	222.3	99.9
	6.01	6.01	224.9	224.6	99.9
MeS	6.02	6.01	226.4	226.0	99.8
	6.01	6.01	226.4	226.0	99.8
BSA	6.02	6.02	225.8	225.5	99.9
	6.02	6.01	225.1	225.2	100.0

Residues after processing

The fate of fluensulfone and its BSA, MeS, and TSA metabolites during processing of raw tomato into processed tomato products was investigated by Jones (2011, Report AA100707) by Burn and Winner (2012, Report FOZ1001), and by Jones (2013, Report R-29577). In all studies, samples of processed commodities were generated using procedures reflective of commercial practices and all samples were analysed by methods equivalent to Method 1977W or Method 2061W.

In Jones 2011, tomatoes were transplanted into plots that had received treatment with fluensulfone seven days prior to transplanting at a rate of 7.93 or 8.02 kg ai/ha. Tomatoes were harvested at maturity from the second trial only (8.02 kg ai/ha) and processed into juice, puree, and paste using simulated commercial practices. RAC and processed commodities were assayed for fluensulfone, BSA, MeS, and TSA. All residues were < 0.01 mg/kg in all samples except for parent fluensulfone at 0.01 mg/kg in tomato juice. Given the results and that other studies are available, further information on processing practices and derivation of processing factors are not addressed in this evaluation.

In Burn and Winner, tomatoes were transplanted in to plots which had received fluensulfone seven days prior to transplanting at a rate of either 3.93 or 7.86 kg ai/ha. Tomatoes were harvested at maturity and processed into peeled, canned, sundried, juice, puree, paste, wet pomace, and dry pomace processed commodities using simulated commercial practices. Raw tomato and processed tomato samples were analysed by a method equivalent to Method 2061W.

Peeled tomatoes were made steaming tomatoes, with stems removed, in a steamer pot for six minutes. After steaming, the skins were removed manually and the tomato cores were removed with a standard kitchen coring tool.

Canned tomatoes were made by placing portions of the peeled tomatoes into containers, topping the containers off with juice from the whole tomato, fitting lids to the containers, and boiling in a water-filled pot for 45 minutes. The canned tomatoes were then cooled rapidly to prevent overcooking.

Juice, puree, paste, and wet pomace were made as follows: Whole tomato samples were chopped in a food processor at low speed. The resulting homogenate was strained using a press and a gauze bag to remove course components (skins, seeds, etc.). The material in the bag made up the wet pomace fraction and the strained liquid made up the juice fraction. An aliquot of juice was concentrated, by rotary evaporation in vacuo at 90 °C, to a moisture content of 86% to form puree, and a separate aliquot of juice was concentrated in the same fashion to a moisture content of 72% to form paste. Dry pomace was made by drying wet pomace in an oven to a moisture content of < 10%.

For sundried tomatoes, whole tomato samples were quartered lengthwise and composited into samples containing at least 1 quarter from 12 different tomatoes. The wedges were laid out onto a tray and lightly covered with salt (NaCl, ca. 10–15 g per kg fresh sample). The samples were dried in the sun over a 5-day period. Samples were checked daily for water content and were considered to be suitably dried when they had dehydrated to < 20% of their original weight.

Residues of fluensulfone were < 0.01 mg/kg in all samples. Quantifiable residues of BSA, MeS, and TSA occurred in RAC tomatoes from at least one of the treatment rates. Residues of BSA and TSA were concentrated, relative to the residues in the RAC, in wet and dry pomace. In addition, BSA showed concentration in sundried tomato. MeS was concentrated in dry pomace from the lower treatment rate only.

Table 79 Residues of fluensulfone, BSA, MeS, and TSA in tomato and processed commodities (Burn and Winner, 2012, Report FOZ1001)

	Residue, mg/kg		Processing Factor	
Tomato Commodity	3.93 kg ai/ha rate	7.86 kg ai/ha rate	3.93 kg ai/ha rate	7.86 kg ai/ha rate
Fluensulfone				
Raw fruit	< 0.01	< 0.01	–	–
Canned	< 0.01	< 0.01	–	–
Dry pomace	< 0.01	< 0.01	–	–
Peeled	< 0.01	< 0.01	–	–
Sundried	< 0.01	< 0.01	–	–
Juice	< 0.01	< 0.01	–	–
Paste	< 0.01	< 0.01	–	–
Puree	< 0.01	< 0.01	–	–
Wet pomace	< 0.01	< 0.01	–	–
BSA				
Raw fruit	0.01	0.03	–	–
Canned	< 0.01	0.01	< 1	0.33
Dry pomace	0.17	0.28	17	9.3
Peeled	< 0.01	0.01	< 1	0.33
Sundried	0.02	0.05	2	1.67
Juice	< 0.01	0.02	< 1	0.67
Paste	0.01	0.03	1	1
Puree	< 0.01	0.02	< 1	0.67
Wet pomace	0.04	0.09	4	3

	Residue, mg/kg		Processing Factor	
Tomato Commodity	3.93 kg ai/ha rate	7.86 kg ai/ha rate	3.93 kg ai/ha rate	7.86 kg ai/ha rate
MeS				
Raw fruit	0.02	< 0.01	–	–
Canned	< 0.01	< 0.01	< 0.5	–
Dry pomace	0.04	0.05	2	–
Peeled	< 0.01	< 0.01	< 0.5	–
Sundried	< 0.01	0.01	< 0.5	–
Juice	< 0.01	< 0.01	< 0.5	–
Paste	< 0.01	< 0.01	< 0.5	–
Puree	< 0.01	< 0.01	< 0.5	–
Wet pomace	< 0.01	0.02	< 0.5	–
TSA				
Raw fruit	0.01	0.02	–	–
Canned	< 0.01	< 0.01	< 1	< 0.5
Dry pomace	0.06	0.09	6.0	4.5
Peeled	< 0.01	0.01	< 1	0.5
Sundried	0.01	0.02	1	1
Juice	< 0.01	< 0.01	< 1	< 0.5
Paste	0.01	0.01	1	0.5
Puree	< 0.01	< 0.01	< 1	< 0.5
Wet pomace	0.02	0.03	2	1.5

In a second study by Jones (2013, R-29577), tomatoes were planted into plots treated at a rate of either 12 kg ai/ha or 20 kg ai/ha seven days prior to transplanting. Tomatoes were harvested from one plot at the higher treatment rate and processed into juice, puree, paste, and wet and dry pomace using simulated commercial practices. Residues of fluensulfone, BSA, MeS, and TSA were assayed using Method 2061W.

Prior to processing, tomatoes were washed (52–57 °C, 3–5 min), hand culled, and suitable fruits were trimmed of defects and/or off-colour areas. Cleaned tomatoes were chopped to a fine consistency and processed through a pulper/finisher with a 2.4 mm screen. Material passing through the screen underwent a hot-break process and was then passed through a pulper/finisher fitted with a 0.84 mm screen. An aliquot of the material passing through the screen was heated (85–91 °C, 3 min), placed into cans, pressure cooked (121–124 °C, 40–45 seconds), and cooled in a water bath (16–27 °C, 28–32 min). The resulting juice fraction was then placed into frozen storage. Separate aliquots of the juice fraction were vacuum-evaporated to form puree (8–24% solids) and paste (24–30% solids). Puree and paste samples were heated, canned, and cooled, as above for juice (no pressure cooking). Material not passing through the screens was collected as wet pomace, of which an aliquot was dried (54–71 °C, 20–24 hrs) to form dry pomace.

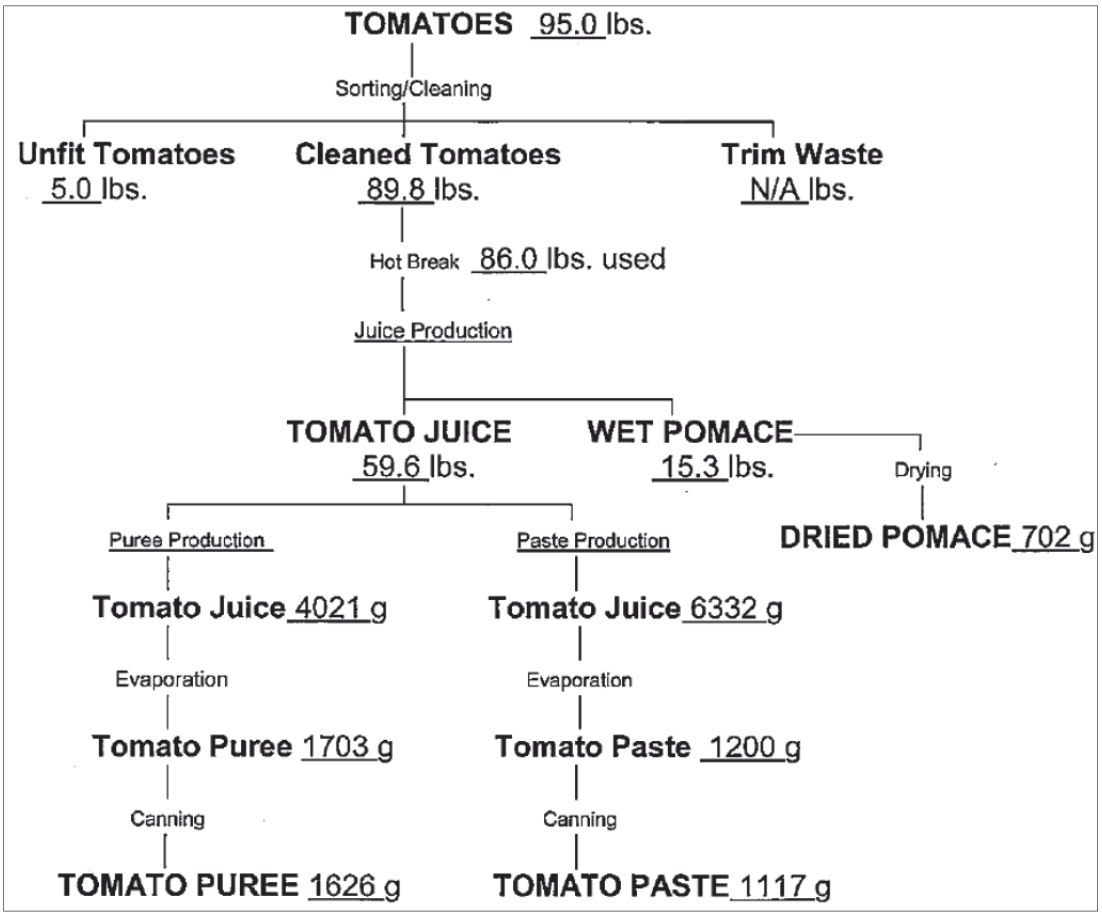


Figure 6 Material balance and processed commodity flowchart for processed tomato commodities (copied without alteration from Jones 2013, Report R-29577)

Residues of fluensulfone and MeS were < 0.01 ppm in all commodities. Residues of BSA and TSA were quantifiable in all commodities and showed concentration, relative to the raw fruit, in dry pomace and paste, and a slight concentration in BSA in puree.

Table 80 Residues of fluensulfone, BSA, MeS, and TSA in tomato and processed commodities (Jones, 2013, Report R-29577)

Tomato Commodity	Average residue, mg/kg	Processing factor
Fluensulfone		
Raw fruit	< 0.01	–
Dry pomace	< 0.01	–
Juice	< 0.01	–
Paste	< 0.01	–
Puree	< 0.01	–
Wet pomace	< 0.01	–
BSA		
Raw fruit	2.17	–
Dry pomace	14.26	6.57
Juice	1.81	0.83
Paste	7.69	3.54
Puree	3.00	1.38
Wet pomace	1.43	0.66
MeS		

Tomato Commodity	Average residue, mg/kg	Processing factor
Raw fruit	< 0.01	–
Dry pomace	< 0.01	–
Juice	< 0.01	–
Paste	< 0.01	–
Puree	< 0.01	–
Wet pomace	< 0.01	–
TSA		
Raw fruit	0.50	–
Dry pomace	1.73	3.46
Juice	0.46	0.92
Paste	1.41	2.82
Puree	0.49	0.98
Wet pomace	0.36	0.72

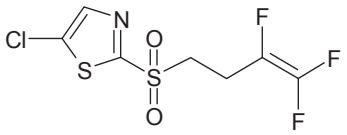
Residues in animal commodities

No feeding studies depicting transfer of residues from animal feeds to animal commodities were provided.

APPRAISAL

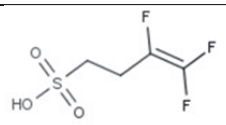
Fluensulfone is a non-fumigant nematicide in the fluoroalkenyl class of pesticides. Fluensulfone shows activity in multiple nematicide physiological systems. It was considered for the first time by the 2013 JMPR for toxicology and by the 2014 JMPR for residues. The 2013 JMPR established an ADI of 0–0.01 mg/kg bw and an ARfD of 0.3 mg/kg bw.

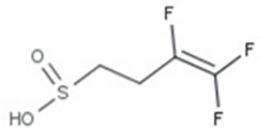
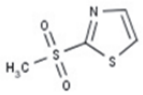
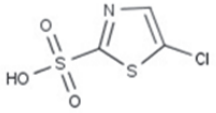
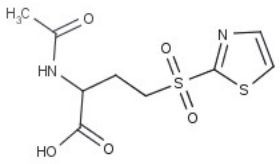
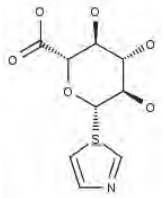
The IUPAC name for fluensulfone is 5-chloro-1,3-thiazol-2-yl 3,4,4-trifluorobut-3-en-1-yl sulfone.



Fluensulfone with ^{14}C radiolabelling in the thiazole ring or in the ethane bridge between the sulfone and trifluorobutene moieties was used in the metabolism and environmental fate studies. In this appraisal, these positions are referred to as the Th and Bu labels, respectively.

The following abbreviations, along with IUPAC names and structures, are used for the metabolites discussed in this appraisal:

BSA	3,4,4-trifluorobut-3-ene-1-sulfonic acid	

Butene sulfinic acid	3,4,4-trifluorobut-3-ene-1-sulfinic acid	
MeS	2-methylsulfonyl-1,3-thiazole	
TSA	5-chloro-1,3-thiazole-2-sulfonic acid	
Thiazole mercapturate	2-acetamido-4-(1,3-thiazole-2-sulfonyl)butanoic acid	
Thiazole glucuronides (α and ß isomers)	Name not specified	

Animal metabolism

The Meeting received studies elucidating the metabolism of fluensulfone in laboratory animals (evaluated by the 2013 Meeting), lactating goats, and laying hens.

In rats, absorption of fluensulfone administered by gavage at 5 mg/kg bw is rapid, with maximal plasma concentrations achieved within 4 hours. At 5 and 500 mg/kg bw, the extent of oral absorption is high (> 80%). Fluensulfone is widely distributed in the body. High concentrations of both butene- and thiazole-labelled material were found in the liver and kidney. The labelled material was rapidly excreted via urine (> 70%), with faecal excretion accounting for no more than 5–13%. Absorbed fluensulfone was extensively metabolized, with almost no unmetabolized parent compound detected. Other than low amounts of thiazole sulfonic acid, no other faecal metabolites were present at levels above 5% of the administered dose. The parent compound probably reacts with glutathione and cleaves, giving rise to thiazole mercapturate, thiazole glucuronide, and butene sulfinic acid, the major urinary metabolites.

In goats dosed for five consecutive days at approximately 28.8 mg/animal/day (10.5 ppm in the diet), most of the recovered radioactivity was in urine and GI tract/faeces, with only 10.7% (Th-14C) or 3.5% (Bu-14C) of the applied dose (AD) accounted for in tissues and body fluids. In excreta, the major identified residues were trifluorobutene sulfinic acid and the MeS metabolite. In other matrices, the highest levels of radioactivity were associated with liver (max. 2.6 mg eq./kg, 1.7% AD), kidney (max 1.4 mg eq./kg, 0.2% AD), and milk fat (2.0 mg eq./kg, 0.31% AD). Seventy-five to

ninety percent of the radioactivity in the goat matrices was extracted with a combination of solvent extraction and alkaline digestion. No BSA, TSA, or fluensulfone was detected in any goat matrix. Radioactivity in milk and tissues was primarily associated with glucose (0.039–0.24 mg/kg; 4–17% TRR), lactose (0.036–0.21 mg/kg; 4–63% TRR), proteins/amino acids (0.015–1.2 mg/kg; 5–37% TRR), and triglycerides/fatty acids (0.009–1.1 mg/kg; 7.6–52% TRR), and the radioactivity appears to be due to incorporation of the radiolabelled carbon.

In hens dosed for seven consecutive days at 1.25 mg/animal/day (9.8 ppm in the diet), total radioactive residues (TRR) in excreta accounted for approximately 80% of the dosed material for both label positions. Total radioactivity in eggs did not plateau within the eight dosing days of the hen study. Radioactive residues in eggs were not identified. Most residues in eggs were associated with aqueous phases in the extraction schemes; however, 0.18 mg eq./kg from the butane label (27% TRR) was extracted with hexane:acetone. Fluensulfone was a major residue (0.009–0.041 mg/kg; 21–55% TRR) in poultry fat; otherwise, parent fluensulfone was not observed in any matrix. Comparison of extraction of radioactivity from liver samples treated with and without protease enzyme indicates that ca. 0.16 mg/kg (24%) of the radioactivity was associated with proteins and/or amino acids and approximately 3% (0.016 mg/kg) was identified as TSA. Incorporation of the radioactivity into triglycerides was noted in both fat matrices and in eggs. In eggs, triglyceride accounted for 7% and 27% of the TRR for the thiazole and butene labels, respectively. In fat matrices, triglycerides accounted for 7–12% and 79–87% of the TRR for the thiazole and butene labels, respectively.

Overall, the animal metabolism studies show that fluensulfone is well absorbed and that the majority (75–90%) of the dosed radioactivity is excreted. Results from rat, goat, and hen studies indicate that fluensulfone is cleaved at the sulfonyl bridge in all three animals; however, the identification of different residues in the studies suggests that there may be different metabolic pathways. In both poultry and goats, fluensulfone can be expected to break down and be incorporated almost entirely into natural products. Based on the residue profile in poultry and the observed incorporation of radioactivity into natural components, the Meeting is of the opinion that the lack of a residue plateau in egg is not of concern.

Plant metabolism

The Meeting received studies depicting the metabolism of fluensulfone in tomato, lettuce, and potato. All of the studies were conducted with fluensulfone which was radiolabelled, separately, in the thiazole ring and the ethane bridge between the sulfonyl and trifluorobutene moieties.

To investigate the metabolism of fluensulfone on tomato, fluensulfone was applied at a rate of 4.07 kg ai/ha to soil. Later that same day, tomato seedlings were planted. Mature fruits were harvested 87 days after treatment. Total radioactive residues in tomato were higher in samples treated with Bu-^{14}C-labelled material (0.52 mg eq./kg) than those from Th-^{14}C treatment (0.27 mg eq./kg). The majority (88.7% Th-^{14}C; 91.3% Bu-^{14}C) of the radioactivity was extracted with acetonitrile:water

(ACN:H_2O). TSA made up 0.12 mg/kg (45.4% TRR), with an additional 0.06 mg eq./kg (21.2% TRR) as salts/related compounds. BSA occurred at 0.22 mg/kg (41.6% TRR) with salts/related compounds making up 0.13 mg eq./kg (26.5% TRR). No other compounds, including parent fluensulfone, were identified in tomato.

Lettuce seeds were planted into soil and then fluensulfone was applied at a rate of 4.07 kg ai/ha. Samples were collected 49 days and 64 days after application to obtain immature and mature lettuce, respectively. Contrary to the results with tomato, TRR were higher from treatment with Th-^{14}C-labelled material (6.1–7.1 mg eq./kg) than with Bu-^{14}C-labelled material (1.5–2.4 mg eq./kg) and were similar in immature and mature foliage. The majority of the radioactivity was extracted with ACN:H_2O, with higher extraction efficiency from samples treated with the Th-^{14}C label. Following treatment with Th-^{14}C-labelled material, 3.57 mg/kg and 4.34 mg/kg (67.5% and 70.6% TRR) was identified as TSA in immature and mature leaves, respectively. An additional 1.39 mg eq./kg and 0.41 mg eq./kg (17.8% and 6.6% TRR) in immature and mature leaves, respectively, was determined to be salts and/or other forms of TSA. Following treatment with Bu-^{14}C-labelled material, BSA occurred at 0.49 mg/kg (23.8% TRR) in immature leaves and at 0.49 mg/kg (37.6% TRR) in mature leaves. As with TSA, salts and other forms occurred for BSA and constituted, in total, 0.75 mg eq./kg (36.0% TRR) in immature foliage and 0.29 mg eq./kg (22.1% TRR) in mature foliage. Fluensulfone occurred at trace levels (0.009 mg/kg, 0.008 mg/kg) in immature lettuce from the Th-^{14}C and Bu-^{14}C treatments, respectively. Aside from BSA and TSA, no other metabolites of fluensulfone were identified.

Potato seed pieces were planted just prior to application of fluensulfone to soil at a rate of 4.04 kg ai/ha (Th-^{14}C) or 4.13 kg ai/ha (Bu-^{14}C). Immature (70 days after treatment) and mature (106 days after treatment) tubers were harvested and analysed. For immature and mature tubers, respectively, TRR were 0.32 and 0.44 mg eq./kg from the Th-^{14}C treatment and 0.22 and 0.17 mg eq./kg from the Bu-^{14}C treatment. Extraction with ACN:H_2O efficiently released residues: 91.9% TRR (Th-^{14}C, immature tuber), 91.7% TRR (Th-^{14}C, mature tuber), 76.9% TRR (Bu-^{14}C, immature tuber), and 79.1% TRR (Bu-^{14}C, mature tuber). Fluensulfone was found at trace levels (0.005 mg/kg) from both label treatments in mature tubers only. Otherwise, the only identified residues were BSA, TSA, and their salts and/or related compounds. BSA constituted 0.069 mg/kg (30.7% TRR) and 0.042 mg/kg (25.8% TRR) in immature and mature tubers, respectively. Salts and related forms of BSA provided an additional 0.041 mg eq./kg (17.8% TRR; immature tubers) and 0.035 mg eq./kg (21.4% TRR; mature tubers). TSA occurred at 0.21 mg/kg (63.0% TRR) and 0.31 mg/kg (65.3% TRR) in immature and mature tubers, respectively. Salts and related forms of TSA gave an additional 0.028 mg eq./kg (8.4% TRR; immature tubers) and 0.025 mg eq./kg (5.3% TRR; mature tubers).

Fluensulfone was extensively metabolised in all of the studies, with the only major residues being the BSA and TSA metabolites. A few chromatographic fractions contained radioactivity in

excess of 10% TRR. Investigation of these fractions indicated that the residues were associated with the BSA or TSA metabolites, as salts of the sulfonic acids or as related forms of the metabolites. The only major residues in the harvested matrices were the BSA and TSA metabolites and, with the exception of trace levels of fluensulfone in immature lettuce and mature potato, no parent compound was detected.

Environmental fate in soil

Fluensulfone is stable to hydrolysis under accelerated conditions (50 °C, pH 4, 7, 9) but is prone to photolysis [DT_{50} of 21days (Th-^{14}C) or 35 days (Bu-^{14}C) in soil], showing first-order kinetics. In an aerobic soil metabolism study, major residues following treatment with fluensulfone were BSA, TSA, and MeS, depending on the duration of incubation. Fluensulfone had DT_{50} estimates ranging from 7 to 17 days across six soils, all following first-order kinetics. BSA formed from fluensulfone generally accumulated for the first ca. 1 month of incubation followed by dissipation (DT_{50} 18–26 days). Residues of TSA accumulated continuously over the incubation period, reaching maxima of 49–74% of the applied radioactivity at the 120-day sampling. Residues of MeS began to be observed after the first 2–4 weeks of incubation, reaching a maximum of not more than 8% of the applied radioactivity; residues of MeS declined to 0% of the applied radioactivity between the 50- and 120-day sampling times, depending on the soil. In a separate study, the DT_{50} estimates for the TSA and MeS metabolites under aerobic soil conditions are 421 and 33 days, respectively. Field dissipation studies were not provided.

Confined rotational crop studies were conducted with radish, lettuce, and wheat at plant-back intervals (PBIs) of 30, 120, and 360 or 390 days. Fluensulfone, radiolabelled as either the Th-^{14}C or Bu-^{14}C, was applied to soil at a rate of approximately 4 kg ai/ha. Lettuce was replanted at 390 days after application due to crop failure at the 360-day PBI. Following treatment with Th-^{14}C-labeled material, TRR generally declined sharply from 30 to 120 days and then remained relatively consistent between the 120 and the 360/390-day PBIs. (e.g., wheat hay: 27 mg eq./kg at 30-Day PBI, 9.4 mg eq./kg at 120-Day PBI, 10.8 mg eq./kg at 360-Day PBI) As with primary crops, the major residues were the BSA and TSA metabolites. A low level of the parent compound was observed in lettuce, radish root, radish foliage, and wheat forage, hay, and straw (but not grain). Fluensulfone, when found, was typically 1 to 2 orders of magnitude less than the BSA or TSA residue levels. In all cases, residues of fluensulfone and BSA were not quantifiable after the 120-day PBI whereas residues of TSA persisted at quantifiable levels for at least one year, ranging from 0.13 mg eq./kg (immature lettuce) to 11 mg eq./kg (wheat hay).

Overall, fluensulfone can be expected to dissipate rather rapidly in the environment, with a concomitant increase in residues of BSA, TSA, and, to a much lesser extent, MeS. BSA residues should then decline; however, TSA appears to be stable for an extended period. The Meeting concluded from the soil metabolism and confined rotational crop studies that TSA may accumulate in

soils following repeated uses of fluensulfone and may occur in follow-on crops at plant-back intervals exceeding one year after treatment.

Methods of residue analysis

The Meeting received analytical methods for the analysis of fluensulfone, BSA, MeS, and TSA in plant and animal matrices. The methods are essentially identical for all samples and the LOQ for all matrices and analytes, defined as the lower limit of method validation, is 0.01 mg/kg.

Extraction of residues is accomplished with ACN:H_2O (1:1, v/v) or ACN (BSA and TSA in eggs only); the extract is then split for analysis of fluensulfone and MeS by one set of procedures and for analysis of BSA and TSA by a second set. For fluensulfone and MeS, there is no clean-up of the extract beyond filtration (except hexane partitioning for analysis of MeS in fatty/oily samples). Residues of fluensulfone and MeS are determined by reverse-phase LC-MS/MS in positive ion spray mode. For BSA and TSA, an aliquot of the initial extract is concentrated and then cleaned-up using C-18 SPE. Residues are determined by reverse-phase LC-MS/MS in negative ion spray mode.

The solvent used for extraction is the same as, or very similar to, that used in the metabolism studies and showed adequate extraction efficiency of incurred residues.

Testing of fluensulfone and the two sulfonic acid metabolites, BSA and TSA, through the FDA PAM multiresidue method protocols demonstrated that the compounds showed poor sensitivity, poor recovery, and/or poor chromatography. Overall, the results indicate that the FDA PAM multiresidue protocols are not suitable for the detection or enforcement of fluensulfone, BSA, or TSA residues in non-fatty foods.

Stability of residues in stored analytical samples

The Meeting received data depicting the stability of residues of fluensulfone, BSA, and TSA in tomato, pepper, cucumber, and melon. In addition, the stability of those analytes and MeS was investigated in frozen, stored tomato puree and paste. No dissipation of any analyte was observed during the storage periods for the various matrices. Stability was demonstrated in tomato raw agricultural commodity (RAC) for at least 469 days (ca. 15 months) and in tomato processed commodities for at least 181 days (ca. 6 months). For pepper, cucumber, and melon, residues were stable for at least 488 days (ca. 16 months).

Definition of the residue

Studies depicting the nature of the residues in animals consistently show fluensulfone to be cleaved at the sulfonyl moiety, presumably via glutathione conjugation, resulting in both halves of the molecule having a sulfonyl functional group. With the exception of poultry fat, fluensulfone was not observed in any animal commodity. In livestock, the majority of the radiolabel was excreted. Retained fluensulfone is extensively metabolized, with the radioactivity being associated primarily with sugars,

amino acids, and fatty acids. MeS and butene sulfinic acid were identified in livestock studies, but were observed only in excreta. In the rats, significant residues were thiazole mercapturate, thiazole glucuronide, BSA, TSA, and butene sulfinic acid. MeS, observed in some field trial samples, was not identified in the rat metabolism study.

Based on the livestock metabolism studies, a residue definition potentially suitable for enforcement by the typical criteria is possible only for poultry fat and poultry liver, which were the only matrices in the animal metabolism studies with quantifiable residues of a fluensulfone-specific compound (fluensulfone in fat and TSA in liver). Although fluensulfone was a major residue in poultry fat (up to 55% TRR), the available residue data indicate that quantifiable residues of the parent compound are not expected in plants; thus exposure to fluensulfone via livestock diets is unlikely, making the parent compound an unsuitable marker for enforcement in any livestock commodity. The other potential marker, TSA, occurred only as a minor component in poultry liver (2.7% TRR). Based on the results of the metabolism studies and on the residue profiles observed in crop metabolism studies, confined rotational crop studies, and supervised residue trials, the Meeting determined that a residue definition for livestock commodities is not necessary.

In both plant and rotational crop metabolism studies, fluensulfone appears to follow the same glutathione-mediated pathway observed in livestock; however, in plants quantifiable residues of the BSA and TSA metabolites were consistently observed. Parent fluensulfone was identified only at trace levels in immature lettuce, mature potato, and rotational lettuce, radish foliage, and wheat hay, forage and straw at short PBIs (30 days). In target crops, BSA ranged from 0.071–1.24 mg/kg (43.6–68.1% TRR) and TSA ranged from 0.17–4.75 mg/kg (66.6–85.3% TRR). In rotational crops, BSA was detected in all matrices except wheat grain at the 30-day PBI (0.004–1.4 mg/kg) and in most matrices at the 120-day PBI (0.001–0.43 mg/kg), and was undetected (< 0.001 mg/kg) by the 360/390-day PBI, except wheat straw at 0.012 mg/kg. In contrast, TSA was detected in all rotational crop matrices at all PBIs, ranging from 0.086 mg/kg to 16 mg/kg across all samples.

In crop field trials, fluensulfone was detected in only one sample (summer squash at 0.017 mg/kg). Across all crops, residues of BSA ranged from < 0.01 to 0.27 mg/kg and TSA ranged from < 0.01 to 0.71 mg/kg. MeS ranged from < 0.01 to 0.08 mg/kg and was less than both BSA and TSA in the corresponding sample. In all trials with only pre-plant applications (per GAP), MeS was < 0.01 mg/kg in all samples of cantaloupe, pepper, and tomato. Although MeS was not found in the plant or rotational crop metabolism studies, it was observed in supervised residue trials in cucumber (< 0.01–0.079 mg/kg) and summer squash (< 0.01–0.050 mg/kg).

The Meeting determined that fluensulfone is NOT a suitable marker for compliance with MRLs in crops. Both BSA and TSA are suitable markers based on results of supervised field trials. The confined rotational crop study, however, demonstrates a potential for TSA to carry over into succeeding crops. Therefore, given that quantifiable residues of fluensulfone are not expected in plant commodities, that a separate analysis is required for the analysis of fluensulfone and BSA/TSA, and

that residues of TSA may occur from previous crop cycle treatments with fluensulfone, the Meeting determined that BSA is the most suitable marker for MRL compliance. A validated method exists for analysis of BSA in plant commodities. The Meeting defined the BSA metabolite as the residue definition for compliance in plants.

Regarding the toxicity of the BSA, TSA, and MeS metabolites, the JMPR has concluded that TSA is unlikely to be of any toxicological relevance; data are insufficient at this time to make a definitive toxicological determination regarding the relevancy of BSA and MeS.

For BSA, the JMPR has determined that the ADI and ARfD for fluensulfone could be used as a screening evaluation of exposure to BSA. Based on a comparison of toxicity data between BSA and fluensulfone, the evaluation may be made directly, without a correction for molecular weight. If additional uses are considered in the future, the use of the fluensulfone points of departure to evaluate exposure to BSA may need to be re-evaluated.

For MeS, the JMPR has determined that the IEDI (0.07 µg/kg bw/day) for MeS should be compared to the Cramer class III TTC value of 1.5 µg/kg bw/day and that the IESTI (3.2 µg/kg bw/day)[2] should be compared to the single-exposure TTC for Cramer class III compounds of 5 µg/kg bw proposed by EFSA. The IESTI is somewhat refined in that for melon, the specific HR (0.01 mg/kg) from melon field trials was used rather than the HR for the fruiting vegetables, Cucurbits group (0.053 mg/kg). On the basis of these comparisons, the Meeting concluded that MeS is not considered to be a relevant metabolite for the crops under consideration. If additional uses are considered in the future, this conclusion may need to be re-evaluated.

Given the residue profile in crops and taking into consideration the available information on the toxicities of the metabolites, the Meeting determined that the residue definition for dietary exposure from crops is BSA. In lieu of BSA-specific toxicological points of departure, dietary intake estimates for BSA should be compared to the ADI and ARfD for fluensulfone, with no correction for molecular weight.

Definition of the residue for compliance with the MRLs and dietary intake for plant commodities: *BSA {3,4,4-trifluorobut-3-ene-1-sulfonic acid}*.

Definition of the residue for compliance with the MRLs and for dietary intake for animal commodities: *Not necessary*

Results of supervised residue trials on crops

Fluensulfone is registered in the USA for use on cucurbit vegetables and on fruiting vegetables. For all crops, the cGAP is an application to the soil at 2.8 kg ai/ha made seven days prior to transplanting

[2] The estimate of 3.2 µg/kg bw is refined, using the observed HR for melon (0.01 mg/kg) rather than the HR for the fruiting vegetables, Cucurbits group (0.053 mg/kg), which resulted in a maximum dietary intake estimate of 5.3 µg/kg bw.

crops into the field. Application may be made by broadcast spray to the soil, by banded spray, or by drip irrigation. The applied material must be mechanically incorporated 15–20 cm into the soil profile for spray applications or by sufficient volume for drip irrigation application.

The Meeting received supervised residue trial data for cucumber, summer squash, cantaloupe, pepper, and tomato. The trials were conducted in North America (USA and Canada). All trials were conducted at a target application rate of 3.9 kg ai/ha, which reflects a nominal exaggeration of 39% relative to the cGAP. Therefore, the Meeting decided to scale residue values for all analytes from trials otherwise meeting the cGAP to an application rate of 2.8 kg ai/ha. Residues scaled to < 0.01 mg/kg were maintained at < 0.01 mg/kg. Reported values are field trial averages unless otherwise noted.

Residues of fluensulfone were < 0.01 mg/kg in all samples.

Fruiting vegetables, Cucurbits

In cucumber, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 7) were: < 0.01, 0.01 (2), 0.063, 0.07, 0.17, and 0.219 mg/kg.

Application rates for these trials ranged from 3.72 kg ai/ha to 4.11 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: < 0.01 (3), 0.041, 0.045, 0.114, and 0.137 mg/kg.

In summer squash, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 8) were: < 0.01, 0.05, 0.06, 0.082, 0.186, 0.196, 0.214, and 0.247 mg/kg.

Application rates for these trials ranged from 3.80 kg ai/ha to 4.14 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: < 0.01, 0.032, 0.038, 0.051, 0.115, 0.12, 0.133, and 0.149 mg/kg.

In melon, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 8) were: < 0.01 (3), 0.021, 0.025, 0.032, 0.049, and 0.064 mg/kg.

Application rates for these trials ranged from 3.85 kg ai/ha to 4.11 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: < 0.01 (3), 0.013, 0.016, 0.019, 0.030, and 0.040 mg/kg.

Noting that the GAP in the USA is for the cucurbit vegetables crop group, which is equivalent to the Codex fruiting vegetables, Cucurbit group, and that the BSA residue data from cucumbers, summer squash, and melons are not significantly different by the Kruskal-Wallis test, the Meeting determined that the residues from the trials are similar and is estimating a group maximum residue level for fruiting vegetables, Cucurbits based on the following scaled BSA residue data set (n = 23): < 0.01 (7), 0.013, 0.016, 0.019, 0.030, 0.032, 0.038, 0.040, 0.041, 0.045, 0.051, 0.114, 0.115, 0.120, 0.133, 0.137, and 0.149 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg for BSA on fruiting vegetables, Cucurbits; the HR is 0.16 mg/kg (from a single sample) and the STMR is 0.032 mg/kg.

Fruiting vegetables, other than Cucurbits

In chilli pepper, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 3) were: 0.040, 0.041, and 0.184 mg/kg.

Application rates for these trials ranged from 3.98 kg ai/ha to 4.10 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: 0.025, 0.025, 0.116 mg/kg.

In sweet pepper, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 8) were: 0.048, 0.055, 0.063, 0.070, 0.073, 0.082, 0.136, and 0.232 mg/kg.

Application rates for these trials ranged from 3.84 kg ai/ha to 410 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: 0.030, 0.034, 0.041, 0.045 (2), 0.050, 0.083, and 0.146 mg/kg.

In tomato, mean field trial residues of BSA (unscaled) from independent field trials treated 7 days prior to transplant (n = 20) were: < 0.01 (3), 0.013, 0.023, 0.026, 0.029, 0.034, 0.042, 0.072, 0.074, 0.078, 0.087, 0.088, 0.094, 0.173, 0.198, 0.231, 0.269, and 0.273 mg/kg.

Application rates for these trials ranged from 3.64 kg ai/ha to 4.12 kg ai/ha. Scaled to an application rate of 2.8 kg ai/ha, the residues of BSA are: < 0.01 (4), 0.014, 0.016, 0.018, 0.021, 0.026, 0.045, 0.046, 0.049, 0.054, 0.055, 0.061, 0.108, 0.132, 0.140, 0.168, and 0.169 mg/kg;

Noting that the GAP in the USA is for the fruiting vegetables crop group, which is equivalent to the Codex group fruiting vegetables, other than Cucurbits except sweet corn and mushroom, and that the residue data from sweet pepper, chilli pepper, and tomato are not significantly different by the Kruskal-Wallis test, the Meeting determined that the residues from the trials are similar and is estimating a group maximum residue level for fruiting vegetables, other than Cucurbits except sweet corn and mushroom based on the following scaled BSA residue data set: (n = 31): < 0.01 (4), 0.014, 0.016, 0.018, 0.021, 0.025, 0.025, 0.026, 0.030, 0.034, 0.041, 0.045 (3), 0.046, 0.049, 0.050, 0.054, 0.055, 0.061, 0.083, 0.108, 0.116, 0.132, 0.140, 0.146, 0.168, and 0.169 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg for BSA on fruiting vegetables, other than Cucurbits except sweet corn and mushroom; the HR is 0.17 mg/kg (from a single sample) and the STMR is 0.045 mg/kg.

Based on the maximum residue level of fruiting vegetables, other than Cucurbits except sweet corn and mushroom (0.3 mg/kg) and a dehydration factor of 7, the Meeting estimated a maximum residue level of 2 mg/kg for BSA in chilli pepper (dry), an HR of 1.2, and an STMR of 0.32.

Fate of residues during processing

High-temperature hydrolysis

The Meeting received a study investigating the high-temperature hydrolysis of fluensulfone, BSA, MeS, and TSA. Samples of aqueous buffered solutions were spiked with fluensulfone, BSA, MeS, or TSA at ca. 1 mg/L and put under conditions simulating pasteurisation (90 °C, pH 4, 20 min.); baking, brewing, boiling (100 °C, pH 5, 60 min); and sterilisation (120 °C, pH 6, 20 min.). Solutions were analysed by HPLC-MS/MS prior to and after processing. All four analytes were shown to be stable under all three conditions, with overall recoveries ranging from 87 to 118% of the initial concentration.

Residues after processing

The Meeting received data depicting the concentration/dilution of residues during processing of tomato into canned, juice, puree, paste, wet and dry pomace, peeled, and sun-dried processed commodities. Processed commodities were derived using simulated commercial practices. Of the three studies that were submitted, two were suitable for deriving processing factors (in one study, all residues were < 0.01 mg/kg). In those two studies, residues of fluensulfone were < 0.01 mg/kg in all samples and processing factors for the parent compound could not be derived.

Crop	Processed commodity	BSA processing factors	Best processing factor estimate (average)	STMR-P, mg/kg	HR-P, mg/kg
Tomato	RAC	--	--	STMR = 0.045	HR = 0.17
	Canned	0.33	0.33	0.015	0.056
	Dry pomace	6.6, 9.3, 17	11	0.50	1.9
	Peeled	0.33	0.33	0.015	0.056
	Sundried	1.67, 2	1.8	0.081	0.31
	Juice	0.67, 0.83	0.75	0.034	0.13
	Paste	1, 1, 3.54	1.8	0.081	0.31
	Puree	0.67, 1.38	1.0	0.045	0.17
	Wet pomace	0.66, 3, 4	2.6	0.12	0.44

Based on the maximum residue estimate for fruiting vegetables, other than Cucurbits except sweet corn and mushroom (0.3 mg/kg) and the processing factor of 1.8 for both dried tomato and tomato paste, the Meeting recommends a maximum residue level of 0.5 mg/kg for BSA in dried tomato and 0.5 mg/kg for BSA in tomato paste.

Residues in animal commodities

The Meeting has determined that residue definitions for compliance and dietary intake are not necessary for animal commodities and that residues in animal commodities are not expected.

RECOMMENDATIONS

Definition of the residue for compliance with the MRLs and dietary intake for plant commodities: *3,4,4-trifluorobut-3-ene-1-sulfonic acid (BSA)*. Note that for dietary intake, exposure estimates should be compared to the ADI and ARfD for fluensulfone, with no correction for molecular weight.

Definition of the residue for compliance with the MRLs and for dietary intake for animal commodities: *Not necessary.*

Commodity		Recommended MRL, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P, mg/kg
CCN	Name	New	Previous		
VC 0045	Fruiting vegetables, Cucurbits	0.3	–	0.032	0.16
VO 0050	Fruiting vegetables, other than Cucurbits except sweet corn and mushroom	0.3	–	0.045	0.17
HS 0444	Peppers chilli, dried	2.1	–	0.32	1.2
VW 0448	Tomato paste	0.5	–	0.081	0.31
DV 0448	Tomato, dried	0.5	–	0.081	0.31

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDIs) of BSA were calculated for the 17 GEMS/Food cluster diets using STMRs/STMR-Ps estimated by the current Meeting. The ADI for fluensulfone is 0–0.01 mg/kg bw. The calculated IEDIs for BSA were 0–3% of the maximum fluensulfone ADI. The Meeting concluded that the long-term intakes of residues of BSA, when fluensulfone is used in ways that have been considered by the JMPR, are unlikely to present a public health concern.

Short-term intake

The International Estimated Short-Term Intakes (IESTI) of BSA were calculated for food commodities and their processed commodities using HRs/HR-Ps or STMRs/STMR-Ps estimated by the current Meeting. The ARfD for fluensulfone is 0.3 mg/kg bw. The calculated maximum IESTI for BSA was 7% of the fluensulfone ARfD for all commodities. The Meeting concluded that the short-term intake of residues of BSA, when fluensulfone is used in ways that have been considered by the JMPR, is unlikely to present a public health concern.

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