SAFLUFENACIL (251)

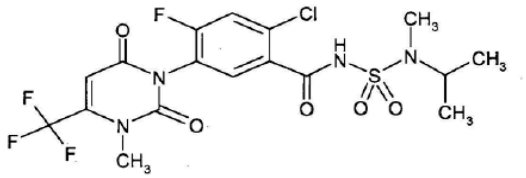
The first draft was prepared by Prof. Dr. Árpád Ambrus, Hungarian Food Safety Office, Budapest

EXPLANATION

Saflufenacil is a new herbicide from the uracil family acting as protoporphyrinogen IX oxidase inhibitor. It is a very effective contact and residual control of broad leaf weeds and is used in many crops in pre- and post-emergence, or desiccation Residue and analytical aspects of emamectin were considered for the first time by the present Meeting. The toxicological and residue evaluation was scheduled for the 2011 JMPR by the Forty-second Session of the 2010 CCPR (ALINORM 10/33/24).

Saflufenacil is used in a variety of crops, including corn, soya bean, sunflower, cotton, canola, citrus fruits, tree nuts, pome fruits, stone fruits, grapes, banana, mango, potato, legume vegetables, wheat, sorghum, rice, barley, coffee, and sugar cane.

IDENTITY

ISO common name	Saflufenacil
Other names	BAS 800 H
IUPAC name	N'-[2-chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)benzoyl]-N-isopropyl-N-methylsulfamide
Chemical Abstracts name	Benzamide, 2-chloro-5-[3,6-dihydro-3-methyl-2,6-dioxo-4-(trifluoromethyl)-1(2H)-pyrimidinyl]-4-fluoro-N-[[methylethyl)amino]sulfonyl]
CAS Number	372137-35-4
CIPAC Number	Not allocated
Molecular formula	$C_{17}H_{17}ClF_4N_4O_5S$
Molecular mass	500.92
Structural formula	

PHYSICAL AND CHEMICAL PROPERTIES

Pure active ingredient (purity 99.6 %)

Parameter	Property	Ref.
Description	white odourless powder	Yacoub R. 2006
Melting point, melting range	189.9 °C	
Boiling point	No boiling point could be detected, because the substance showed decomposition at approx. 230 °C.	
Temperature of decomposition or sublimation	It is stable under N_2 for up to 220 °C. The substance showed decomposition at approx. 230 °C.	
Density	1.595 g/mL at 20 °C	Kroehl T. 2005a
Vapour pressure	at 20 °C: 4.5×10^{-15} Pa; at 25 °C to 2.0×10^{-14} Pa.	
Henry's law constant	1.07×10^{-20} atm-m^3/mol	Paulick R.C. 2009a

Parameter	Property	Ref.
Water solubility at 25 °C,	pH 5: 0.0025 g/100 mL pH 4: 0.0014 g/100 mL pH 7: 0.21 g/100 mL At pH 9 the solubility could not be determined due to degradation.	Vanhook C.R. 2005
Dissociation in water	$pK_a = 4.41 \pm 0.025$.	Beery J. 2007
Octanol/water partition coefficient at 25 °C, (purity 95.4%)	log P_{ow} =2.6	Vanhook C. 2005b
		Ta C., Trollinger J. 2009
Solubility in organic solvents	Acetonitrile: 19.4 g/100 mL Dichloromethane: 24.4 g/100 mL N,N,dimethylformamide: 55.4 g/100 mL Acetone: 27.5 g/100 mL Ethyl acetate: 6.55 g/100 mL Tetrahydrofuran: 36.2 g/100 mL Butyrolactone: 35.0 g/100 mL Methanol: 2.98 g/100 mL Isopropyl alcohol: 0.25 g/100 mL Toluene: 0.23 g/100 mL Olive oil: 0.01 g/100 mL 1-octanol: < 0.01 g/100 mL n-heptane: < 0.005 g/100 mL	Vanhook C.R. 2007
Explosive properties (2.13)	An exothermic peak maximum of 236 °C with an energy release of approx. 131 J/g was observed with the pressure DSC.	Yacoub R. 2007
Surface Tension (2.14)	At a concentration of 23 mg/L in pure water a surface tension of 72 mN/m was determined.	Kroehl T. 2005b
Oxidizing properties (2.15)	Saflufenacil is considered a strong reducing agent and should not be mixed with or stored near strong oxidizers. Saflufenacil does not react with water or with reducing agents (iron fillings) and is non-hazardous when contact with monoammonium phosphate, a fire-extinguishing agent.	Yacoub R. 2007
pH (2.16)	At 25 °C 1% Saflufenacil in distilled water: 4.4	
Storage stability (2.17.1)	Saflufenacil was chemically and physically stable after two years of storage at the warehouse conditions and at 5 °C. There was no corrosive effect to the LDPE containers as a result of this long term storage.	Yacoub R. 2010

No data were available on effect of pH on octanol/water partition coefficient, and hydrolysis rate at pH 4, 7 and 9 under sterile and dark conditions, quantum yield of direct photo-transformation in sterile water using artificial light.

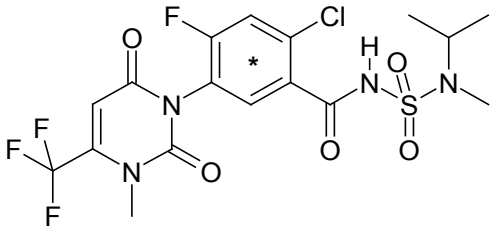
FORMULATIONS

Saflufenacil is applied as a solo or combination product

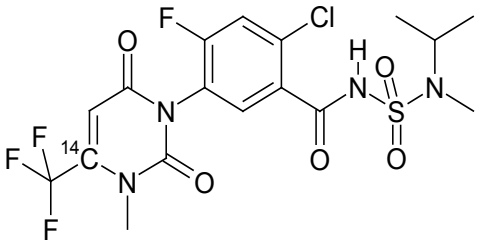
METABOLISM

The metabolism and distribution of saflufenacil in plants and animals were investigated using the active substance radio labelled in the phenyl ring and the uracil ring. The molecular structures and the positions of the labels are shown below:

Saflufenacil Phenyl-U-C^{14} label

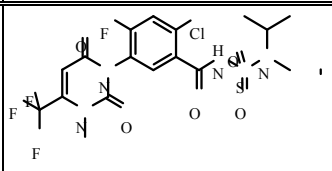
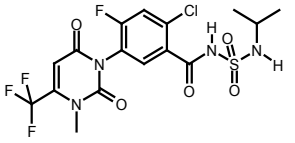
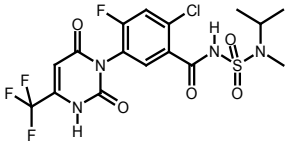
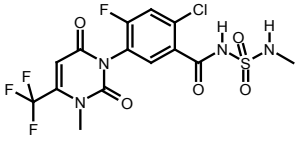
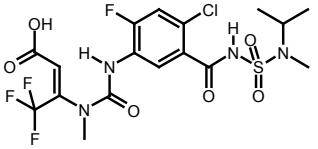
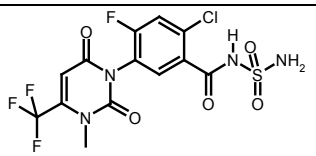


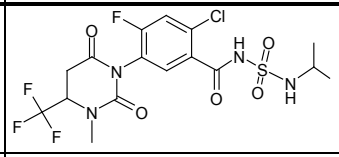
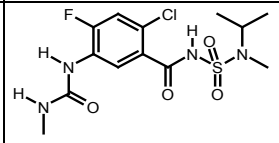
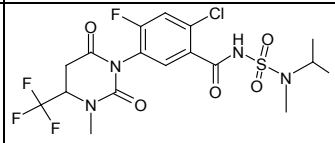
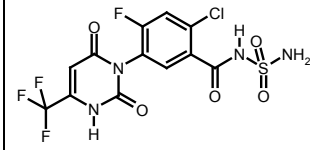
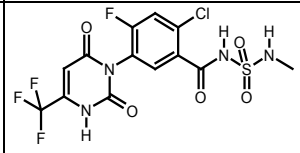
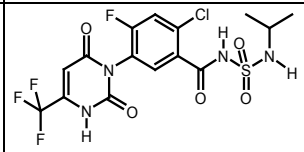
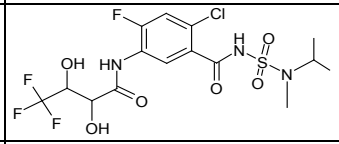
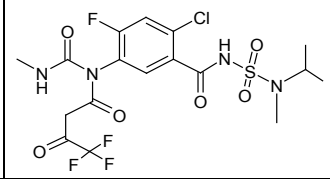
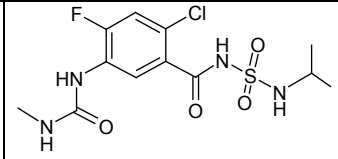
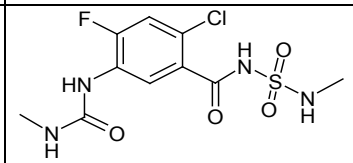
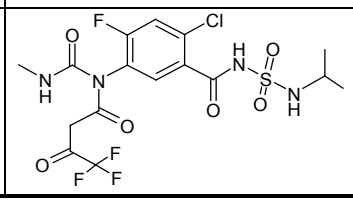
Saflufenacil Uracil-4-^{14}C Label

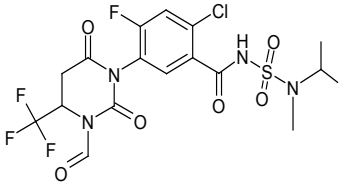
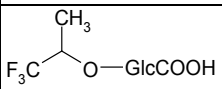
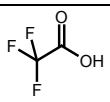
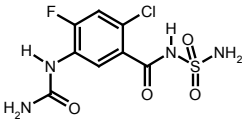
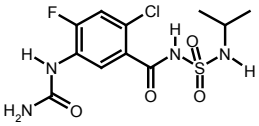
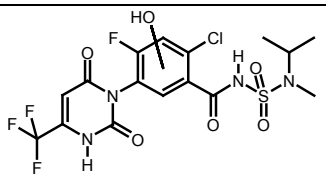
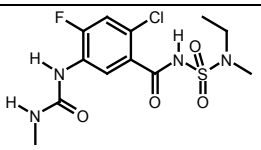


The code names and the structural formula of metabolites identified in metabolism studies are given in Table 2

Table 2 Summary of metabolites identified

Metabolite Code	Chemical Structure	MW	Rat	Goat	Hen	Soya bean	Corn	Tomato	Rot Crop
Saflufenacil Saflufenacil		500	x	Y	Y	Y	x	Y	x
M800H01		486	x	x	Y	x	x	x	x
M800H02		486	x	x	x	Y	x	x	x
M800H03		458	x	x	x	x	x	-	x
M800H04		518	x	Y	-	-	-	-	-
M800H05		444	x	x	x	x	x	-	Y

Metabolite Code	Chemical Structure	MW	Rat	Goat	Hen	Soya bean	Corn	Tomato	Rot Crop
M800H06		488	x	-	-	-	-	-	-
M800H07		380	x	x	-	-	-	Y	-
M800H08		502	x	-	-	-	-	-	-
M800H09		430	x	-	-	-	Y	x	x
M800H10		444	x	x	x	x	Y	x	x
M800H11		472	x	x	x	Y	x	Y	x
M800H16		479	x	-	-	-	-	-	-
M800H17		518	x	-	-	-	-	-	-
M800H18		366	x	-	-	-	-	-	-
M800H19		338	x	-	-	-	-	-	-
M800H20		504	x	-	-	-	-	-	-

Metabolite Code	Chemical Structure	MW	Rat	Goat	Hen	Soya bean	Corn	Tomato	Rot Crop
M800H21		514	x	-	-	-	-	-	-
M800H23		290	x	-	-	-	-	-	-
M800H29 (TFA)		114	-	-	-	Y	Y	Y	Y
M800H34		310	-	-	-	-	Y	-	-
M800H35		352	x	-	-	Y	-	x	Y
M800H36		502	-	-	-	x	-	-	-
M800H37		366	x	-	-	x	-	-	-

MW = molecular weight

Y represents compounds at quantities of more than 10% TRR and 0.01 mg/kg,

X represents compounds at quantities of less than 10% TRR and 0.01 mg/kg

"--" represents compound not found

The chemical names of the metabolites identified are:

Metabolite Code	Chemical Name
M800H01	N'-[2-chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)benzoyl]-N-isopropylsulfamide
M800H02	N'-[2-chloro-5-(2,6-dioxo-4-(trifluoromethyl)-3,6-dihydropyrimidin-1(2H)-yl)-4-fluorobenzoyl]-N-isopropyl-N-methylsulfamide
M800H03	N'-[2-chloro-5-(2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)-4-fluorobenzoyl]-N-isopropyl-N-methylsulfamide
M800H04	(2E)-3-{4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino) carbonyl]phenyl)amino]carbonyl(methylamino)}-4,4,4-trifluorobut-2-enoic acid
M800H05	N'-[2-chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)benzoyl]-sulfamide
M800H06	N'-[2-chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)tetrahydro-1(2H)-pyrimidinyl)benzoyl]-N-isopropylsulfamide
M800H07	N-{4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino)carbonyl]phenyl}-N'-methylurea
M800H08	N'-[2-chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)tetrahydro-1(2H)-pyrimidinyl)benzoyl]-N-isopropyl-N-methylsulfamide
M800H09	N'-[2-chloro-5-(2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)-4-fluorobenzoyl]-sulfamide
M800H10	N'-[2-chloro-5-(2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)-4-fluorobenzoyl]-N-methylsulfamide

Metabolite Code	Chemical Name
M800H11	N'-[2-chloro-5-(2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)-4-fluorobenzoyl]-N-isopropylsulfamide
M800H15	N-{4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino)carbonyl]phenyl}-4-4-4-trifluoro-3,3-dihydroxybutanamide
M800H16	N-{4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino)carbonyl]phenyl}-4,4,4-trifluoro-2,3-dihydroxybutanamide
M800H17	N-{4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino)carbonyl]phenyl}-N-(methylamino)carbonyl-4,4,4-trifluoro-3-oxo-butanamide
M800H18	N-{4-chloro-2-fluoro-5-[({[isopropylamino]sulfonyl}amino)carbonyl]phenyl}-N'-methylurea
M800H19	N-{4-chloro-2-fluoro-5-[({[methylamino]sulfonyl}amino)carbonyl]phenyl}-N'-methylurea
M800H20	N-{4-chloro-2-fluoro-5-[({[isopropylamino]sulfonyl}amino)carbonyl]phenyl}-N-(methylamino)carbonyl-4,4,4-trifluoro-3-oxo-butanamide
M800H21	N'-[2-chloro-4-fluoro-5-(3-formyl-2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)benzoyl]-N-isopropyl-N-methylsulfamide
M800H22	3-[({4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino)carbonyl]anilino}carbonyl)(methyl)amino]-4,4,4-trifluorobutanoic acid
M800H23	1,1,1-trifluoro-2-propanol-glucoside
M800H26	N-Methyl-2,2,2-trifluoroacetamide
M800H29 (TFA)	Trifuoroacetic acid (or its Na salt)
M800H31	3-[carboxy(methyl)amino]-4,4,4-trifluorobutanoic acid
M800H33	Trifluoroacetone
M800H34	N-{4-chloro-2-fluoro-5-[([aminosulfonyl]amino)carbonyl]phenyl}-N'-methylurea
M800H35	N-[4-chloro-2-fluoro-5-({[(isopropylamino)sulfonyl]amino} carbonyl)phenyl]urea
M800H36	Not IUPAC classified due to ambiguous hydroxyl position
M800H37	N-{4-chloro-2-fluoro-5-[({[ethyl(methyl)amino]sulfonyl}amino)carbonyl]phenyl}-N'-methylurea

Animal metabolism

Animal metabolism studies were conducted with saflufenacil on lactating goat and laying hen, and as part of toxicological studies the metabolism was also examined in rats.

Rats

Several metabolism studies were conducted on laboratory animals. The parent compound was metabolized by three major transformation steps, which are demethylation of the uracil ring system, degradation of the N-methyl-N-isopropyl group to NH_2 and cleavage of the uracil ring, forming a phenyl-N-methyl urea group.

The predominant compounds were the metabolites M800H01, M800H03 and M800H07, and the parent compound for male and female rats. In addition, the metabolite M800H05 was a major metabolite for male rats. Metabolites M800H16, M800H17, M800H18, M800M19 and M800M20 were present only in bile. Details are given in the toxicological evaluation.

Lactating goats

The studies were conducted with 2-year old goats of 37.8 kg and 36.9 kg which were fed with 1.5 kg hay per day (Fabian E, Landsiedel R, 2006). The animals were kept in air-conditioned individual metabolism cages. [Phenyl-U-^{14}C]-saflufenacil and [uracil-4-^{14}C] saflufenacil were administered to the goats via gavage on 8 consecutive days.

The animal dosed with [phenyl-U-^{14}C] saflufenacil received a dose of 18.4 mg/day, equivalent to 13.9 ppm feed. The animal dosed with [uracil-4-^{14}C] saflufenacil received a dose of 17.8 mg/day, equivalent to 13.4 ppm feed.

Production of urine and faeces was recorded once daily, production of milk twice daily (in the afternoon and in the morning before application). Animals were sacrificed within 24 h after the last dose. Liver, kidney, blood, adipose tissue, muscle, GI tract with contents, and bile were collected. The

total recovery of radioactivity was found to be 94.28% in the phenyl-label group and 91.72% in the uracil-label group.

Milk samples were pooled throughout day 1–8, whereas samples of urine and homogenized faeces were pooled from Day 2-8 for both labels. The pooled samples of milk, urine and faeces and tissue homogenates of liver, kidney, muscle and fat were also analysed for total radioactive residues.

Milk, liver and faeces were extracted (Hafemann C., Glaessgen E.W., 2007) three times with acetonitrile. Kidney was extracted three times with acetonitrile, and the acetonitrile residues were further extracted three times with water. Muscle and fat samples were initially extracted three times with acetonitrile followed (in most cases) by a single extraction with isohexane.

In the cases of liver and kidney (uracil label), the supernatants of the three extraction steps with acetonitrile were separately collected in volumetric cylinders, adjusted to defined volumes, and aliquots were radioassayed (LSC). The evaluation of the individual extraction steps showed that no fourth extraction step with acetonitrile was necessary for exhaustive extraction.

For metabolic profiling, homogenized subsamples of the tissues and organs and subsamples of the pooled milk samples were generally extracted with acetonitrile. A further extraction step was added using water in the case of kidney, or isohexane in some work ups of muscle and fat. The extractable radioactive residues (ERR) for the phenyl and the uracil label ranged from 81% to 108% TRR for all edible matrices. The non-extractable residues accounted for 4 and 14% TRR in milk, 3 and 2% TRR in liver, 4 and 3% TRR in kidney, 17 and 1% TRR in muscle, and 12 and 9% TRR in fat, for the phenyl and the uracil label, respectively.

During the course of work-ups, the extracts were stored in a refrigerator overnight, or for longer periods they were stored in a freezer at -18 °C or below.

All samples were extracted and analysed within approximately four months after sampling. The storage stability of residues was not tested.

The total radioactive residues measured in milk, tissues and excreta are summarized in Table 3.

Table 3 Total saflufenacil radioactive residues in milk, tissues and excreta

Matrix	Collection Timing [day]	Phenyl-U-^{14}C-label		Uracil-4-^{14}C-label	
		% of dose	mg/kg	% of dose	mg/kg
Total urine		62.04		45.57	
Total faeces		28.48		41.90	
Excreta		90.52		87.47	
Milk	1 p.m.	0.002	0.007	0.002	0.006
	1 a.m.	0.002	0.005	0.004	0.007
	2 p.m.	0.005	0.019	0.006	0.020
	2 a.m.	0.002	0.005	0.005	0.011
	3 p.m.	0.002	0.011	0.007	0.022
	3 a.m.	0.003	0.005	0.007	0.013
	4 p.m.	0.003	0.015	0.006	0.023
	4 a.m.	0.002	0.004	0.008	0.013
	5 p.m.	0.003	0.015	0.005	0.022
	5 a.m.	0.002	0.004	0.008	0.014
	6 p.m.	0.003	0.014	0.005	0.022
	6 a.m.	0.002	0.004	0.009	0.016
	7 p.m.	0.003	0.016	0.005	0.024
	7 a.m.	0.001	0.004	0.006	0.013
	8 p.m.	0.004	0.013	0.006	0.023
	8 a.m.	0.001	0.004	0.006	0.011
Total milk		0.040		0.100	
Muscle	9	0.020	0.008	0.024	0.011
Fat		0.001	0.010	0.001	0.017
Kidney		0.009	0.130	0.012	0.171
Liver		0.366	0.962	1.532	3.832
Stomach		0.024	0.009	0.061	0.024
Gut		0.064	0.340	0.149	0.077

Matrix	Collection Timing [day]	Phenyl-U-^{14}C-label		Uracil-4-^{14}C-label	
		% of dose	mg/kg	% of dose	mg/kg
Stomach + gut contents		0.771	0.071	0.520	0.033
Blood		0.007	0.013	0.009	0.024
Bile		0.006	0.634	0.012	1.461
Sum of tissues		1.268		2.321	
Sum of Administered Dose (%)		91.828		89.891	

Saflufenacil was transformed to a number of metabolites after administration to the goats. However, unchanged parent compound was found as the predominant compound in almost all goat matrices. The metabolites identified and their concentrations are shown in Tables 4 and 5.

Table 4: Summary of characterization and identification of radioactive residues in goat matrices following application of [Phenyl-U-^{14}C]-Saflufenacil

Table 4 Summary of characterization and identification of radioactive residues in goat matrices following application of [Phenyl-U-^{14}C]-saflufenacil

Compound	Muscle		Fat		Kidney		Liver		Milk [a]	
	TRR = 0.008 mg/kg		TRR = 0.010 mg/kg		TRR = 0.130 mg/kg		TRR = 0.962 mg/kg		TRR = 0.006 mg/kg	
	%TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	%TRR	mg/kg
Saflufenacil	44.2	0.004	44.1	0.004	73.8	0.096	80.2	0.772	47.0	0.003
M800H01	–	–	–	–	2.2	0.003	1.2	0.011	9.1	0.001
M800H03	–	–	–	–	–	–	–	–	7.8	< 0.0005
M800H04	–	–	–	–	12.9	0.017	13.2	0.127	–	–
M800H10	37.5	0.003	14.7	0.001	1.7	0.002	–	–	39.1	0.002
Total identified	81.7	0.007	58.8	0.006	90.6	0.118	94.7	0.911	103.0	0.006
Total characterized [b]	0.3	< 0.0005	26.8	0.005	4.5	0.008	1.5	0.015	2.7	< 0.0005
Total extractable	82.0	0.007	82.4	0.008	96.4	0.126	96.2	0.925	105.7	0.006
Unextractable (PES) [c]	16.5	0.001	12.0	0.001	3.5	0.006	2.7	0.026	4.0	0.0002
Accountability [d]	98.4		94.5		100.1		98.9		109.7	

[a] Calculated for Day 1-8 in the case of the pooled milk samples. TRR values were calculated assuming a density of 1.0 g/mL

[b] Characterised but not identified substances

[c] Residues remaining after exhaustive extractions

[d] Accountability = (Total extractable + Total unextractable)/(TRRs from combustion analysis × 100)

Table 5 Summary of characterization and identification of radioactive residues in goat matrices following application of [Uracil-U-^{14}C] saflufenacil

Compound	Muscle		Fat		Kidney		Liver		Milk [a]	
	TRR = 0.011 mg/kg		TRR = 0.017 mg/kg		TRR = 0.171 mg/kg		TRR = 3.832 mg/kg		TRR = 0.012 mg/kg	
	%TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	%TRR	mg/kg
Saflufenacil	56.7	0.006	65.1	0.011	71.3	0.122	75.7	2.900	25.4	0.003
M800H01	–	–	–	–	5.2	0.009	1.4	0.054	6.7	0.001
M800H03	–	–	–	–	3.7	0.006	–	–	8.8	0.001
M800H04	–	–	–	–	10.0	0.017	14.2	0.543	–	–
M800H10	49.6	0.005	15.1	0.003	2.5	0.004	–	–	39.9	0.005
Total identified	106.3	0.012	80.2	0.014	92.8	0.159	91.3	3.497	80.9	0.009
Total characterized [b]	1.4	< 0.0005	26.8	0.005	4.5	0.008	1.9	0.073	–	–
Total extractable	107.7	0.012	107.0	0.018	97.3	0.167	93.2	3.570	80.9	0.009
Unextractable (PES) [c]	1.0	0.0001	9.2	0.002	3.5	0.006	2.4	0.094	14.1	0.002
Accountability [d]	108.7		116.2		100.8		95.6		95.0	

[a] Calculated for Day 1-8 in the case of the pooled milk samples. TRR values were calculated assuming a density of 1.0 g/mL

[b] Characterised but not identified substances

[c] Residues remaining after exhaustive extractions

[d] Accountability = (Total extractable + Total unextractable)/(TRRs from combustion analysis × 100)

In addition to the parent compound M800H01 was the major metabolite in urine and faeces, other metabolites M800H02, M800H03, M800H05 (only in urine), M800H11 were identified in varying proportion.

Saflufenacil was transformed to a number of metabolites after administration to the goats. All relevant metabolites were identified and a comprehensive metabolic pathway was elucidated (Figure 1). The accountability in all matrices was high (> 95%).

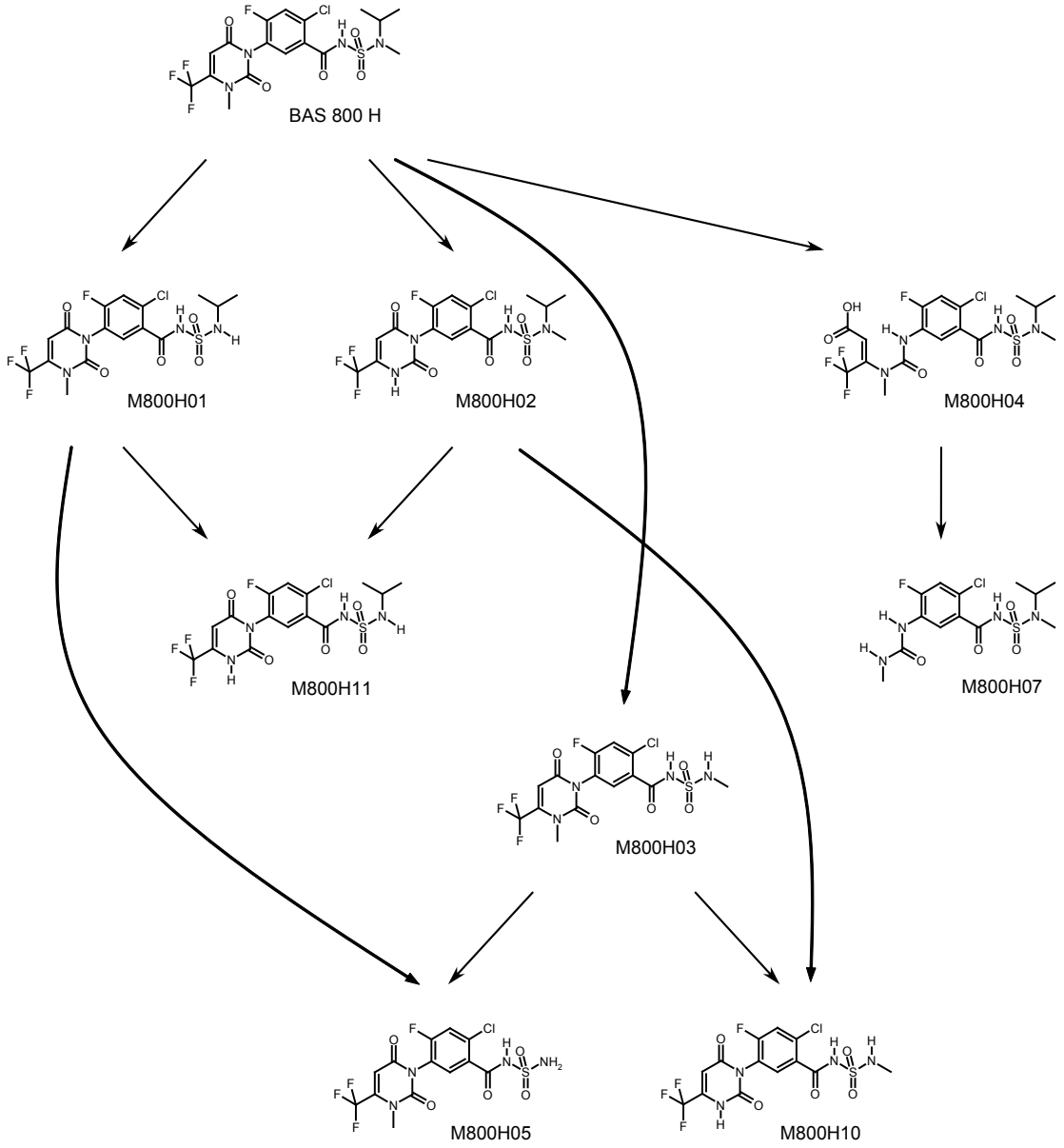


Figure 1 Propose metabolic pathway of Saflufenacil in goat

Table 6 Summary of identified components in goat matrices: phenyl label upper raw and uracil label lower row

Metabolite Code	Milk [mg/kg] (% TRR)	Liver [mg/kg] (% TRR)	Kidney [mg/kg] (% TRR)	Muscle [mg/kg] (% TRR)	Fat [mg/kg] (% TRR)	Urine [mg/kg] (% TRR)	Faeces [mg/kg] (% TRR)
Saflufenacil	0.003 (47.0)	0.772 (80.2)	0.096 (73.8)	0.004 (44.2)	0.004 (44.1)	8.119 (91.8)	0.432 (41.5)

Metabolite Code	Milk [mg/kg] (% TRR)	Liver [mg/kg] (% TRR)	Kidney [mg/kg] (% TRR)	Muscle [mg/kg] (% TRR)	Fat [mg/kg] (% TRR)	Urine [mg/kg] (% TRR)	Faeces [mg/kg] (% TRR)
	0.003 (25.4)	2.900 (75.7)	0.122 (71.3)	0.006 (56.7)	0.011 (65.1)	7.010 (69.4)	0.460 (33.8)
M800H01	0.001 (9.1)	0.011 (1.2)	0.003 (2.2)	nd nd	0.463 (5.2)	0.316	(30.3)
	0.001 (6.7)	0.054 (1.4)	0.009 (5.2)	nd	nd	0.893 (8.8)	0.538 (39.5)
M800H02	nd	nd	nd	nd	nd	nd	nd
	nd	nd	nd	nd	nd	nq	0.070 (5.1)
M800H03	< 0.0005 (7.8)	nd nd	nd nd	0.262	(3.0)	0.077	(7.4)
	0.001 (8.8)	nd	0.006 (3.7)	nd	nd	1.027 (10.2)	0.150 (11.0)
M800H04	nd 0.127	(13.2) 0.017	(12.9)	nd	nd	nd	nd
	nd	0.543 (14.2)	0.017 (10.0)	nd	nd	nd	nd
M800H05	nd	nd	nd	nd	nd	nd	nd
	nd	nd	nd	nd	nd	0.184 (1.8)	nd
M800H07	nd	nd	nd	nd	nd	0.065	(6.2)
	not detected with the Uracil Label						
M800H10	0.002 (39.1)	nd 0.002	(1.7) 0.003	(37.5) 0.001	(14.7)	nd	nd
	0.005 (39.9)	nd	0.004 (2.5)	0.005 (49.6)	0.003 (15.1)	nd	nd
M800H11	nd	nd	nd	nd	nd	nd	n. q.
	nd	nd	nd	nd	nd	0.268 (2.7)	0.127 (9.3)

nd = not detected / identified

nq = not quantitated by radio-HPLC, obtained from LC-MS/MS

Laying hens

Phenyl-U-^{14}C saflufenacil or uracil-^{14}C saflufenacil was administered orally by gavage once a day to two groups of eight Brown Leghorn laying hens for 10 consecutive days at a nominal rate of 12 ppm feed. The feed consumption was 132.5 g/day. The animals were sacrificed 23 hours after the last dose (Fabian E., Landsiedel R. 2007, Rabe U., Glaessgen W.E. 2007).

The eggs were collected in the afternoon after administration and in the morning before the administration (except for weekend when records on egg production were only made once per day). Excreta were collected in time intervals of 24 hours. The radioactivity was determined in liver, adipose tissue, blood, muscles (leg and chest muscles), gastrointestinal tract (skin and contents). All tissues/organs were processed as one pool sample of 8 animals per label. All samples were extracted and analysed within approximately four months after sampling. Stability of residues was not investigated.

Subsamples of the pooled eggs, muscle and excreta samples (Day 1-10, both labels; 50 g each) were extracted three times with 150–250mL acetonitrile.

Subsamples of the liver homogenates were extracted three times with 250 mL acetonitrile. The residual material was dried, homogenized and extracted twice with 240 mL water. Aliquots of the combined supernatants were radioassayed. The residues after acetonitrile and water extraction were subject to pronase incubation, the supernatants were centrifuged and radioassayed. The solid final residues were freeze-dried, weighed and homogenized.

Subsamples of the fat homogenates were extracted with 150 mL acetonitrile. The extraction mixtures were centrifuged and the supernatants were filtered through paper filters into volumetric flasks. This procedure was repeated twice. The residues were extracted three times with 150 mL isohexane, the filtered supernatants were combined and its aliquots were radioassayed. The remaining acetonitrile extracts were concentrated and radioassayed. The residues after extraction with acetonitrile and isohexane were freeze-dried, weighed and homogenized. Five representative aliquots were combusted for the determination of the radioactive residues.

Radioactivity in homogenized samples was determined by combustion analysis with liquid scintillation counting. For metabolic profiling, homogenized subsamples of the tissues and organs and subsamples of the pooled excreta and egg samples were generally extracted with acetonitrile. A further extraction step was added using water in the case of liver, or isohexane for fat. Sample extracts were subjected to Reversed-Phase-HPLC with UV-VIS and radioactivity detection. Identification of metabolites was accomplished using ESI-MS or ECI-MS/MS coupled to an HPLC system.

The results of the analyses are shown in the following tables.

Table 7 Total radioactive residues (TRRs) in eggs, tissue

Matrix	Collection Timing [day]	Phenyl-U-^{14}C-label		Uracil-4-^{14}C-label	
		% of dose	mg/kg	% of dose	mg/kg
Cage wash	10	2.93		4.86	
Eggs	1	0.001	0.003	0.002	0.004
	2	0.002	0.008	0.004	0.012
	3	0.003	0.008	0.004	0.011
	4	0.003	0.010	0.005	0.015
	5	0.004	0.011	0.006	0.017
	6	0.004	0.012	0.005	0.018
	7	0.003	0.010	0.005	0.017
	8	0.004	0.012	0.006	0.017
	9	0.004	0.011	0.005	0.017
	10	0.003	0.010	0.005	0.016
	Sum of eggs	0.029		0.046	
Blood	10	0.01	0.043	0.01	0.040
Liver		0.02	0.062	0.02	0.060
GI-Tract (skin)		0.43	0.255	0.54	0.324
GI-Tract (contents)		0.19	0.625	0.08	0.284
Musle		0.03	0.011	0.02	0.011
Adipose tissue		0.00	0.011	0.00	0.011
Sum of tissues		0.68		0.67	
Total sum:		88.76		83.67	

Table 8 Extractability of Residues of saflufenacil in Hen Matrices (Phenyl Label and Uracil Label)

Matrix	TRR $_{co}$ [a] [mg/kg]	ERR [b] [mg/kg]	[% TRR]	PES [c] [mg/kg]	[% TRR]	TRR$_{cal}$ [d] [mg/kg]	Recovery [e] [%]
(Phenyl Label)							
Excreta	4.586	4.690	98.9	0.051	1.1	4.742	103.4
Egg	0.011	0.011	94.8	0.001	5.2	0.012	101.7
Liver [f]	0.062	0.057	95.2	0.003	5.0	0.060	97.8
Muscle	0.011	0.010	93.4	0.001	6.6	0.010	94.6
Fat [g]	0.011	0.008	94.7	0.0004	5.3	0.008	78.4
(Uracil Label)							
Excreta	3.825	3.970	98.7	0.052	1.3	4.022	105.2
Egg	0.016	0.015	87.7	0.002	12.3	0.018	112.1
Liver [h]	0.060	0.056	91.6	0.005	8.2	0.061	101.9
Muscle	0.011	0.011	81.9	0.003	18.1	0.014	128.0
Fat [i]	0.011	0.009	93.7	0.001	6.3	0.010	88.2

[a] TRR$_{co}$TRR combusted: Total Radioactive Residue, determined by direct combustion

[b] ERR Extractable Radioactive Residue; % TRR values refer to TRR calculated

[c] PES Post-Extraction Solid (residue after solvent extraction); % TRR values refer to TRR calculated

[d] TRR_{cal} TRR calculated: Total Radioactive Residue, calculated as sum of ERR and PES

[e] Recovery Calculated as (ERR [mg/kg] + PES [mg/kg]) • 100 / TRR_{co} [mg/kg]

[f] In the case of liver (Phenyl Label), 0.051 mg/kg corresponding to 83.9% TRR were extracted with acetonitrile, and additional 0.007 mg/kg or 11.3% TRR were extracted with water. The sum of acetonitrile and water extracts 0.057 mg/kg is reported as ERR. The sum of the acetonitrile extract and the acetonitrile residue (0.010 mg/kg or 16.1% TRR) was referred to as TRR calculated;
The residue after extraction with acetonitrile and water ("PES") was calculated as the sum of the pronase supernatant and the pronase residue.

[g] In the case of fat (Phenyl Label), 0.008 mg/kg corresponding to 90.4% TRR were extracted with acetonitrile, and additional 0.0004 mg/kg or 4.3% TRR were extracted with isohexane

[h] In the case of liver (Uracil Label), 0.048 mg/kg corresponding to 78.5% TRR were extracted with acetonitrile, and additional 0.008 mg/kg or 13.1% TRR were extracted with water; The sum of the acetonitrile extract and the acetonitrile residue (0.013 mg/kg or 21.5% TRR) was referred to as TRR calculated;
The residue after extraction with acetonitrile and water ("PES") was calculated as the sum of the pronase supernatant and the pronase residue

[i] In the case of fat (Uracil Label), 0.008 mg/kg corresponding to 81.0% TRR were extracted with acetonitrile, and additional 0.001 mg/kg or 12.7% TRR were extracted with isohexane

Table 9 Summary of characterization and identification of radioactive residues in hen matrices following application of [Phenyl-U-^{14}C] saflufenacil

Compound	Excreta		Muscle		Fat		Liver		Eggs	
	TRR = 4.586 mg/kg		TRR = 0.011 mg/kg		TRR = 0.011 mg/kg		TRR = 0.062 mg/kg		TRR = 0.011 mg/kg	
	%TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	%TRR	mg/kg
Saflufenacil	53.2	2.525	54.7	0.006	26.1	0.002	47.4	0.029	20.8	0.002
M800H01	20.6	0.979	3.2	< 0.0005	1.7	< 0.0005	24.0	0.014	–	–
M800H02 [a]	6.7	0.316	1.0	< 0.0005	–	–	3.2	0.002	–	–
M800H03	3.9	0.186	1.2	< 0.0005	–	–	2.0	0.001	–	–
M800H05	7.6	0.362	1.0	< 0.0005	2.3	< 0.0005	2.2	0.001	–	–
M800H10	1.6	0.074	23.1	0.002	15.8	0.001	7.6	0.005	67.6	0.008
M800H11	3.9	0.185	1.0	< 0.0005	–	–	2.6	0.002	–	–
Total identified	97.6	4.626	85.2	0.009	46.0	0.004	89.0	0.054	88.4	0.010
Total characterized [b]	1.4	0.064	3.3	< 0.0005	48.0	0.004	6.5	0.004	9.2	0.001
Total ident.+charact.	98.9	4.690	88.5	0.009	94.0	0.008	95.5	0.058	97.6	0.011
Total extractable	98.9	4.690	93.4	0.010	94.7	0.008	95.2	0.057	94.8	0.011
Unextractable (PES) [c]	1.1	0.051	6.6	0.001	5.3	0.0004	5.0	0.003	5.2	0.001
Accountability [d]	103.4		94.6		78.4		97.8		101.7	

[a] The excreta extract contained metabolite M800H02 (ident. by LC-MS/MS) and potentially in addition the metabolite M800H06 (not separated by HPLC) -

[b] Characterised but not identified

[c] Residues remaining after exhaustive extractions.

[d] Accountability = (Total extractable + Total unextractable)/(TRRs from combustion analysis) × 100)

Table 10 Summary of characterization and identification of radioactive residues in hen matrices following application of [Uracil-U-^{14}C] saflufenacil

Compound	Excreta		Muscle		Fat		Liver		Eggs	
	TRR = 3.825 mg/kg		TRR = 0.011 mg/kg		TRR = 0.011 mg/kg		TRR = 0.060 mg/kg		TRR = 0.016 mg/kg	
	%TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	%TRR	mg/kg
Saflufenacil	50.4	2.027	38.2	0.005	24.0	0.002	47.0	0.029	9.9	0.002
M800H01	22.1	0.888	2.4	< 0.0005	1.8	< 0.0005	20.9	0.013	0.8	< 0.0005
M800H02 [a]	7.6	0.305	0.3	< 0.0005	2.4	< 0.0005	1.9	0.001	–	–
M800H03	3.8	0.153	1.3	< 0.0005	–	–	2.4	0.001	–	–
M800H05	7.2	0.289	–	–	0.7	< 0.0005	1.2	0.001	1.3	< 0.0005
M800H10	0.9	0.037	22.0	0.003	12.7	0.001	7.3	0.004	51.6	0.009
M800H11	4.4	0.177	–	–	1.9	< 0.0005	1.4	0.001	2.2	< 0.0005
Total identified	96.4	3.876	64.2	0.009	43.4	0.004	82.1	0.050	65.7	0.012
Total characterized [b]	2.3	0.094	18.3	0.003	49.3	0.005	8.3	0.005	17.5	0.003

Compound	Excreta		Muscle		Fat		Liver		Eggs	
	TRR = 3.825 mg/kg		TRR = 0.011 mg/kg		TRR = 0.011 mg/kg		TRR = 0.060 mg/kg		TRR = 0.016 mg/kg	
	%TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	%TRR	mg/kg
Total ident.+charact.	98.7	3.970	82.6	0.012	92.7	0.009	90.5	0.055	83.3	0.015
Total extractable	98.7	3.970	81.9	0.011	93.7	0.009	90.5	0.055	87.7	0.009
Unextractable (PES) [c]	1.3	0.052	18.1	0.003	6.3	0.001	8.2	0.005	12.3	0.002
Accountability [d]	105.2		128.0		88.2		101.9		112.1	

[a] The excreta extract contained metabolite M800H02 (ident. by LC-MS/MS) and potentially in addition the metabolite M800H06 (not separated by HPLC) -

[b] Characterised but not identified

[c] Residues remaining after exhaustive extractions.

[d] Accountability = (Total extractable + Total unextractable)/(TRRs from combustion analysis) × 100)

The parent compound was metabolized by different dealkylation steps occurring at two sites of the molecule: loss of the N-methyl group of the N-isopropyl-N-methylsulfamide side chain formed metabolite M800H01, while loss of methyl from the uracil ring formed metabolite M800H02.

Loss of both methyl groups resulted in the formation of metabolite M800H11. Elimination of the N-isopropyl group from the sulfamide chain yielded metabolite M800H03 and subsequent loss of the uracil methyl produced M800H10.

Loss of the sulfamide methyl group from metabolite M800H03 yielded metabolite M800H05. The metabolites M800H05 and M800H10 could also be formed via elimination of the isopropyl group from the sulfamide chain of M800H01 or M800H02, respectively. Metabolite M800H06 was possibly formed in excreta only under reductive conditions by hydrogenation of M800H01.

The proposed metabolic pathway is depicted in Figure 2.

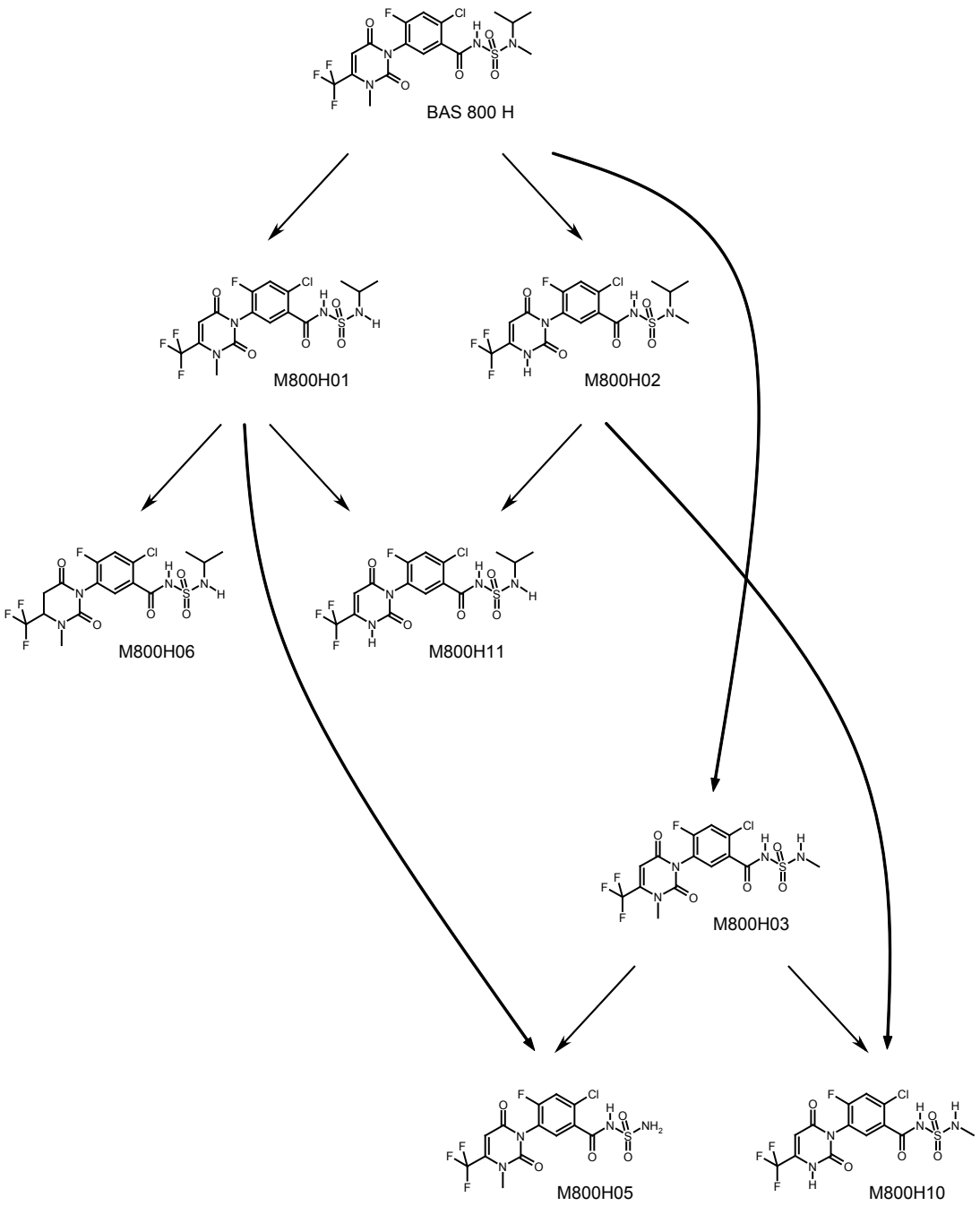


Figure 2 Proposed Metabolic Pathway of Saflufenacil in Laying Hen

The concentration of metabolites identified and determined in various matrices are shown in Table 12.

Table 11 Summary of identified components in hen matrices (phenyl label upper row, uracil label lower raw)

Metabolite Code	Excreta [mg/kg] (% TRR)	Egg [mg/kg] (% TRR)	Liver [mg/kg] ([% TRR])	Muscle [mg/kg] (% TRR)	Fat [mg/kg] (% TRR)
Saflufenacil	2.525 (53.2)	0.002 (20.8)	0.029 (47.4)	0.006 (54.7)	0.002 (26.1)
	2.027 (50.4)	0.002 (9.9)	0.029 (47.0)	0.005 (38.2)	0.002 (24.0)
M800H01	0.979 (20.6)	nd 0.014	(24.0) < 0.0005	(3.2) < 0.0005	(1.7)

Metabolite Code	Excreta [mg/kg] (% TRR)	Egg [mg/kg] (% TRR)	Liver [mg/kg] ([% TRR])	Muscle [mg/kg] (% TRR)	Fat [mg/kg] (% TRR)
	0.888 (22.1)	< 0.0005 (0.8)	0.013 (20.9)	< 0.0005 (2.4)	< 0.0005 (1.8)
M800H02	0.316 (6.7) [a]	nd 0.002	(3.2) < 0.0005	(1.0)	nd
	0.305 (7.6) [1)]	nd	0.001 (1.9)	< 0.0005 (0.3)	< 0.0005 (2.4)
M800H03	0.186 (3.9)	nd 0.001	(2.0) < 0.0005	(1.2)	nd
	0.153 (3.8)	nd	0.001 (2.4)	< 0.0005 (1.3)	nd
M800H05	0.362 (7.6)	nd 0.001	(2.2) < 0.0005	(1.0) < 0.0005	(2.3)
	0.289 (7.2)	< 0.0005 (1.3)	0.001 (1.2)	nd	< 0.0005 (0.7)
M800H07	nd	nd	nd	nd	nd
	nd	nd	nd	nd	nd
M800H10	0.074 (1.6)	0.008 (67.6)	0.005 (7.6)	0.002 (23.1)	0.001 (15.8)
	0.037 (0.9)	0.009 (51.6)	0.004 (7.3)	0.003 (22.0)	0.001 (12.7)
M800H11	0.185 (3.9)	nd	0.002 (2.6)	< 0.0005 (1.0)	nd
	0.177 (4.4)	< 0.0005 (2.2)	0.001 (1.4)	nd	< 0.0005 (1.9)

[a] The excreta extract contained the metabolite M800H02 (identified by LC-MS/MS) and potentially in addition the metabolite M800H06 (not separated by HPLC)

nd = not detected / identified

Plant metabolism

Metabolism studies were conducted with phenyl and uracil labelled Saflufenacil and reported on corn soya beans and tomato.

Corn

The metabolism of saflufenacil was investigated in corn after one single spray application of the test substance in an EC formulation at a nominal application rate of 200 g ai/ha directly on the bare soil after sowing (pre-emergence treatment) (Hoefs R. *et al*. 2007). Corn plants were grown in climatic chambers (phytotrons) simulating the weather conditions of a typical corn-growing area in the USA.

Forage samples were taken 42 and 101/102 days after treatment (DAT) (at the growth stages BBCH 18 and 85). Corn husks, cob, grain and straw (stover) were harvested at 133 days after treatment (BBCH 89).

Prior to extraction and determination of the total radioactive residues (TRR), subsamples of corn forage, husks, cob, grain or straw (stover) were frozen with liquid nitrogen and homogenized using a mill. Subsamples were stored at -18 °C or below. Small aliquots were combusted for the determination of the total radioactive residues. Weighed subsamples of homogenized plant material were extracted three times at ambient temperature with sufficient volumes of methanol. The methanol extractions were followed by two extraction steps with water. Aliquots of the extracts were measured by LSC. The results of the methanol extracts and the water extracts were summarized and referred to as total extractable radioactive residues (ERR). The residue after solvent extraction of each sample was freeze-dried or dried in a fume hood, homogenized using a mill or mortar, and aliquots were combusted for the determination of the residual radioactive residue (post extraction solids) (RRR). The total radioactive residues (TRR) were the result of combustion analyses or the calculated sum of

ERR and RRR values (the data are shown as TRR combusted and TRR calculated in Table 13. All calculations throughout the study (including tables) were based on TRR calculated.

Prior to HPLC analyses, aliquots of the extracts were concentrated using a rotary evaporator, dissolved in a mixture of HPLC eluent and Triton X100, and centrifuged. In some cases, an additional clean-up of the methanol extract using a C-18 Mega Bond Elute column was performed. Isolation of metabolites was achieved by HPLC fractionation of methanol extracts from corn stover (phenyl label, several fractionation steps) and corn husks (uracil label).

The residual radioactive residues after solvent extraction of corn husks, cob, grain or straw (stover) were subjected to sequential solubilisation procedures. Subsamples of the residual radioactive residues were treated twice with a 1% ammonia solution under continuous shaking. After centrifugation the combined supernatants were analysed by LSC. The residues were dried, and aliquots were combusted for the determination of the radioactive residues. The remaining dried residues were subjected to the next solubilisation procedure. One to several enzymatic treatments were sequentially performed using Macerozyme R-10, Tyrosinase/Laccase, and α-Amylase/β-Amylase/Amyloglucosidase, each in an appropriate aqueous buffer.

Aliquots of homogenized solid plant samples were combusted by means of an automatic sample oxidizer. The $^{14}CO_2$ evolved during combustion was trapped by an absorption liquid, and the collected radioactivity was measured by liquid scintillation counting (LSC). In order to determine the background radioactivity, aliquots of untreated corn matrices were combusted under the same conditions. The limits of quantification were determined at 0.00007 to 0.00009 mg/kg for corn forage and 0.00085 mg/kg to 0.00111 mg/kg for corn grain. The radioactive residues in liquid samples were also determined by LSC.

The nature of the radioactive residues in the methanol extracts was investigated using two different radio HPLC methods both with gradient elution on reversed-phase columns.

Metabolite identification was mainly based on LC-MS/MS investigations performed with isolated fractions from corn straw (stover) (phenyl label) and corn husks (uracil label). Furthermore, co-chromatography experiments and retention time comparison were performed in two HPLC systems with either metabolites identified from corn straw (stover) and corn husks by LC-MS/MS or with radio-labelled reference items obtained from a rat metabolism study with Saflufenacil.

The results of the study are summarised in the following tables.

Table 12 Total radioactive residues (TRRs) in corn samples after pre-emergence treatment with ^{14}C-saflufenacil

Matrix	Days after treatment	TRR (mg/kg)			
		Phenyl Label		Uracil Label	
		combusted	calculated*	combusted	calculated*
Forage	42	0.025	0.018	0.038	0.039
Forage	101/102	0.038	0.029	0.164	0.149
Husks	133	0.257	0.215	0.276	0.226
Cob	133	0.018	0.016	0.067	0.065
Grain	133	0.019	0.020	0.052	0.049
Straw	133	0.118	0.096	0.675	0.553

* sum of extractable and unextractable residues, ERR + RRR

Table 13 Extractability of radioactive residues in corn samples after treatment with ^{14}C-Saflufenacil

Matrix	TRR calc. [mg/kg]	Methanol [mg/kg]	[% TRR]	Water [mg/kg]	[% TRR]	ERR [mg/kg]	[% TRR]	RRR [mg/kg]	[% TRR]
Phenyl-label									
Forage 42 DAT	0.018	0.010	56.4%	0.002	9.7%	0.012	66.1%	0.002	13.8%
Forage 101 DAT	0.029	0.021	73.6%	0.002	7.9%	0.024	81.5%	0.007	22.8%
Husks	0.215	0.136	62.9%	0.029	13.3%	0.164	76.2%	0.051	23.8%
Cob	0.016	0.003	16.0%	0.001	3.1%	0.003	19.2%	0.013	80.8%
Grain	0.020	0.003	12.9%	0.001	5.5%	0.004	18.4%	0.017	81.6%

Matrix	TRR calc. [mg/kg]	Methanol [mg/kg]	[% TRR]	Water [mg/kg]	[% TRR]	ERR [mg/kg]	[% TRR]	RRR [mg/kg]	[% TRR]
Straw	0.096	0.069	71.8%	0.011	11.3%	0.080	83.2%	0.016	16.8%
Uracil-label									
Forage 42 DAT	0.039	0.037	93.5%	0.001	2.5%	0.038	96.0%	0.002	4.0%
Forage 102 DAT	0.149	0.134	90.5%	0.006	4.3%	0.141	94.8%	0.008	5.2%
Husks	0.226	0.206	91.3%	0.007	2.9%	0.213	94.3%	0.013	5.7%
Cob	0.065	0.045	69.3%	0.005	8.1%	0.050	77.4%	0.015	22.6%
Grain	0.049	0.024	48.6%	0.006	11.5%	0.029	60.1%	0.019	39.9%
Straw	0.553	0.509	92.1%	0.024	4.3%	0.533	96.4%	0.020	3.6%

Table 14 Summary of characterization and identification of radioactive residues in corn forage following application of phenyl labelled saflufenacil

Compound	Corn Forage (42 DAT) TRR = 0.018 mg/kg		Corn Forage (101 DAT) TRR = 0.029 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg
Saflufenacil	2.1	< 0.0005	nd	nd
M800H01	14.6	0.003	1.6	< 0.0005
M800H02	3.8	0.001	nd	nd
M800H03	13.5	0.002	1.1	< 0.0005
M800H05	11.1	0.002	nd	nd
M800H09	20.0	0.004	21.4	0.006
M800H10	16.0	0.003	20.4	0.006
M800H11	8.9	0.002	7.3	0.002
M800H34	1.2	< 0.0005	21.0	0.006
Further polar HPLC peaks	1.8	< 0.0005	6.9	0.002
Further medium polar HPLC peaks	7.7	0.001	13.0	0.004
Further non-polar HPLC peaks	not detected	not detected	0.7	< 0.0005
Total identified from ERR [a]	91.1	0.017	72.7	0.020
Total characterized from ERR [a]	19.2	0.003	28.5	0.008
Total identified and/or characterized from ERR [a]	110.3	0.020	101.2	0.028
Water extract (unidentified compounds)	9.7	0.002	7.9	0.002
Unextractable (RRR) [b]	13.8	0.002	22.8	0.007
Grand total [c]	124.1%		124.0%	

[a] ERR: extractable radioactive residue

Remark: For metabolite identification and characterization by HPLC, the methanol extracts were concentrated. Amounts of identified and/or characterized metabolites were calculated using the measured residue levels of the concentrated extracts.

[b] RRR: residual radioactive residue, remaining after extraction with solvents like methanol and water.

[c] Grand total = (total identified and/or characterized from ERR + RRR) * 100% / calculated TRR

Table 15 Summary of Characterization and identification of radioactive residues in corn matrices (harvested at 133 DAT) following application of phenyl labelled saflufenacil

Compound	Corn Husks TRR=0.215 mg/kg		Corn Cob TRR=0.016 mg/kg		Corn Grain TRR=0.020 mg/kg		Corn Straw (Stover) TRR=0.096 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Saflufenacil	0.7	0.001	nd	nd	nd	nd	0.3	< 0.0005
M800H03	nd	nd	nd	nd	nd	nd	0.3	< 0.0005
M800H05	1.2	0.002	nd	nd	nd	nd	nd	nd
M800H09	1.4	0.003	7.0	0.001	0.3	< 0.0005	12.6	0.012
M800H10	4.1	0.009	3.1	< 0.0005	0.5	< 0.0005	12.8	0.012
M800H11	1.6	0.003	1.9	< 0.0005	0.6	< 0.0005	4.6	0.004
M800H34	6.0	0.013	16.7	0.003	2.0	< 0.0005	12.2	0.012
Further polar HPLC peaks	3.7	0.008	8.5	0.001	14	< 0.0005	1.7	0.02
Further medium polar HPLC peaks	33.7 [1]	0.073	14.8 [b]	0.002	0.7	< 0.0005	8.8	0.008
Further non-polar HPLC peaks	5.3	0.011	nd	nd	nd	nd	1.2	0.001
Total identified from ERR [a]	14.9	0.031	28.8	0.005	3.4	0.001	42.8	0.041
Total characterized from ERR [a]	55.9	0.120	26.4	0.004	7.6	0.001	23.1	0.022
Total ident./ charact. from ERR [a]	70.8	0.151	55.2	0.008	11.0	0.002	65.9	0.063

Compound	Corn Husks		Corn Cob		Corn Grain		Corn Straw (Stover)	
	TRR=0.215 mg/kg		TRR=0.016 mg/kg		TRR=0.020 mg/kg		TRR=0.096 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Water extract (unidentified comp.)	13.3	0.029	3.1	0.001	5.5	0.001	11.3	0.011
Unextractable (RRR) [c]	23.8	0.051	80.8	0.013	81.6	0.017	16.8	0.016
Total charact. after release from RRR	9.8	0.021	16.0	0.003	49.7	0.010	5.5	0.005
Total identified and/or characterized	80.6	0.172	71.2	0.011	60.6	0.012	71.4	0.068
Final residue after extraction + release	not determined		not determined		20.6	0.004	8.7	0.008
Grand total [d]	94.6%		136.0%		81.3%		80.1%	

[a] According to confirmatory HPLC analysis, several medium polar components were characterized in husks, each at less than 10% TRR.

[b] Each of the characterized medium polar peaks in cob represented a portion below 7% TRR.

[c] RRR: residual radioactive residue, remaining after extraction with solvents like methanol and water

[d] Grand total = (total identified and/or characterized from ERR + RRR) * 100% / calculated TRR

nd = not detected na = not applied

Table 16 Summary of characterization and identification of radioactive residues in corn forage following application of uracil labelled saflufenacil

Compound	Corn Forage (42 DAT)		Corn Forage (102 DAT)	
	TRR = 0.039 mg/kg		TRR = 0.149 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg
Saflufenacil	1.1	< 0.0005	not detected	not detected
M800H01	4.4	0.002	not detected	not detected
M800H02	1.0	< 0.0005	not detected	not detected
M800H03	3.4	0.001	not detected	not detected
M800H05	1.8	0.001	not detected	not detected
M800H09	3.1	0.001	2.2	0.003
M800H10	3.1	0.001	2.9	0.004
M800H11	2.0	0.001	1.9	0.003
M800H29 [a]	63.7	0.006	75.7	0.026
Further polar HPLC peaks	1.1	< 0.0005	1.3	0.002
Further medium polar HPLC peaks	1.2	< 0.0005	not detected	not detected
Water extract (unidentified compounds)	2.5	0.001	4.3	0.006
Unextractable (RRR) [d]	4.0	0.002	5.2	0.008
Total identified from ERR [b, c]	83.7	0.013	82.6	0.036
Total characterized from ERR [2]	4.8	0.001	5.6	0.008
Total identified and/or characterized from ERR [b, c]	88.4	0.014	88.3	0.044
Unextractable (RRR) [d]	4.0	0.002	5.2	0.008
Grand total [e]	92.5%		93.4%	

[a] mg/kg calculated using the molecular mass of trifluoroacetic acid

[b] ERR = extractable radioactive residue

Remark: For metabolite identification and characterization by HPLC, the methanol extracts were concentrated and cleaned-up. Amounts of identified and/or characterized metabolites were calculated using the measured residue levels of the conc. extracts.

[c] Total identified was summed up using the values for M800H29 which were calculated using the molecular mass of TFA.

[d] RRR = residual radioactive residue, remaining after extraction with solvents like methanol and water.

[e] Grand total = (total identified and/or characterized from ERR + RRR) * 100% / calculated TRR

Table 17 Summary of Characterization and Identification of Radioactive Residues in Corn Matrices (Harvested 133 DAT) Following Application uracil labelled saflufenacil

Compound	Corn Husks		Corn Cob		Corn Grain		Corn Straw (Stover)	
	TRR=0.226 mg/kg		TRR=0.065 mg/kg		TRR=0.049 mg/kg		TRR=0.553 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Saflufenacil	nd	nd	nd	nd	nd	nd	nd	nd
M800H09	0.3	0.001	0.3	< 0.0005	nd	nd	1.8	0.010
M800H10	0.6	0.001	nd	nd	nd	nd	2.7	0.015
M800H11	0.5	0.001	nd	nd	nd	nd	0.8	0.004

Table 17 Summary of Characterization and Identification of Radioactive Residues in Corn Matrices (Harvested 133 DAT) Following Application uracil labelled saflufenacil

Compound	Corn Husks		Corn Cob		Corn Grain		Corn Straw (Stover)	
	TRR=0.226 mg/kg		TRR=0.065 mg/kg		TRR=0.049 mg/kg		TRR=0.553 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
M800H29 [a]	87.7	0.045	66.0	0.010	30.5	0.004	77.4	0.098
Further polar HPLC peaks	1.0	0.002	0.8	0.001	0.5	< 0.0005	1.3	0.007
Further medium polar HPLC peaks	0.5	0.001	0.5	< 0.0005	nd	nd	0.5	0.003
Further non-polar HPLC peaks	0.4	0.001	nd	nd	nd	nd	nd	nd
Total identified from ERR [b, c]	89.1	0.048	66.3	0.010	30.5	0.004	82.7	0.127
Total characterized from ERR [b]	4.7	0.011	9.4	0.006	12.0	0.006	6.1	0.034
Total ident./ charact. from ERR [b, c]	93.8	0.059	75.7	0.016	42.5	0.010	88.8	0.161
Water extract (unidentified comp.)	2.9	0.007	8.1	0.005	11.5	0.006	4.3	0.024
Unextractable (RRR) [d]	5.7	0.013	22.6	0.015	39.9	0.019	3.6	0.020
Total charact. after release from RRR	1.3	0.003	4.4	0.003	18.7	0.009	1.8	0.010
Total identified and/or characterized	95.1	0.062	80.1	0.019	61.2	0.019	90.6	0.171
Final residue after extraction + release	4.0	0.009	17.6	0.011	18.2	0.009	1.5	0.008
Grand total [e]	99.1%		97.7%		79.4%		92.1%	

[a] mg/kg calculated using the molecular mass of 800H29 trifluoroacetic acid

[b] ERR: extractable radioactive residue

Remark: For metabolite identification and characterization by HPLC, the methanol extracts were concentrated and cleaned-up. Amounts of identified and/or characterized metabolites were calculated using the measured residue levels of the conc.extracts.

[c] Total identified was summed up using the values for M800H29 which were calculated using the molecular mass of TFA.

[d] RRR = residual radioactive residue, remaining after extraction with solvents like methanol and water.

[e] Grand total = (total identified and/or characterized from ERR and RRR + Final residue) * 100% / calculated TRR

Saflufenacil is metabolized in corn plants by the following main transformation reactions:

- N-demethylation at the uracil ring
- stepwise degradation (N-dealkylation) of the N-methyl-N-isopropyl group to NH_2 forming a sulfonamide group
- hydrolytic cleavage of the uracil ring generating a urea side chain

The predominant metabolites in the case of the phenyl label were M800H09, M800H10, M800H11 and M800H34. The metabolite M800H09 was identified as a derivative of the parent compound in which the uracil ring was demethylated and the N-methyl-N-isopropyl group was degraded to NH_2. Furthermore, the metabolite M800H10 was identified as a derivative of BAS 800 H in which the uracil ring was demethylated and the N-methyl-N-isopropyl group was degraded. Metabolite M800H11 was formed by demethylation of the N-methyl group in the uracil ring and demethylation of the methyl group of the N-methyl-N-isopropyl unit. Metabolite M800H34 was identified as a derivative of the parent compound in which the uracil ring was cleaved and the N-methyl-N-isopropyl group was degraded to NH_2 to form an N-sulfonamide group. Further identified metabolites were M800H01, M800H02, M800H03 and M800H05.

In the uracil-labelled corn matrices, the highly polar component M800H29 (trifluoroacetic acid, TFA) was the major metabolite. It is label-specific and therefore, it was not detectable in the phenyl-labelled substrates. Comparing the residue levels of both radiolabels, the total radioactive residues were higher for the uracil label in all matrices. These quantitative differences and the comparison of the metabolite patterns for both labels suggest an uptake of the polar metabolite M800H29 or a respective precursor molecule from soil into corn plants after pre-emergence application of saflufenacil.

The metabolic pathway is shown in Figure 3.

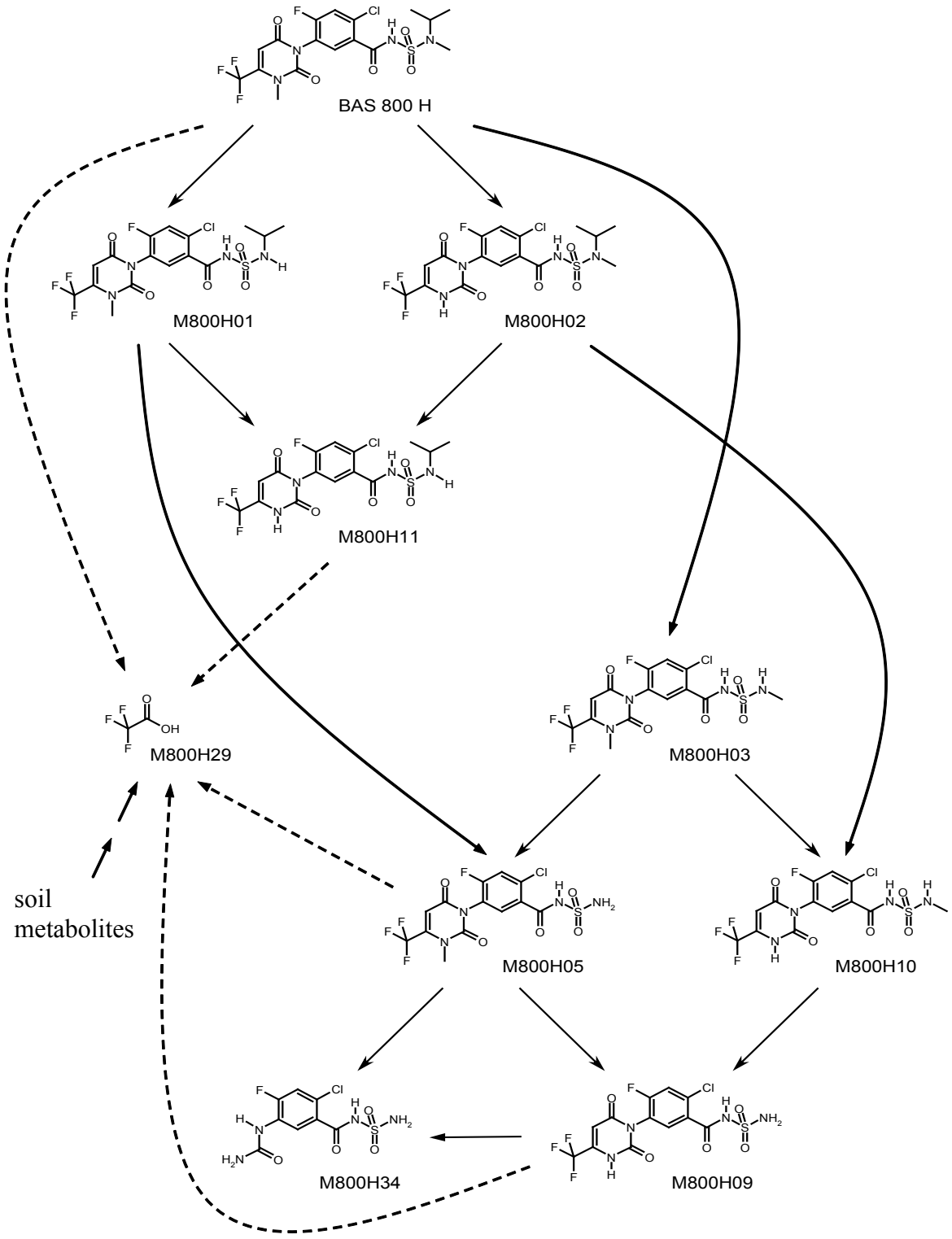


Figure 3 Proposed metabolic pathway of saflufenacil in corn

Table 18 Summary of identified components in corn forage and husks after treatment with ^{14}c-saflufenacil (phenyl label)

Metabolite Code	Corn Matrix (Days After Treatment)					
	Forage (42 DAT)		Forage (101 DAT)		Husks (133 DAT)	
	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Saflufenacil	0.000	2.1	nd	nd	0.001	0.7
	0.000	1.1	nd	nd	nd	nd
M800H01	0.003	14.6	0.000	1.6	nd	nd
	0.002	4.4	nd	nd	nd	nd
M800H02	0.001	3.8	nd	nd	nd	nd
	0.000	1.0	nd	nd	nd	nd
M800H03	0.002	13.5	0.000	1.1	nd	nd
	0.001	3.4	nd	nd	nd	nd
M800H05	0.002	11.1	nd	nd	0.002	1.2
	0.001	1.8	nd	nd	nd	nd
M800H09	0.004	20.0	0.006	21.4	0.003	1.4
	0.001	3.1	0.003	2.2	0.001	0.3
M800H10	0.003	16.0	0.006	20.4	0.009	4.1
	0.001	3.1	0.001	2.9	0.001	0.6
M800H11	0.002	8.9	0.002	7.3	0.003	1.6
	0.001	2.0	0.003	1.9	0.001	0.5
M800H29 * (TFA)	0.006	63.7	0.026	75.7	0.045	87.7
M800H34	0.000	1.2	0.006	21.0	0.013	6.0
	nd	nd	nd	nd	nd	nd

nd - not detected * Concentration [mg/kg] of M800H29 was calculated using the molecular mass of M800H29 (TFA).

Table 19 Summary of identified components in corn cob, grain and straw after treatment with ^{14}C-phenyl- and uracil-labelled saflufenacil

Metabolite Code	Corn Matrix (Days After Treatment)					
	Cob (42 DAT)		Grain (101 DAT)		Straw (133 DAT)	
	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
saflufenacil	nd	nd	nd	nd	0.000	0.3
	nd	nd	nd	nd	nd	nd
M800H01	nd	nd	nd	nd	nd	nd
	nd	nd	nd	nd	nd	nd
M800H02	nd	nd	nd	nd	nd	nd
	nd	nd	nd	nd	nd	nd
M800H03	nd	nd	nd	nd	0.000	0.3
	nd	nd	nd	nd	nd	nd
M800H05	nd	nd	nd	nd	nd	nd
	nd	nd	nd	nd	nd	nd
M800H09	0.001	7.0	0.000	0.3	0.012	12.6
	0.000	0.3	nd	nd	0.010	1.8
M800H10	0.000	3.1	0.000	0.5	0.012	12.8
	nd	nd	nd	nd	0.015	2.7
M800H11	0.000	1.9	0.000	0.6	0.004	4.6
	nd	nd	nd	nd	0.004	0.8
M800H29 * (TFA)	0.010	66.0	0.004	30.5	0.098	77.4
M800H34	0.003	16.7	0.000	2.0	0.012	12.2
	nd	nd	nd	nd	nd	nd

nd - not detected * Concentration [mg/kg] of M800H29 was calculated using the molecular mass of M800H29 (TFA).

Soya bean

Phenyl-U-^{14}C saflufenacil and uracil-4-^{14}C saflufenacil were applied in EC formulation on bare soil on the day of sowing as pre-emergence treatment at a rate of 150 g ai/ha (Rabe U., Glaessgen W.E. 2007a). Soya bean plants (variety: Pioneer 9091) were grown in climatic chambers (phytotrons), simulating the natural climatic conditions of a typical US soya bean-growing area) and in a greenhouse. Soya bean forage samples were taken at growth stage 70 (BBCH code), 39/40 DAT (days after treatment). Soya bean seed, pod (hull), and straw were harvested at GS 96 (95 DAT).

Frozen samples were homogenized and extracted with methanol and water. The extractable radioactive residues (ERR) were measured by LSC, and the residual radioactive residues after solvent extraction (RRR) (post extraction solids) were determined by combustion analysis. The total radioactive residues (TRR) were the result of combustion analysis or the sum of ERR and RRR values.

Table 20 Total radioactive residues (TRRS) in soya bean samples after pre-emergence treatment with ^{14}C-saflufenacil

Matrix	Days after treatment	TRR (mg/kg)			
		Phenyl Label		Uracil Label	
		combusted	calculated*	combusted	calculated*
Forage	39 / 40	0.086	0.081	0.404	0.383
Bean	95	0.041	0.038	0.238	0.221
Pod	95	0.182	0.179	2.123	2.031
Straw	95	0.382	0.431	1.466	1.183

* sum of extractable and unextractable residues, ERR + RRR

The nature of the residues in methanol and water extracts and in the NH_4OH solubilizate of soya bean pod (uracil label) was investigated using HPLC with radiodetection in two/three systems (RP, HILIC). In some cases, appropriate clean-up steps such as C-18 extraction, protein precipitation and partition were applied prior to HPLC analysis. Isolation of metabolites was achieved by clean-up (removal of chlorophyll) and HPLC fractionation of methanol extracts from straw (phenyl label) and forage (uracil label). Identification of metabolites was performed by LC-MS/MS analyses of the purified methanol extracts of soya bean forage and straw as well as of purified fractions from straw and forage, by co-chromatography with the respective reference items and by comparison of retention times and chromatographic patterns. The RRR of soya bean seed, pod and straw (phenyl label only) were further characterized by means of sequential solubilisation procedures using base hydrolysis and enzyme hydrolysis. The protein precipitates from the water extracts of bean and from the NH_4OH solubilizates of bean and pod were incubated with protease to release radioactive residues associated with proteins.

The samples were stored in a freezer at -18 °C during the course of the study. Storage stability investigations were performed on two representative matrices: soya bean pod (95 DAT, phenyl label) and soya bean forage (40 DAT, uracil label). No significant changes of the extraction behaviour and the HPLC patterns were observed. The composition of the residues in the plant materials remained stable for a period of approximately 17 to 23 months. The residues in the stored extracts were shown to be stable for a period of approximately 15 to 17 months under the chosen conditions.

Table 21 Extractability of radioactive residues in soya bean samples after pre-emergence treatment with ^{14}C-saflufenacil

Matrix	DAT [a]	TRR calc. [b]	Methanol Extract		Water Extract		ERR [c]		RRR [d]	
		[mg/kg]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Phenyl Label										
Forage	39	0.081	0.070	87.1	0.004	4.7	0.074	91.8	0.007	8.2
Bean	95	0.038	0.010	26.7	0.013	33.1	0.023	59.7	0.015	40.3
Hull	95	0.179	0.063	35.2	0.048	26.9	0.111	62.0	0.068	38.0
Straw	95	0.431	0.329	76.3	0.040	9.2	0.369	85.4	0.063	14.6
Uracil Label										

Matrix	DAT [a]	TRR calc. [b]	Methanol Extract		Water Extract		ERR [c]		RRR [d]	
		[mg/kg]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Forage	40	0.383	0.371	96.9	0.005	1.3	0.376	98.2	0.007	1.8
Bean	95	0.221	0.043	19.5	0.136	61.7	0.180	81.2	0.042	18.8
Hull	95	2.031	0.801	39.4	0.805	39.6	1.605	79.0	0.426	21.0
Straw	95	1.183	1.054	89.1	0.082	6.9	1.137	96.1	0.046	3.9

[a] DAT = Days After Treatment

[b] TRR was calculated as the sum of ERR + RRR

[c] ERR = Extractable Radioactive Residue (sum of methanol and water extractable residues)

[d] RRR = Residual Radioactive Residue (after solvent extraction)

Table22 Summary of characterization and identification of radioactive residues in soya bean matrices following application of phenyl labelled saflufenacil

Compound	Forage (39 DAT)		Bean (95 DAT)		Pod (95 DAT)		Straw (95 DAT)	
	TRR = 0.081 mg/kg		TRR = 0.038 mg/kg		TRR = 0.179 mg/kg		TRR = 0.431 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
saflufenacil	23.5	0.019	2.3	0.001	1.5	0.003	2.5	0.011
M800H01	6.0	0.005	2.1	0.001	1.0	0.002	3.0	0.013
M800H02	18.2	0.015	6.3	0.002	5.6	0.010	8.2	0.035
M800H03	1.2	0.001	nd	nd	nd	nd	nd	nd
M800H05	nd	nd	3.2	0.001	nd	nd	2.3	0.010
M800H10 and / or M800H36	6.6	0.005	14.5	0.006	12.3	0.022	11.5	0.049
M800H11	6.0	0.005	1.8	0.001	9.0	0.016	24.9	0.107
M800H35	5.2	0.004	3.7	0.001	12.9	0.023	15.6	0.067
M800H36 see M800H10	s. a.	s. a.	s. a.	s. a.	s. a.	s. a.	s. a.	s. a.
M800H37	6.5	0.005	nd	nd	nd	nd	nd	nd
Total identified from ERR [a]	73.2	0.059	34.0	0.013	42.2	0.076	68.0	0.293
Total characterized from ERR [a]	14.8	0.012	37.7	0.014	19.9	0.036	14.1	0.061
Total identified and/or characterized from ERR [a]	88.0	0.071	71.7	0.027	62.1	0.111	82.1	0.354
Unextractable (RRR) [b]	8.2	0.007	40.3	0.015	38.0	0.068	14.6	0.063
Total characterized after release from RRR	n. a.	n. a.	26.9	0.010	27.3	0.049	7.4	0.032
Total identified and/or characterized	88.0	0.071	98.6	0.038	89.4	0.160	89.6	0.386
Final residue (after extraction and release)	8.2 (s. a.)	0.007 (s. a.)	10.8	0.004	9.8	0.017	6.3	0.027
Grand total [c]	96.2%		109.4%		99.2%		95.9%	

[a] ERR = extractable radioactive residue (calculated as sum of the methanol and water extracts).

Remark: For metabolite identification and characterization by HPLC, methanol and water extracts were cleaned-up and/or concentrated. Amounts of identified and/or characterized metabolites were calculated using the measured residue levels of the concentrated extracts.

[b] RRR = residual radioactive residue, remaining after extraction with solvents like methanol and water.

[c] Grand total = (total identified and/or characterized from ERR + RRR) * 100% / calculated TRR

nd = not detected - s. a. = see above - n. a. = not applied

Table 23 Summary of characterization and identification of radioactive residues in soya bean matrices following application of uracil labelled saflufenacil

Compound	Forage (40 DAT)		Bean (95 DAT)		Pod (95 DAT)		Straw (95 DAT)	
	TRR = 0.383 mg/kg		TRR = 0.221 mg/kg		TRR = 2.031 mg/kg		TRR = 1.183 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
saflufenacil	4.0	0.015	0.8	0.002	nd	nd	2.9	0.034
M800H01	2.3	0.009	1.1	0.002	nd	nd	2.0	0.024
M800H02	5.0	0.019	1.4	0.003	1.0	0.021	5.3	0.062
M800H11	2.5	0.010	nd	nd	1.3	0.027	14.6	0.172
M800H29 [a]	85.2	0.074	65.4	0.033	75.9	0.351	69.2	0.187
Total identified from ERR [b]	99.1	0.128	68.8	0.040	78.2	0.399	93.9	0.479

Compound	Forage (40 DAT)		Bean (95 DAT)		Pod (95 DAT)		Straw (95 DAT)	
	TRR = 0.383 mg/kg		TRR = 0.221 mg/kg		TRR = 2.031 mg/kg		TRR = 1.183 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Total characterized from ERR [b]	3.1	0.012	9.7	0.021	nd	nd	6.7	0.079
Total identified and/or characterized from ERR [b]	102.2	0.139	78.5	0.062	78.2	0.399	100.5	0.558
Unextractable (RRR)[d]	1.8	0.007	18.8	0.042	21.0	0.426	3.9	0.046
Total identified after release from RRR (M800H29 [a])	n. a.	n. a.	n. a.	n. a.	16.5	0.077	n. a.	n. a.
Total characterized after release from RRR [d]	n. a.	n. a.	13.7 [e]	0.030 [e]	2.3	0.048	n. a.	n. a.
Total identified and/or characterized after release from RRR [d]	n. a.	n. a.	13.7	0.030	18.9	0.124	n. a.	n. a.
Total identified	99.1	0.128	68.8	0.040	94.7	0.476	93.9	0.479
Total identified and/or characterized	102.2	0.139	92.2	0.092	97.1	0.523	100.5	0.558
Final Residue (after extraction and release)	1.8 (s. a.)	0.007 (s. a.)	6.0	0.013	1.0	0.020	3.9 (s. a.)	0.046 (s. a.)
Grand total [f]	104.0%		98.1%		98.1%		104.5%	

[a] mg/kg calculated using the molecular mass of trifluoroacetic acid

[b] ERR = extractable radioactive residue (calculated as sum of the methanol and water extracts).

Remark: For metabolite identification and characterization by HPLC, the methanol and water extracts were cleaned-up and/or concentrated. Amounts of identified and/or characterized metabolites were calculated using the measured residue levels of the concentrated extracts.

[c] Total identified was summed up using the values for M800H29 which were calculated using the molecular mass of TFA.

[d] RRR = residual radioactive residue, remaining after extraction with solvents like methanol and water.

[e] Sum of fractions characterized from RRR after protein precipitation from NH_4OH solubilizate.

[f] Grand total = (total identified and/or characterized from ERR + RRR) * 100% / calculated TRR

nd = not detected - n. a. = not applied - s. a. = see above

The metabolic pathway is shown in Figure 4.

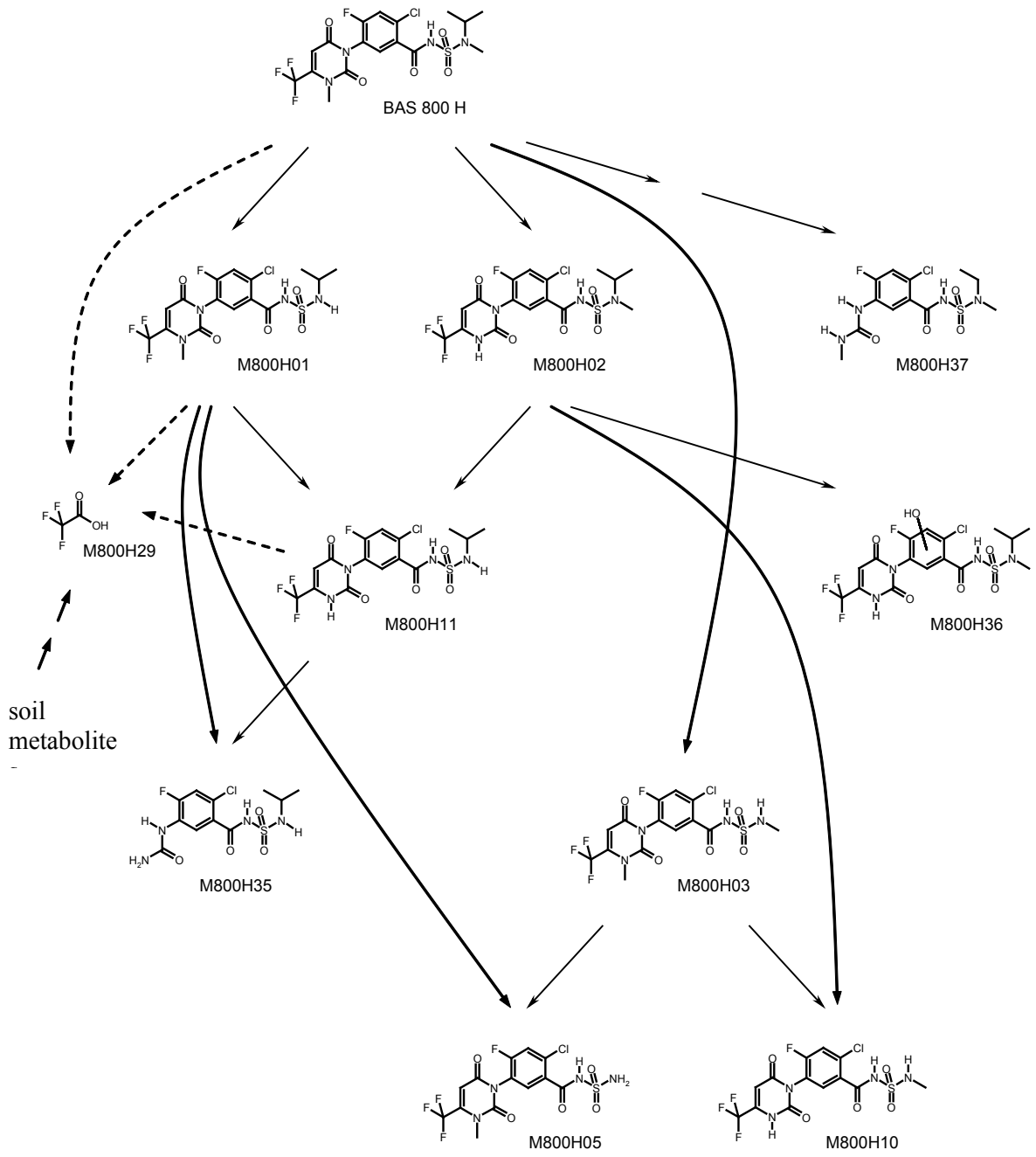


Figure 4 Proposed Metabolic Pathway of Saflufenacil in Soya bean

Table 24 Summary of identified components in soya bean matrices after pre-emergence treatment with phenyl- (upper row) and uracil (lower row) labelled saflufenacil

Metabolite Code	Soya bean Matrix (Days After Treatment)							
	Forage (40 DAT)		Bean (95 DAT)		Hull (95 DAT)		Straw (95 DAT)	
	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Saflufenacil	0.019	23.5	0.001	2.3	0.003	1.5	0.011	2.5
	0.015	4.0	0.002	0.8	nd	nd	0.034	2.9
M800H01	0.005	6.0	0.001	2.1	0.002	1.0	0.013	3.0
	0.009	2.3	0.002	1.1	nd	nd	0.024	2.0
M800H02	0.015	18.2	0.002	6.3	0.010	5.6	0.035	8.2
	0.019	5.0	0.003	1.4	0.021	1.0	0.062	5.3
M800H03	0.001	1.2	nd	nd	nd	nd	nd	nd
	nd	nd	nd	nd	nd	nd	nd	nd
M800H05	nd	nd	0.001	3.2	nd	nd	0.010	2.3
	nd	nd	nd	nd	nd	nd	nd	nd
M800H10 and/or M800H36	0.005	6.6	0.006	14.5	0.022	12.3	0.049	11.5
	nd	nd	nd	nd	nd	nd	nd	nd
Metabolite Code	Soya bean Matrix (Days After Treatment)							
	Forage (40 DAT)		Bean (95 DAT)		Hull (95 DAT)		Straw (95 DAT)	
	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
M800H11	0.005	6.0	0.001	1.8	0.016	9.0	0.107	24.9
	0.010	2.5	nd	nd	0.027	1.3	0.172	14.6
M800H29 (TFA)	Only detectable with the Uracil Label							
	0.074	85.2	0.033	65.4	0.428[3)]	92.4 [3)]	0.187	69.2
M800H35	0.004	5.2	0.001	3.7	0.023	12.9	0.067	15.6
	Only detectable with the Phenyl Label							
M800H37	0.005	6.5	nd	nd	nd	nd	nd	nd
	Only detectable with the Phenyl Label							

nd = not detected

Concentration of M800H29 calculated in consideration of the molecular mass of trifluoroacetic acid

Including the combined NH_4OH solubilizate from the non-extractable residues (Sample No. Lab0182)

Soya bean (pre-harvest desiccation)

The soya bean metabolism study was conducted with ^{14}C-Uracil Labelled saflufenacil after foliar spray application at a rate of 1 × 100 g ai/ha at BBCH growth stage 87–89. Harvest of soya bean leaves, stems, pods and seeds was at a PHI of 7 days after application (Grosshans F. *et al*. 2010a).

Leaves and seeds were taken from the plant. Mature and immature seeds were separated and only the mature seeds were further investigated. Additionally, the pods were separated from the seeds. After collection of leaves and seeds the stems were cut just above the soil line and shredded into pieces. The samples were stored in a freezer immediately after they were taken.

All plant samples were homogenized and the radioactive residues were determined by combustion analysis. The homogenized samples were successively extracted with methanol and water. The Total Radioactive Residues (TRR) were determined by summarizing the Extractable Radioactive Residues (ERR) and the Residual (non-extractable) Radioactive Residues (RRR) (post extraction solids).

After the extraction procedures with methanol and water, HPLC analyses were carried out for the extracts with a sufficient level of radioactivity. In some cases of seed samples, the extracts were additionally purified by protein precipitation. The non-extractable residues were treated with aqueous ammonia solution and the respective solubilizates were partitioned with ethyl acetate. The residues obtained after NH_4OH solubilisation were subsequently incubated with Macerozyme / Cellulase,

Amylase / Amyloglucosidase and Tyrosinase / Laccase for further characterization of the residual radioactive residues. For seed samples the residues obtained after enzyme treatment were additionally treated with hydrochloric acid.

Table 25 Total radioactive residues in soya bean samples after foliar treatment with ^{14}C-uracil-saflufenacil

Matrix	Days after treatment	TRR (mg/kg)	
		Uracil Label	
		combusted	calculated*
Stem	7	0.412	0.419
Pod	7	1.744	1.859
Seed	7	0.049	0.043
Leaves	7	19.592	17.922

* sum of extractable and unextractable residues, ERR + RRR

Table 26 Extractability of radioactive residues in soya bean samples after foliar treatment with ^{14}C-uracil labelled saflufenacil

Matrix	DAT [a]	TRR calc. [b]	Methanol extract		Aqueous extract		ERR [c]		RRR [d]	
			[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Stem	7	0.419	0.395	94.4	0.009	2.2	0.405	96.7	0.014	3.3
Pod	7	1.859	1.369	73.7	0.299	16.1	1.668	89.7	0.191	10.3
Seed	7	0.043	0.018	41.5	0.015	34.1	0.032	75.6	0.010	24.4
Leaves	7	17.922	16.623	92.7	0.874	4.9	17.497	97.6	0.426	2.4

[a] DAT = Days After last Treatment

[b] TRR was calculated as the sum of ERR + RRR

[c] ERR = Extractable Radioactive Residue (sum of methanol and water extractable residues)

[d] RRR = Residual Radioactive Residue (after solvent extraction)

The identification of the metabolites was based on LC-MS and LC-MS/MS analyses of HPLC fractions derived from the purified methanol extract (ethyl acetate phase) of soya bean leaves and on co-chromatography of methanol and aqueous extracts of soya bean leaves with reference compounds. Peak assignment in the other samples was done by comparison of the HPLC retention times and the elution profiles / metabolite patterns with those of the extracts investigated by LC-MS or co-chromatography and with the reference compounds. If identification was not possible (e.g. because of the low residue levels), the peaks were characterized by their retention times. The quantitation of the parent compound and metabolites is based on the HPLC analysis of the methanol and aqueous extracts and of the ethyl acetate phases obtained after liquid/liquid partition of the NH_4OH solubilizate from the RRR of pod, seed and leaves using HPLC method LC01 with a Synergy Hydro RP column. HPLC method LC02 (Phenyl-Hexyl column) was used for confirmatory purposes.

The total identified and characterized radioactive residues accounted for 100.3 % TRR in soya bean stem, 95.1 % TRR in pod, 84.6 % TRR in seed, and 108.8% TRR in leaves.

The metabolic pathway of saflufenacil following post-emergence treatment is qualitatively the same as in case of pre-emergence application (Figure 3) but only M800-H01, M800-H02, M800-H03 and M800-H011 were identified (Table 29).

Table 27 Summary of characterization and identification of radioactive residues in soya bean matrices following pre-harvest desiccant-application of ^{14}C-uracil labelled saflufenacil

Compound	Stem (7 DAT)		Pod (7 DAT)		Seed (7 DAT)		Leaves (7 DAT)	
	TRR = 0.419 mg/kg		TRR = 1.859 mg/kg		TRR 0.043 mg/kg		TRR = 17.922 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Saflufenacil	73.2	0.306	76.4	1.420	25.8	0.011	63.7	11.423
M800H01	nd	nd	2.6	0.048	nd	nd	13.6	2.441
M800H02	18.2	0.076	5.3	0.098	25.5	0.011	14.8	2.658
M800H03	nd	nd	0.6	0.010	nd	nd	8.9	1.589
M800H11	7.5	0.031	2.7	0.050	10.2	0.004	5.2	0.936

Compound	Stem (7 DAT)		Pod (7 DAT)		Seed (7 DAT)		Leaves (7 DAT)	
	TRR = 0.419 mg/kg		TRR = 1.859 mg/kg		TRR 0.043 mg/kg		TRR = 17.922 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Total identified from ERR [a]	98.8	0.414	87.4	1.626	61.5	0.026	106.3	19.046
Total characterized from ERR [a]	0.3	0.001	2.9	0.053	8.2	0.003	1.2	0.216
Total identified and/or characterized from ERR [a]	99.1	0.415	90.3	1.679	69.7	0.029	107.5	19.263
Unextractable (RRR) [b]	3.3	0.014	10.3	0.191	24.4	0.010	2.4	0.426
Saflufenacil	n.a.	n.a.	nd	nd	0.3	0.0001	0.04	0.008
M800H02	n.a.	n.a.	0.9	0.018	0.8	0.0004	0.32	0.058
M800H11	n.a.	n.a.	0.2	0.004	0.7	0.0003	0.09	0.016
Total identified after release from RRR [b]	n.a.	n.a.	1.2	0.022	1.7	0.0007	0.5	0.082
Total characterized after release from RRR [b]	1.2	0.005	3.7	0.068	13.2	0.0056	0.8	0.148
Total identified and/or characterized after release from RRR [b]	1.2	0.005	4.8	0.090	14.9	0.0064	1.3	0.230
Total identified	98.8	0.414	88.6	1.648	63.2	0.027	106.7	19.129
Total identified and/or characterized	100.3	0.420	95.1	1.769	84.6	0.036	108.8	19.493
Final Residue (after extraction and release)	2.0	0.009	3.3	0.061	5.1	0.002	0.6	0.103
Grand total [c]	102.3		98.4		89.7		109.3	

[a] ERR = extractable radioactive residue (calculated as sum of the methanol and water extracts).

Remark: For metabolite identification and characterization by HPLC, the methanol and water extracts were cleaned-up and/or concentrated. Amounts of identified and/or characterized metabolites were calculated using the measured residue levels of the concentrated extracts.

[b] RRR = residual radioactive residue, remaining after extraction with solvents like methanol and water.

[c] Grand total = (total identified and/or characterized from ERR + RRR) * 100% / calculated TRR

nd = not detected - n. a. = not applied - s. a. = see above

Table 28 Summary of identified components in soya bean matrices after foliar pre-harvest desiccant treatment with ^{14}C-uracil labelled saflufenacil

Component	Soya bean Matrix (Days after Treatment)							
	stem (7 DAT)		pod (7 DAT)		seed (7 DAT)		leaf (7 DAT)	
	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Saflufenacil	0.306	73.2	1.420	76.4	0.011	25.8	11.431	63.8
M800H01	-	-	0.048	2.6	-	-	2.441	13.6
M800H02	0.076	18.2	0.115	6.2	0.011	25.5	2.716	15.2
M800H03	-	-	0.010	0.6	-	-	1.589	8.9
M800H11	0.031	7.5	0.054	2.9	0.004	10.2	0.952	5.3

Tomato

The metabolism of saflufenacil was investigated in tomato after one single spray application of the test substance in an EC formulation at a nominal application rate of 100 g ai/ha. The active substance was applied to soil directly before planting of tomato plants (pre-plant treatment). Treatment was performed with either phenyl-U-^{14}C saflufenacil (Phenyl-Label) or ^{14}C-saflufenacil -[uracil-4-^{14}C] saflufenacil (uracil-label) (Hafemann C., Kloeppner U. 2007). Tomato plants at BBCH growth stage 16/17 (variety: Goldene Königin) were planted into the sprayed soil and were grown in climatic chambers (phytotrons) and later in the greenhouse. Tomato plants at BBCH growth stage 62/63 were sampled 68 days after application (68 DAT). Mature tomato fruits were harvested 113 days after treatment (113 DAT). Additionally, tomato plant material at harvest (113 DAT) was sampled for further investigations.

Frozen samples were homogenized and extracted with methanol and water. The extractable radioactive residues (ERR) were measured by LSC, and the residual radioactive residues after solvent extraction (post extraction solids) (RRR) were determined by combustion analysis. The total radioactive residues (TRR) were the result of combustion analysis or the sum of ERR and RRR values.

Table 29 Total radioactive residues (TRRs) in tomato after pre-plant treatment with ^{14}C saflufenacil

Matrix	Days after treatment	TRR (mg/kg)			
		Phenyl Label		Uracil Label	
		combusted	calculated*	combusted	calculated*
Tomato Plant at GS 62/63	68 DAT	0.089	0.103	0.131	0.143
Tomato Plant at Harvest	113 DAT	0.113	0.108	0.138	0.140
Tomato Fruit	113 DAT	0.015	0.015	0.037	0.035

* sum of extractable and unextractable residues, ERR + RRR

Table 30 Extractability of radioactive residues in tomato samples after pre-plant application of ^{14}C-saflufenacil

Matrix	DAT [a]	TRR comb. [b]	TRR calc. [c]	Methanol Extract		Aqueous Extract		ERR [d]		RRR [e]	
					TRR		TRR		TRR		TRR
		[mg/kg]	[mg/kg]	[mg/kg]	[%]	[mg/kg]	[%]	[mg/kg]	[%]	[mg/kg]	[%]
Phenyl Label											
Tomato plant at GS 62/63	68	0.089	0.103	0.090	101.0	0.003	2.9	0.093	103.8	0.011	12.1
Tomato plant at harvest	113	0.113	0.108	0.087	76.6	0.004	3.9	0.091	80.5	0.017	15.3
Tomato fruit	113	0.015	0.015	0.010	64.0	0.001	4.1	0.010	68.1	0.005	32.2
Uracil Label											
Tomato plant at GS 62/63	68	0.131	0.143	0.132	100.8	0.002	1.8	0.135	102.5	0.008	6.4
Tomato plant at harvest	113	0.138	0.140	0.118	85.5	0.005	3.3	0.122	88.8	0.018	13.0
Tomato fruit	113	0.037	0.035	0.030	83.2	0.001	1.8	0.031	85.0	0.004	11.8

[a] DAT = Days after Treatment

[b] TRR combusted

[c] TRR was calculated as the sum of ERR + RRR

[d] ERR = Extractable Radioactive Residue

[e] RRR = Residual Radioactive Residue (after solvent extraction)

The TRR values combusted were used as 100% TRR for all further calculations.

The samples were stored at approximately -18 °C during the course of the study. For all matrices the storage stability of the residues in the stored extracts and the stored sample material was investigated. No significant changes of the HPLC patterns were observed. The residues in the stored extracts were stable over a period of approximately 9 to 10 months under the chosen conditions. The composition of the residues in the plant materials remained stable over a period of approximately 10 to 11 months. All tomato plant matrices were extracted within 10-55 days after sampling. The metabolite profiles used for quantification of metabolites were obtained by HPLC analysis not later than 3-22 days after extraction. The maximum time period between sampling and HPLC analysis (metabolite profile used for quantification) was 59 days.

The nature of the residues in the methanol extracts was investigated using two methods of HPLC radiodetection. Metabolite identification is based on HPLC co-chromatography experiments performed with reference items obtained from other metabolism studies in corn, rotational crops and

rat. The RRR of tomato plant at GS 62/63 (phenyl label) and tomato plant at harvest (phenyl label and uracil label) were further characterized by means of sequential solubilisation procedures using base and acid hydrolysis and microwave treatment. Storage stability has been demonstrated for all samples. For metabolite identification and characterization by HPLC, the methanol extracts were concentrated. Amounts of identified and / or characterized metabolites were calculated using the measured residue levels of the concentrated extracts.

Table 31 Summary of characterization and identification of radioactive residues in tomato matrices following application of phenyl labelled saflufenacil

Compound	Tomato Plant (GS 62/63)		Tomato Plant (Harvest)		Tomato Fruit	
	TRR=0.089 mg/kg		TRR= 0.113 mg/kg		TRR=0.015 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Saflufenacil	28.6	0.026	10.9	0.012	0.7	< 0.0005
M800H01	1.9	0.002	1.5	0.002	nd	nd
M800H02	5.9	0.005	2.3	0.003	nd	nd
M800H07	14.1	0.013	5.8	0.007	nd	nd
M800H09 [a]	5.2 [a]	0.005 [a]	5.0	0.006	nd	nd
M800H10 and unknown [b]	9.4	0.008	10.2	0.012	nd	nd
M800H11	12.6	0.011	5.9	0.007	nd	nd
M800H35 [a]	5.2 [a]	0.005 [a]	5.8	0.007	nd	nd
Sugar (most probably fructose)	nd	nd	nd	nd	52.9	0.008
ERR	103.8	0.093	80.5	0.091	68.1	0.010
Total identified from ERR	68.2	0.061	37.3	0.042	53.6	0.008
Total characterized from ERR	30.4	0.027	40.2	0.046	14.9	0.002
Total identified and/or characterized from ERR	98.6	0.088	77.5	0.088	68.4	0.010
Unextractable (RRR)	12.1	0.011	15.3	0.017	32.2	0.005
Total characterized after release from RRR	5.3	0.005	3.4	0.004	n.a.	n.a.
Total identified and/or characterized	103.9	0.093	80.9	0.091	68.4	0.010
Final residue (after extraction and release)	3.9	0.003	7.1	0.008	32.2	0.005
Grand Total [c]	107.7		88.0		100.7	

[a] M800H09 and M800H035 co-eluted and were quantified together

[b] M800H10 was counted as characterized

(M800H10 co-eluted with another unknown metabolite; both metabolites were separated using a second HPLC method, ratio M800H10 : unknown approximately 1:2 for tomato plant at GS 62/63 and ratio 1:1.2 for tomato plant at harvest.
The ratio specifies no correlation to the peak identity.)

[c] Grand total = (total identified and/or characterized from ERR + RRR) * 100% / calculated TRR

n.a.	not applicable
nd	not detected
ERR	extractable radioactive residue (calculated from the residues in combined methanol extract and combined water extract)
RRR	residual radioactive residue, remaining after solvent extraction with methanol and water.

Table 32 Summary of characterization and identification of radioactive residues in tomato matrices following application of uracil labelled saflufenacil

Compound	Tomato Plant (GS 62/63)		Tomato Plant (Harvest)		Tomato Fruit	
	TRR=0.131 mg/kg		TRR= 0.138 mg/kg		TRR=0.037 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Saflufenacil	4.8	0.006	8.5	0.012	nd	nd
M800H10	2.4	0.003	2.9	0.004	nd	nd
M800H11	3.9	0.005	3.6	0.005	nd	nd
M800H29 [a]	82.2	0.025	51.7	0.016	48.6	0.004
Sugar (most probably fructose)	nd	nd	nd	nd	33.7	0.012
ERR	102.5	0.135	88.8	0.122	85.0	0.031
Total identified from ERR	93.2	0.039	66.8	0.037	82.3	0.016

Compound	Tomato Plant (GS 62/63)		Tomato Plant (Harvest)		Tomato Fruit	
	TRR=0.131 mg/kg		TRR= 0.138 mg/kg		TRR=0.037 mg/kg	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Total characterized from ERR	9.3	0.012	20.8	0.029	1.8	0.001
Total identified and/or characterized from ERR	102.5	0.051	87.6	0.066	84.0	0.017
Unextractable (RRR)	6.4	0.008	13.0	0.018	11.8	0.004
Total characterized after release from RRR	n.a.	n.a.	2.9	0.004	n.a.	n.a.
Total identified and/or characterized	102.5	0.051	90.5	0.070	84.0	0.017
Final residue (after extraction and release)	6.4	0.008	6.4	0.009	11.8	0.004
Grand Total [b]	109.0		97.0		95.8	

[a] mg/kg calculated using the molecular mass of trifluoroacetic acid

[b] Grand total = (total identified and/or characterized from ERR + RRR) * 100% / calculated TRR

n.a. not applicable - nd - not detected

ERR extractable radioactive residue (calculated from the residues in combined methanol extract and combined water extract)

RRR residual radioactive residue, remaining after solvent extraction with methanol and water.

The proposed metabolic pathway is shown in Figure 5.

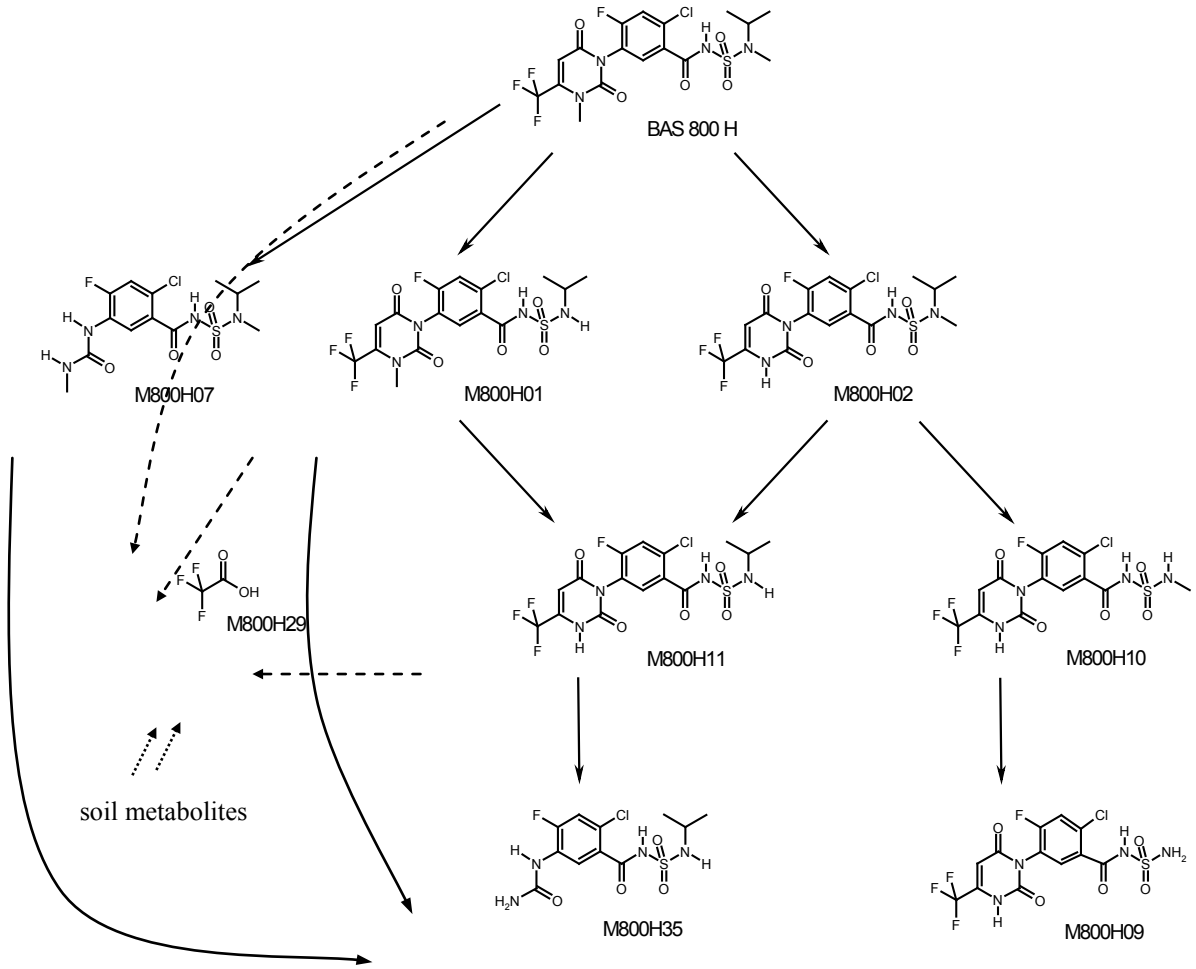


Figure 5 Proposed Metabolic Pathway of Saflufenacil in Tomato

Table 33 Summary of identified components in tomato matrices after pre-plant application of ^{14}C phenyl labelled (upper row) and ^{14}C-uracil labelled saflufenacil

Metabolite Code	Tomato Matrix (Days After Treatment)					
	Tomato Plant at GS 62/63 (68 DAT)		Tomato Plant at Harvest (113 DAT)		Tomato Fruit (113 DAT)	
	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Saflufenacil	0.026	28.6	0.012	10.9	< 0.0005	0.7
	0.006	4.8	0.012	8.5	--	--
M800H01	0.002	1.9	0.002	1.5	--	--
M800H02	0.005	5.9	0.003	2.3	--	--
M800H07	0.013	14.1	0.007	5.8	--	--
M800H09	M800H09 and M800H35 0.005 M800H09	and M800H35 5.2	0.006	5.0	--	--
M800H10 and unknown	0.008	9.4	0.012	10.2	--	--
	0.003	2.4	0.004	2.9	--	--
M800H11	0.011	12.6	0.007	5.9	--	--
	0.005	3.9	0.005	3.6	--	--
M800H35	M800H09and M800H350.005 M800H09	and M800H35 5.2	0.007	5.8	--	--
Fructose [a]	--	--	--	--	0.008	52.9
	--	--	--	--	0.012	33.7

[a] Concentration expressed in parent equivalents

Environmental fate in soil

Soil metabolism

The aerobic degradation of 14C-uracil and phenyl-labelled saflufenacil was studied on soils obtained from Idaho, Illinois, New Jersey and Wisconsin (Singh, 2008). According to USDA Textural Classification, the soils were classified as sandy loam, silty clay loam, silt loam, and loamy sand soils, respectively.

The soils were treated with ^{14}C-saflufenacil at approximately 400 g ai/ha, the proposed maximum use rate. The treated soils were incubated in polypropylene centrifuge flasks in darkness in a growth chamber maintained at 25 ± 1 °C. During the incubation of the treated samples, CO_2-free air was continuously purged over the samples and through traps of NaOH to collect volatile radioactive residues. Soil moisture was maintained at 75% of 1/3 bar by adding water as needed.

Samples were taken at 0, 7, 14, 25, 43, 57-62, 91–99, 147-153, 246-251 and 330–334 days after treatment (DAT) for analysis. Each time-course soil sample was extracted successively with acetonitrile and a mixture of acetonitrile (ACN) and water (7:3, v/v). All the extracts were pooled and assayed by LSC prior to further processing.

An aliquot of the pooled extract was concentrated to near dryness on a rotary evaporator. The concentrated sample was dissolved in a mixture of ACN and water (3 mL, 1:2), centrifuged and filtered. Aliquots of the filtered sample were assayed by LSC and analysed by HPLC. The radioactivity remaining in the soil after extraction was determined by combustion.

For metabolite identification, extracts from all the test soils (ID, IL, NJ and WI soils) were pooled for each label then concentrated on a rotary evaporator. The remaining aqueous portion was partitioned using EtOAc. The EtOAc fractions were concentrated to near dryness, re-dissolved in a mixture of ACN/H2O then used for the isolation of various degradation products by HPLC fraction

collection. Selected HPLC fractions were combined, concentrated, and assayed by LSC and HPLC. The identity of the degradation products found in the study was established with a combination of HPLC co-chromatography with reference standards, full scan LC/MS and LC/MS/MS and NMR. One metabolite, M800H26, was identified by GC/MS.

Examples for the proportion of metabolites formed are given in Tables 34 to 35. Qualitatively the degradation in other soils is similar. For these tables values are the average of two replicates:

- %TAR Others consists of several products, some identified, none > 5% TAR
- %TAR Others = %TAR Extractable (from material balance Table) - %TAR Identified
- %TAR Identified = Sum %TAR [M800H31, 26, 7, 22, 2, 1, 8, and Saflufenacil]
- % Extractable Identified = (%TAR Identified / %TAR Extractable)*100

Table 34 Biotransformation of [^{14}C-Uracil]-saflufenacil in Idaho soil (sandy loam) under aerobic conditions

Metabolite Code (HPLC Retention, min)	%TAR Distribution of Degradation Products with Time									
	0 DAT	7 DAT	14 DAT	25 DAT	43 DAT	62 DAT	91 DAT	147 DAT	251 DAT	334 DAT
M800H31		1.40	3.86	4.71	2.58	3.89	1.08	4.40	5.64	10.85
M800H26		0.88								
M800H22		0.36	2.03	2.46	2.04	1.82	2.05	3.36	5.02	5.02
M800H02		2.42	1.37	3.46	7.04	13.58	25.24	29.04	24.04	26.35
M800H01		1.91	2.20	4.86	8.22	6.73	6.16	1.14	2.82	2.11
M800H08		6,.2	6.54	14.57	15.58	16.11	17.80	13.61	18.04	10.35
Saflufenacil	98.34	72.40	60.22	44.00	39.80	30.07	17.09	5.42	4.87	3.75
% TAR Others	0.01	2.06	1.04	1.40	4.25	7.86	13.99	24.36	20.87	20.47
%TAR Extractable	98.33	87.75	77.26	75.46	79.51	80.06	83.41	81.33	81.30	78.90
%TAR (V+ O)[1]	0.00	1.58	3.14	3.70	4.32	4.81	5.23	5.58	6.04	5.59
%TAR NER[2]	0.47	6.44	12.29	18.70	12.78	12.71	9.98	12.08	9.29	16.67
%TAR Recovered	98.80	95.77	92.69	97.86	96.61	97.58	98.62	98.99	96.63	101.16
Total %TAR Identified	98.34	85.69	76.22	74.06	75.26	72.20	69.42	56.97	60.43	58.43
% Extractable Identified	100.01	97.65	98.65	98.15	94.66	90.19	83.23	70.05	74.33	74.05

[a] (V + O): Volatiles (CO2+ Organic);

[b]: NER: non extractable residues

Table 35 Biotransformation of [^{14}C-Phenyl]-saflufenacil in Idaho soil (sandy loam) under aerobic conditions

Metabolite Code (HPLC Retention, min)	%TAR Distribution of Degradation Products with Time (%TAR Extractable)									
	0 DAT	7 DAT	14 DAT	25 DAT	43 DAT	57 DAT	99 DAT	153 DAT	246 DAT	330 DAT
M800H07		12.26	26.32	21.56	15.83	11.56	10.98	12.42	14.25	17.72
M800H22		2.23	2.53	3.27	3.02	2.74	5.33	5.87	12.25	4.11
M800H02		0.92	1.61	2.20	5.89	8.68	14.40	12.77	17.94	16.25
M800H01		1.34	0.78	3.17	7.66	10.46	7.40	3.79	2.03	1.27
M800H08		3.09	3.68	10.61	13.01	15.18	21.16	27.76	35.50	14.47
Saflufenacil	98.95	73.24	51.16	41.67	34.53	28.34	18.86	10.91	4.95	3.68
% TAR Others	0.01	4.29	5.57	2.48	5.43	8.47	7.12	8.73	14.83	16.70
%TAR Extractable	98.94	97.37	91.65	84.96	85.37	85.43	85.25	82.25	101.75	74.20
%TAR (V + O)[1]		0.04	0.08	0.17	0.25	0.30	0.42	0.47	0.75	0.07
%TAR NER[2]	0.41	2.77	6.13	12.93	13.02	18.43	11.68	13.40	10.76	22.99

Metabolite Code (HPLC Retention, min)	%TAR Distribution of Degradation Products with Time (%TAR Extractable)									
	0 DAT	7 DAT	14 DAT	25 DAT	43 DAT	57 DAT	99 DAT	153 DAT	246 DAT	330 DAT
%TAR Recovered	99.35	100.18	97.86	98.06	98.64	104.16	97.35	96.12	113.26	97.26
Total %TAR Identified	98.95	93.08	86.08	82.48	79.94	76.96	78.13	73.52	86.92	57.50
% Extractable Identified	100.01	95.60	93.93	97.08	93.64	90.09	91.65	89.39	85.43	77.50

[a] (V + O): Volatiles (CO2+ Organic);

[b]: NER: non extractable residues

The half-life of saflufenacil was calculated using the non-linear first order model. The average aerobic degradation DT_{50} values for saflufenacil were approximately 22 days for the Idaho soil, 17 days for the Illinois soil, 4 days for the New Jersey soil and 17 days for the Wisconsin soil.

The proposed pathway for aerobic soil metabolism is shown in Figure 6.

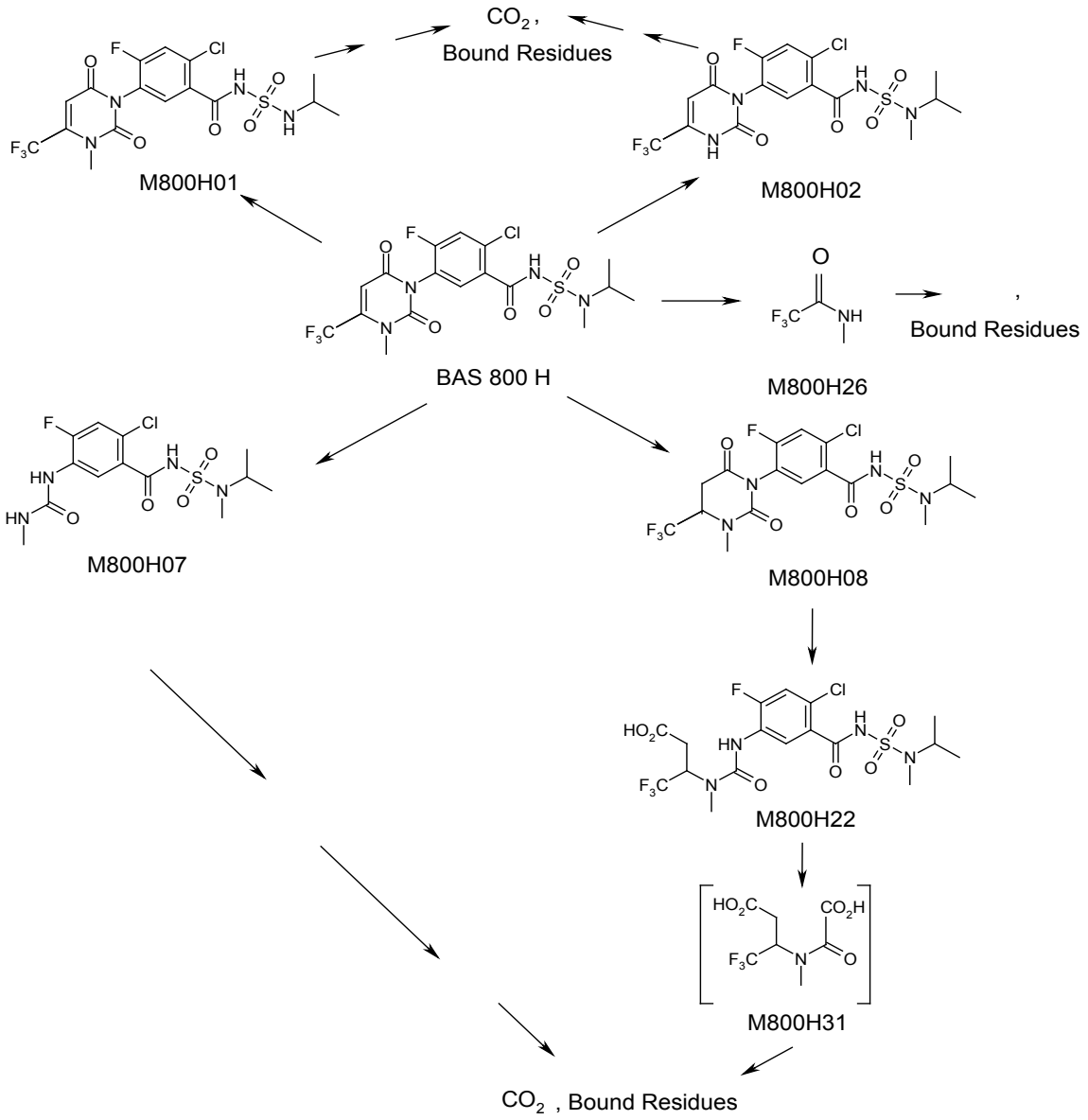


Figure 6 Degradation Pathway for Saflufenacil in Aerobic Soil

Seven field trials were conducted at various locations in the United States and Canada covering a range of soil types and application rates. The primary aim of these studies was to provide data on the levels of saflufenacil and several of its metabolites (M800H01, M800H02, M800H07, M800H08, M800H15 and M800H22) in different soils under several use patterns: pine/vegetation management, typical row crops and orchard/vineyard use (Jordan J.M. *et al*. 2007).

Saflufenacil was applied once to bare soil at a target application rate of 0.4 kg ai/ha with an approximate spray volume of 370 L/ha, the proposed label for pine control use. Soil samples were taken to a depth of 122 cm one day prior to the application and 0, 1, 2, 4, 6, 8, 10, 15, 20, 32, 46, 59, 75, 90, 121, 150, 182, 271, 360, and 451 days following the application. (Jordan J. *et al*. 2007)

The behaviour of saflufenacil was studied following three broadcast application of 50g ai/ha on bare loam, and loamy sand soils in three location of USA. Soil cores were taken to a depth of 122 cm just prior to each of the three applications (-T1, -T2, -T3); immediately after each application (T1, T2, T3); at 3, 5, 10 and 15 days after the first application; and at 2, 4, 6, 10, 15, 20, 30, 45, 60, 75, 90, 121, 150, 180, 270 and 360 days following the last application.

The soil cores were divided into segments prior to freezing and shipment and were stored up to 19 months before analysis. BASF Method D0503 was used to determine the residues of saflufenacil and its metabolites, M800H01, M800H02, M800H07, M800H08, M800H15, and M800H22 in soil using LC/MS/MS (Saha, 2007).

The major route of dissipation of saflufenacil in this bare soil field trial was degradation by aerobic processes. Despite favourable leaching conditions, saflufenacil was not observed below 61 cm in the pine vegetation management study and below 15 cm (with one exception) in the other studies , indicating that mobility in the loamy sand soil was limited by the rapid degradation (DT_{50} = 10.7 days).

Different metabolite were either present at very low concentrations or were not detectable at all, and showed very low mobility

In the pine study, detections of M800H08 in successive depth segments over time coincided with the accumulative excess water flux. M800H08 appears to be more persistent than saflufenacil under field conditions resulting in greater mobility, which is consistent with laboratory studies. However, there was no carryover of Saflufenacil or any metabolites. All measured residue values were < LOQ (0.01 mg/kg) at the end of the 360-day study period.

Table 36 DT_{50}, DT_{75} and DT_{90}-Values for the Degradation of saflufenacil in various soils (laboratory and field studies)

Study	Kinetic endpoint (days)[a]		
	DT_{50}	DT_{75}	DT_{90}
Aerobic soil metabolism			
Idaho	16.4	45.4	122
Illinois	21.4	56.3	138
New Jersey	3.80	14.8	66.4
Wisconsin	17.4	41.1	85.8
Field soil dissipation			
GA (400 g ai/ha)	10.7	21.4	35.5
AR (150 g ai/ha)	6.25	24.4	50.4
IL (150 g ai/ha)	11.1	22.1	36.7
MB (150 g ai/ha)	35.5	71.1	118
WA (50 g ai/ha × 3)	1.36	2.72	4.52
ON (50 g ai/ha × 3)	23.6	47.3	78.6
CA (50 g ai/ha × 3)	32.2	64.5	107

[a] For summary purposes, the kinetic endpoints reported in this Table represent the average from separate kinetic analysis of ^{14}C-phenyl and ^{14}C-uracil radiolabels for the aerobic soil metabolism study.

The metabolic pathway is the same as determined based on the aerobic degradation studies (Figure 6)

Photolysis

Photolysis of U-^{14}C phenyl label] saflufenacil in a light/dark experiment and [^{14}C uracil and U-^{14}C phenyl label] saflufenacil in a continuous irradiation experiment was studied using a loamy sand soil. The soil used was the same as one used in the aerobic soil metabolism study (Ta C, 2007).

Approximately 20 g aliquots of the test soil were treated at a concentration of 0.26 mg/kg, which is equivalent to the maximum application rate of 400 g ai/ha based on application to a soil segment of 1 cm deep. The treated soil samples were subjected to a light/dark cycle of 12 h irradiation/12 h darkness for 30 days or continuous irradiation for 15 days. The average of pre- and post-study Xenon lamp light intensity, measured during the duration of the study, was approximately 597 W/m^2, which is comparable to the natural sunlight intensity in the spring at 40° N latitude (584 W/m^2). The temperature of the soil was maintained at 22 ± 1 °C during the irradiation and darkness periods. The soil moisture was maintained by weighing samples daily and adding water as necessary. Control soil samples were similarly treated and were incubated in the dark at a temperature of 22 ± 1 °C during the course of the study.

The light/dark and dark control samples from the first experiment (Experiment 1) were analysed concurrently at 0, 6, 14, 22, and 30 days after treatment (DAT). The continuously irradiated and the dark control samples from the second experiment (Experiment 2) were analysed concurrently at 0, 1, 3, 7, 11 and 15 DAT. Volatile residues were collected and analysed at the soil sampling intervals.

The samples were extracted immediately after sampling with acetonitrile (one time) and a mixture of acetonitrile and water (70:30, v/v, two times). The soil extracts were pooled and concentrated to dryness on a turbo vap. The residual materials were redissolved in an acetonitrile/water mixture (1:1, v/v) and analysed by LSC and HPLC. The radioactivity remaining in the soil after extraction (Non Extractable Residues, NER) was determined by combustion.

Parent and transformation products were quantitated by HPLC with radiomatic detector. Confirmation of parent and identification of transformation products was done by LC/MS/MS and NMR.

Table 37 Degradation of saflufenacil in photolysis experiments

Product	Days After Treatment					
	0	6	14	22	30	
^{14}C-Phenyl saflufenacil dark control 1st exp.	97.7	77.5	51.7	62.4	65.2	
^{14}C-Phenyl saflufenacil dark control 2nd exp	97.34	94	91.6	86.36	80.23	
^{14}C-Uracil saflufenacil dark control 2nd exp	96.91	94.58	91.5	82.64	75.38	
^{14}C-Phenyl saflufenacil light/dark cycle 1st exp.	97.7	69.1	59.3	57.9	43.1	
	Days After Treatment					
	0	1	3	7	11	15
^{14}C-Phenyl saflufenacil continuous irradiation 2nd exp.	97.34	87.3	78.86	69	60.39	57.02
^{14}C-Uracil saflufenacil continuous irradiation 2nd exp.	96.91	91.8	76.25	72.02	61.88	52.35

The degradation rate constants for saflufenacil under the test conditions were calculated assuming first-order kinetics. The calculated photolysis DT_{50} value of saflufenacil was approximately 29 days for the light/dark cycle and 18 to 20 days for continuous irradiation.

The DT_{50} for true phototransformation could be calculated from data in the report as 66 days for the phenyl labelled saflufenacil in the light/dark cycle and 43 and 41 days for the phenyl and uracil labels, respectively, for continuous irradiation.

For the light/dark experiment, conditions similar to the real field situation, there were no major degradation products from the irradiated samples, for either label, which were greater than 10% TAR at anytime during the experimental. There were 10 minor products (< 10% TAR) observed. There was one major degradation product from the dark samples, and 7 other minor products, none of

which exceeded 5% TAR at any time during the experimental period. The major dark control product was identified by both LC/MS/MS and proton NMR as M800H08.

For the continuous irradiation experiment, the only one major transformation product was an unidentified and unstable product that degraded quickly to M800H01. Minor amounts of M800H01, M800H07, M800H08 and M800H17 were also tentatively identified by HPLC.

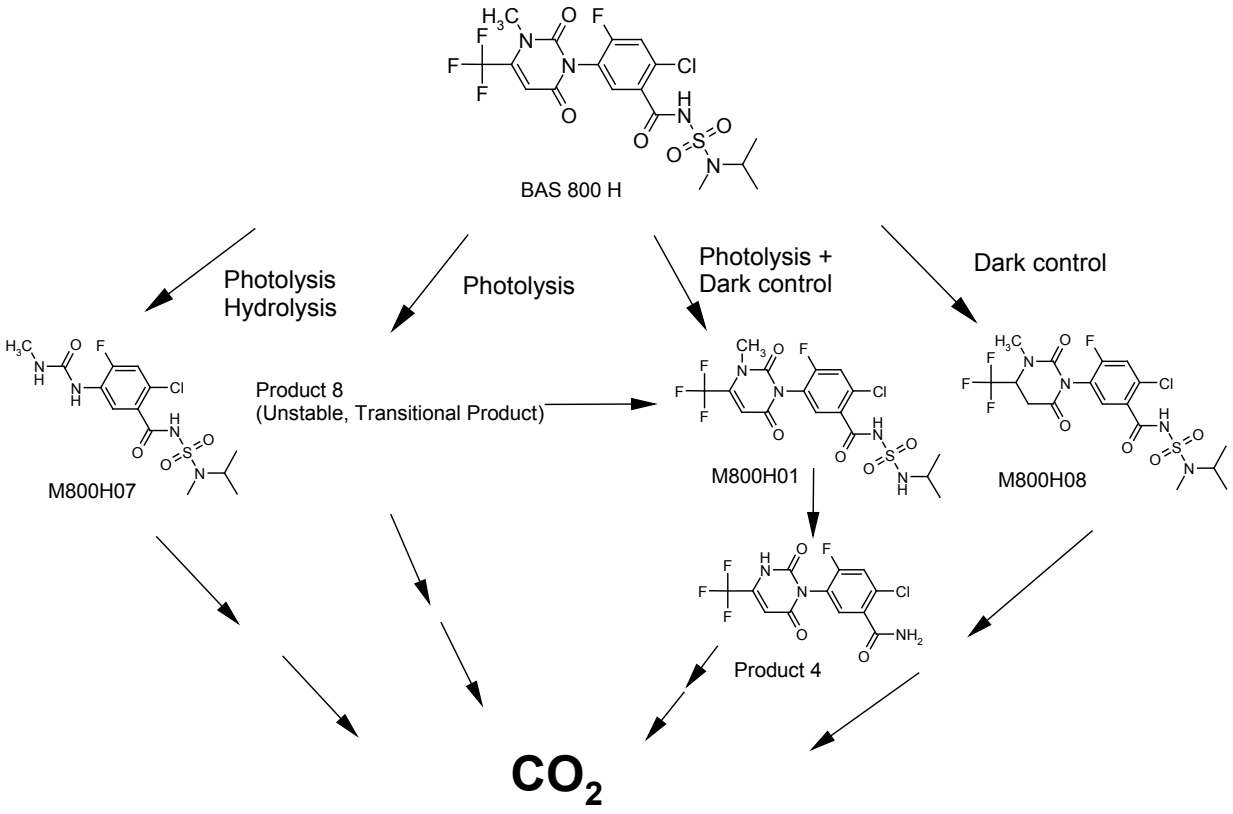


Figure 7 Photolytic degradation pathways for Saflufenacil in soil

Degradation in aquatic system

The hydrolysis of U-^{14}C phenyl label] saflufenacil and [^{14}C-uracil label] saflufenacil investigated in the dark at 25 °C in 0.01 N sterile buffer solutions at pH 5 (acetate), 7 (TRIS) and 9 (TRIS).

For the degradations in all buffers, replicate samples were taken at 0, 1, 3, 8, 15, 21(24) and 30 DAT (Panek M. 2006). For the degradation at pH 9, sampling intervals in addition to those listed above were needed to provide sufficient information on the degradation prior to the half-life. For the uracil label in pH 9 buffer, individual samples were taken at 0.75, 1.75 and 2 DAT, and for the phenyl label, at 0.12, 0.17, 0.25, 0.33 and 2 DAT. Aliquots were removed from the samples in pH 9 buffer for immediate HPLC analysis. After HPLC analysis was initiated for the pH 9 samples, aliquots from all samples were taken for LSC and direct HPLC analysis. The metabolites were identified with HPLC-MS/MS, NMR and GC/MS techniques.

For the uracil label treated samples, the material balance in % TAR ranged from 100.0 to 104.7% with an average of 102.1% for pH 5 buffer; from 99.8 to 106.5% with an average of 101.9% for pH 7 buffer and from 94.8 to100.1% with average of 97.7% for pH 9 buffer. For the phenyl label treated samples, the material balance in % TAR ranged from 98.6 to 101.8% with average of 100.2% for pH 5 buffer; from 98.3 to 102.0% with average of 100.4% for pH 7 buffer and from 98.5 to 106.3% with average of 100.6% for pH 9 buffer.

Table 38 Hydrolysis data of saflufenacil in buffer solutions as TAR%

Interval (DAT)	0	1	3	8	15	21	30
^{14}C-Phenyl, pH 5	100.1	99.5	99.7	100.4	99.5	100.4	100.8
^{14}C-Uracil, pH 5	100.7	101.0	102.2	102.7	101.4	101.7	101.1
^{14}C-Phenyl, pH 7	100.2	99.2	99.2	99.6	94.7	94.4	89.3
^{14}C-Uracil, pH 7	100.29	100.48	101.41	99.12	99.67	98.81	93.80

DAT	0	0.12	0.17	0.25	0.33	1
^{14}C-Phenyl, pH 9	99.75	Na	95.76	na	89.09	74.59
DAT	2	3	8	15	24	30
^{14}C-Phenyl, pH 9	57.51	48.19	24.99	11.97	11.06	3.07
DAT	0	0.75	1	1.75	2	
^{14}C-Uracil, pH 9	100.0		72.29			
DAT	3	8	15	21	30	
^{14}C-Uracil, pH 9	41.38	14.37	3.84	1.29	1.08	

[a] Average of 2 replicate measurements

The DT_{50} of saflufenacil at different pH values were calculated using a simple first order model. The results are given in Table 45.

Table 39 DT_{50} Values for the Hydrolysis of Saflufenacil

pH	label	k ($days^{-1}$)	R^2	DT_{50} (days)
5	both	Stable (not calculated)		
7	phenyl	0.0036	0.905	192.5
	uracil	0.002	0.745	346.5
9	phenyl	0.1168	0.835	5.9
	uracil	0.1643	0.946	4.2

The degradation pathway for hydrolysis of Saflufenacil is shown in Figure 8.

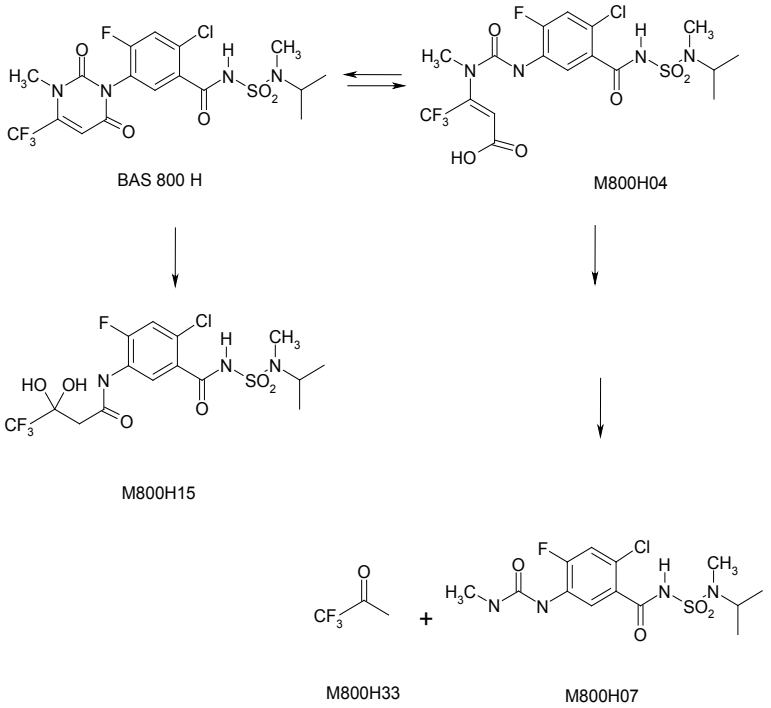


Figure 8 Hydrolysis pathway of saflufenacil

Photochemical degradation

The photolysis of ^{14}C-Saflufenacil (phenyl and uracil label) was conducted in aqueous buffer (pH 5, 0.01 M) and natural water (pH 7.1) at 22 ± 1 °C (Ta C., Trollinger J. 2009).

The concentration of saflufenacil in the treated waters was approximately 10 mg/kg. The treated solutions were continuously exposed to artificial sunlight for about 20 days for the photolysis conducted in aqueous buffer and 21 days for the natural water. The light spectrum and intensity of the Xenon arc lamp was measured at the beginning and end of the irradiation period. The measured intensity and spectrum were comparable to natural sunlight at 40º N latitude. During the irradiation, CO_2-free sterile air was purged over the samples and through NaOH traps. The dark control samples consisted of the test buffer (pH 5) and natural water treated with ^{14}C-phenyl and uracil labelled saflufenacil and were stored in a dark incubator maintained at 22±1 °C.

Treated samples, (irradiated and dark control) were analysed concurrently by LSC and HPLC after about 0, 2, 7, 10, 15, and 20 days after treatment (DAT) for the photolysis in aqueous buffer and about 0, 1, 2, 4, 7, 10, 15, and 21 days after treatment (DAT) for the photolysis in natural water.

Quantitation was done by HPLC and a radiometric solid cell LiGl, 200 μm and UV 270 nm detectors. Confirmation of parent and identification of transformation products was done by LC/MS/MS and NMR spectrometer with standard probe.

The material balance for saflufenacil in pH 5 aqueous buffer under dark conditions ranged from 99.89–103.31% TAR and 96.82–101.72% TAR, respectively, for the phenyl and uracil labels. The material balance for the irradiated samples ranged from 89.44–102.76% TAR for the phenyl label and 92.99–101.72% for the uracil label. Less than 3% TAR was found as cumulative volatile radioactivity by the end of the photo-period for both labels.

The material balance for saflufenacil in natural water under dark conditions ranged from 96.68–101.19% TAR and 95.44-101.91% TAR, respectively, for the phenyl and uracil labels. The material balance for the irradiated samples ranged from 96.54–102.26% TAR for the phenyl label and 82.13–100.74% for the uracil label. Less than 3% TAR was found as cumulative volatile radioactivity by the end of the photo-period in both labels.

Saflufenacil degraded rapidly under photolytic conditions with half-lives of 26.8–35.2 and 9.7–9.8 days from the pH5 buffer and the natural water, respectively. Saflufenacil is fairly stable in both pH5 buffer and the natural water in the dark, although trifluoroacetone and M800H07 were found in the latter.

From the pH5 buffer there are several minor photoproducts formed from both the phenyl and uracil labels; however, only one of them exceeds 10% TAR, but only after 20 days of constant irradiation. This unknown was < 10% TAR in the natural water. In the natural water, there are two major photoproducts formed from the uracil label and identified as trifluoroacetic acid and trifluoroacetone and several other minor photoproducts (none of them exceeds 10% TAR) from both labels.

Saflufenacil degrades in water under photolytic conditions by the opening of the uracil ring followed by the fragmentation of the uracil ring to form M800H04, M800H15, M800H07, trifluoroacetone, and trifluoroacetic acid. Hydroxylation of the trifluoromethyl group and the cleavage of the sulfonylurea side chain result in other minor degradation products.

Crop rotation studies

The metabolism and distribution of saflufenacil in succeeding crops were investigated using the active substance, radiolabelled (^{14}C) either in the 4-position of the uracil ring ("Uracil label") or in the phenyl ring ("Phenyl label") in lettuce, white radish and spring wheat grown in plastic containers filled with a loamy sand soil. The aging of the soil and the cultivation of the crops took place under natural climatic conditions without the influence of rain in a glass roofed vegetation hall or in the glass house depending on the climatic conditions outside (Veit, P., Glaessgen W.E. 2007).

A single spray application of either Uracil- or Phenyl-^{14}C-saflufenacil at a nominal application rate of 150 g ai/ha was performed. The active substance was applied as EC formulation to the bare soil. The nature and level of the residues were investigated after plant-back intervals of 30, 120 and 365 days. An additional soil aging period was inserted for lettuce and white radish because of early growth inhibition after 30 days. Plant samples were harvested at maturity and additional wheat forage samples were taken 48 to 68 DAP. Soil samples were taken after ploughing and after harvest of the mature crops for each plant-back interval.

Ripe lettuce heads were harvested and the roots remained in the soil. Mature white radishes were pulled from the soil and separated into the edible parts (root) and the remaining green parts (tops). Mature wheat was harvested by cutting the plants just above the soil line. The plant material was separated into wheat straw, chaff and grain, and the roots remained in the soil. In addition, immature green plants were harvested (forage). Soil samples were taken after application, after the individual plant-back intervals, and after harvest of the mature crops. All samples were stored in a freezer at -18°C or below immediately after they were taken and until they were transferred to the metabolism laboratory.

Aliquots of homogenized solid plant samples were dried and combusted to determine the total radioactive residues with liquid scintillation counting (LSC). The limits of quantitation were determined at 0.00059–0.00077 mg/kg for lettuce head and 0.00157–0.00204 mg/kg for spring wheat straw.

Weighed subsamples of plant material were homogenized and extracted three times with methanol followed by extraction with water twice. Combined extracts were assayed by LSC and referred as extractable radioactive residues (ERR). The residue after solvent extraction was combusted for the determination of the residual radioactive residue (post extraction solids) (RRR). The total radioactive residues (TRR) were the result of combustion analyses of the sum of ERR and RRR.

For metabolite identification and characterization, HPLC-MS/MS analysis was performed from purified methanol extracts of spring wheat chaff (30 DAT, phenyl label, organic phases from liquid/liquid partitioning and 120 DAT, uracil label samples). Further metabolites were identified by co-chromatography with reference items, including an extract prepared in a biotransformation experiment with corn cell cultures incubated with Saflufenacil. Peak assignment in the other samples was done by comparison of retention times and metabolite patterns.

Table 40 Total radioactive residues in soil samples following treatment with ^{14}C-saflufenacil and plant-back intervals of 30, 58,120 and 365 days

Matrix	Plant-back interval (days)	Phenyl label		Uracil label	
		TRR (%) combusted	TRR (%) calculated	TRR (%) combusted	TRR (%) calculated
Lettuce head	30	0.007	0.007	0.092	0.085
White radish root		0.004	0.003	0.036	0.034
White radish top		0.032	0.025	0.207	0.167
Spring wheat forage		0.055	0.048	0.204	0.183
Spring wheat straw		0.132	0.125	0.362	0.314
Spring wheat chaff		0.399	0.383	1.752	1.604
Spring wheat grain		0.017	0.017	0.376	0.370
Soil after ploughing		0.061	n. a.	0.031	n. a.
Lettuce soil after harvest		0.042	n. a.	0.035	n. a.
White radish soil after harvest		0.031	n. a.	0.006	n. a.
Spring wheat soil after harvest		0.008	n. a.	0.008	n. a.
Lettuce head	58	0.008	0.010	0.078	n. e.
White radish root		0.004	n. e.	0.038	n. e.
White radish top		0.021	0.014	0.205	n. e.
Soil after ploughing*		0.035	n. a.	0.027	n. a.
Soil after ploughing		0.052	n. a.	0.041	n. a.
Lettuce soil after harvest		0.016	n. a.	0.012	n. a.
White radish soil after harvest		0.058	n. a.	0.015	n. a.

Matrix	Plant-back interval (days)	Phenyl label		Uracil label	
		TRR (%) combusted	TRR (%) calculated	TRR (%) combusted	TRR (%) calculated
Lettuce head	120	0.007	n. e.	0.091	0.089
White radish root		0.002	n. e.	0.010	0.010
White radish top		0.012	0.014	0.050	0.046
Spring wheat forage		0.019	0.020	0.064	0.051
Spring wheat straw		0.089	0.089	0.217	0.196
Spring wheat chaff		0.076	0.068	0.661	0.629
Spring wheat grain		0.006	n. e.	0.096	0.094
White radish soil after harvest		0.018	n. a.	0.011	n. a.
Spring wheat soil after harvest		0.009	n. a.	0.016	n. a.
Lettuce head	365	0.001	n. e.	0.002	n. e.
White radish root		0.004	n. e.	0.008	n. e.
White radish top		0.007	n. e.	0.092	0.087
Spring wheat forage		0.012	0.011	0.018	0.017
Spring wheat straw		0.101	0.095	0.453	0.356
Spring wheat chaff		0.118	0.114	0.419	0.439
Spring wheat grain		0.045	0.044	0.116	0.116
Soil after ploughing		0.020	n. a.	0.019	n. a.
Lettuce soil after harvest		0.065	n. a.	0.076	n. a.
White radish soil after harvest		0.015	n. a.	0.013	n. a.
Spring wheat soil after harvest		0.015	n. a.	0.012	n. a.

n. a. - not applied n. e. - no extraction performed * - white radish removed

Table 41 Summary of identified components in extractable and residual radioactive residues from rotational crop matrices following their cultivation in soil treated with ^{14}C-Phenyl- and Uracil labelled saflufenacil after plant-back intervals of 30, 120 and 365 days

Metabolite	Crop parts													
	Lettuce heads		White radish roots		White radish tops		Wheat forage		Wheat straw		Wheat chaff		Wheat grain	
	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
Phenyl label														
Plant-back interval 30 days														
TRR	0.007	100	0.003	100	0.025	100	0.048	100	0.125	100	0.383	100	0.017	100
ERR[1]	0.006	80.4	0.003	91.4	0.024	96.2	0.047	97.4	0.117	93.9	0.353	92.1	0.010	57.3
identified in ERR	0.004	54.4	0.000	0.0	0.013	49.7	0.026	54.5	0.075	60.1	0.251	65.5	0.004	20.7
Saflufenacil	0.003	34.2			0.004	13.8	0.001	1.9	0.000	0.0	0.000	0.0	0.000	0.0
M800H01	0.001	13.7			0.004	16.0	0.004	7.7	0.003	2.2	0.007	1.9	0.000	2.1
M800H03	0.000	2.4			0.001	3.9	0.004	8.1	0.007	5.9	0.029	7.5	0.000	2.1
M800H11	0.000	3.0	n. a.		0.003	13.1	0.002	4.2	0.005	4.1			0.000	1.3
M800H05	0.000	0.0			0.000	0.0	0.008	17.6	0.014	11.4	0.053	13.8	0.000	2.1
M800H35 (and M800H09)[1]	0.000	1.0			0.001	3.0	0.007	15.1	0.045	36.5	0.162	42.3	0.002	13.1
characterized in ERR	0.002	26.1	0.003	91.4	0.012	46.5	0.021	42.9	0.042	33.8	0.102	26.6	0.006	36.6
further polar[2]	0.000	3.5	0.000	5.6	0.001	3.2	0.000	0.0	0.000	0.0	0.006	1.5	0.001	3.9
M800H10 and/or unknown	0.000	3.2	0.000	0.0	0.004	15.9	0.007	14.2	0.017	13.6	0.044	11.4	0.000	2.7
further medium polar[3]	0.001	16.2	0.003	85.5	0.005	21.6	0.012	24.8	0.014	11.0	0.053	13.7	0.001	6.3
further non-polar[4]	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
aqueous extract	0.000	3.1	0.000	0.3	0.001	5.9	0.002	3.9	0.011	9.2	n. a.	n. a.	0.004	23.7
RRR	0.001	19.6	0.000	8.6	0.001	3.8	0.001	2.6	0.008	6.1	0.030	7.9	0.007	42.7
Plant-back interval 120 days														
TRR					0.014	100	0.020	100	0.089	100	0.068	100		
ERR[1]					0.013	96.6	0.020	96.8	0.084	94.9	0.062	90.7		
identified in ERR					0.005	38.2	0.011	52.3	0.047	53.1	0.032	46.7		
Saflufenacil					0.001	8.4	0.000	0.0	0.000	0.0	0.000	0.0		
M800H01					0.001	10.5	0.001	4.9	0.002	2.7	0.001	1.5		
M800H03					0.000	2.2	0.001	4.1	0.005	5.4	0.002	3.2		
M800H11					0.001	9.0	0.001	3.3	0.003	3.2	0.000	0.0		
M800H05					0.000	0.0	0.001	7.4	0.007	7.5	0.003	3.8		
M800H35 (and M800H09)[1]	n. a.		n. a.		0.001	8.2	0.007	32.5	0.030	34.3	0.026	38.3	n. a.	
characterized in ERR					0.008	58.3	0.009	44.5	0.037	41.8	0.030	44.0		
further polar[2]					0.001	10.1	0.000	0.0	0.000	0.0	0.000	0.0		
M800H10 and/or unknown					0.003	20.0	0.004	20.7	0.012	13.1	0.004	6.1		
further medium polar[3]					0.003	24.3	0.004	19.8	0.017	18.9	0.008	12.2		
further non-polar[4]					0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0		
aqueous extract					0.001	3.9	0.001	3.9	0.009	9.8	0.017	25.7		
RRR					0.000	3.4	0.001	3.2	0.005	5.1	0.006	9.3		
Plant-back interval 365 days														
TRR							0.011	100	0.095	100	0.114	100	0.044	100
ERR[1]							0.010	86.7	0.057	60.0	0.066	57.8	0.007	16.5
identified in ERR							0.004	33.8	0.032	34.2	0.035	31.0	0.001	3.3
Saflufenacil							0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
M800H01							0.000	1.8	0.000	0.0	0.000	0.0	0.000	0.0
M800H03							0.000	1.2	0.000	0.0	0.000	0.0	0.000	0.0
M800H11							0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
M800H05							0.000	2.7	0.002	2.0	0.000	0.0	0.000	0.2
M800H35 (and M800H09)[1]	n. a.		n. a.		n. a.		0.003	28.1	0.031	32.2	0.035	31.0	0.001	3.2
characterized in ERR							0.006	52.9	0.024	25.8	0.031	26.8	0.006	13.1
further polar[2]							0.001	4.7	0.003	3.1	0.002	1.6	0.001	2.9
M800H10 and/or unknown							0.002	17.3	0.006	6.3	0.003	2.7	0.000	0.3
further medium polar[3]							0.003	27.5	0.009	9.9	0.011	10.0	0.001	2.7
further non-polar[4]							0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
aqueous extract							0.000	3.4	0.006	6.5	0.014	12.4	0.003	7.2
RRR							0.002	13.3	0.038	40.0	0.048	42.2	0.036	83.5
Uracil label														
Plant-back interval 30 days														
TRR	0.085	100	0.034	100	0.167	100	0.183	100	0.314	100	1.604	100	0.370	100
ERR[1]	0.084	99.3	0.034	98.9	0.166	99.5	0.182	99.2	0.305	97.2	1.534	95.6	0.351	94.7
identified in ERR	0.024	98.1	0.007	88.4	0.044	95.7	0.048	93.7	0.079	84.8	0.387	92.1	0.074	87.8
Saflufenacil	0.004	4.4	0.000	0.0	0.002	1.1	0.001	0.5	0.000	0.0	0.000	0.0	0.000	0.0
M800H01	0.002	2.8	0.000	0.0	0.005	2.8	0.002	1.2	0.002	0.07	0.003	0.2	0.000	0.0
M800H03	0.000	0.0	0.000	0.0	0.000	0.0	0.003	1.5	0.003	0.9	0.016	1.0	0.000	0.0

Metabolite	Crop parts													
	Lettuce heads		White radish roots		White radish tops		Wheat forage		Wheat straw		Wheat chaff		Wheat grain	
	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
M800H11	0.001	1.2	0.000	0.0	0.004	2.2	0.001	0.6	0.004	1.4			0.000	0.0
M800H05	0.000	0.0	0.000	0.0	0.000	0.0	0.005	2.5	0.011	3.6	0.037	2.3	0.000	0.0
M800H09	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.003	0.8	0.009	0.6	0.000	0.0
M800H29[5]	0.017	89.8	0.007	88.4	0.034	83.6	0.037	87.4	0.055	77.4	0.322	88.1	0.074	87.8
characterized in ERR	0.001	1.2	0.004	10.6	0.006	3.9	0.010	5.5	0.039	12.4	0.056	3.5	0.025	6.9
further polar[2]	0.000	0.0	0.000	0.9	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.025	6.9
M800H10 and/or unknown	0.000	0.0	0.000	0.0	0.000	0.0	0.002	1.0	0.006	1.8	0.015	0.9	0.000	0.0
further medium polar[3]	0.001	0.6	0.003	9.3	0.004	2.2	0.005	2.5	0.023	7.2	0.041	2.6	0.000	0.0
further non-polar[4]	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
aqueous extract	0.000	0.6	0.000	0.3	0.003	1.7	0.004	2.1	0.011	3.4	n. a.	n. a.	n. a.	n. a.
RRR	0.001	0.7	0.000	1.1	0.001	0.05	0.001	0.8	0.009	2.8	0.070	4.4	0.020	5.3
Plant-back interval 120 days														
TRR	0.089	100	0.010	100	0.046	100	0.051	100	0.196	100	0.629	100	0.094	100
ERR[1]	0.089	99.7	0.010	97.2	0.045	97.0	0.051	99.7	0.194	99.0	0.619	98.3	0.090	95.1
identified in ERR	0.021	97.6	0.003	93.8	0.011	90.0	0.012	93.3	0.051	84.5	0.122	85.0	0.017	78.2
Saflufenacil	0.001	1.7	0.000	3.1	0.001	3.2	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
M800H01	0.000	0.0	0.000	1.3	0.001	2.0	0.001	1.2	0.003	1.5	0.000	0.0	0.000	0.0
M800H03	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.003	1.6	0.000	0.0	0.000	0.0
M800H11	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.003	1.3	0.000	0.0	0.000	0.0
M800H05	0.000	0.0	0.000	0.0	0.000	0.0	0.001	1.2	0.006	3.1	0.000	0.0	0.000	0.0
M800H09	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.002	1.2	0.000	0.0	0.000	0.0
M800H29[5]	0.019	95.9	0.002	89.3	0.009	84.8	0.011	90.9	0.034	75.8	0.122	85.0	0.017	78.2
characterized in ERR	0.002	2.1	0.000	3.4	0.003	7.0	0.003	6.4	0.028	14.5	0.084	13.3	0.016	16.9
further polar[2]	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
M800H10 and/or unknown	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.006	3.1	0.000	0.0	0.000	0.0
further medium polar[3]	0.000	0.0	0.000	2.9	0.002	4.0	0.001	1.3	0.012	6.1	0.000	0.0	0.000	0.0
further non-polar[4]	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
aqueous extract	0.002	2.1	0.000	0.5	0.001	3.0	0.003	5.1	0.010	5.3	0.084	13.3	0.016	16.9
RRR	0.000	0.3	0.000	2.8	0.001	3.0	0.000	0.3	0.002	1.0	0.011	1.7	0.005	4.9
Plant-back interval 365 days														
TRR					0.087	100	0.017	100	0.356	100	0.439	100	0.116	100
ERR [a]					0.084	96.0	0.015	87.1	0.300	84.4	0.380	86.4	0.064	55.3
identified in ERR					0.019	93.2	0.003	80.1	0.060	73.7	0.082	81.6	0.010	37.3
Saflufenacil					0.001	0.6	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
M800H01					0.000	0.4	0.000	0.4	0.000	0.0	0.000	0.0	0.000	0.0
M800H03					0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
M800H11					0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
M800H05					0.000	0.0	0.000	0.3	0.000	0.0	0.000	0.0	0.000	0.0
M800H09					0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
M800H29[e]	n. a.		n. a.		0.018	92.2	0.003	79.4	0.060	73.7	0.082	81.6	0.010	37.3
characterized in ERR					0.002	2.8	0.001	7.0	0.038	10.7	0.021	4.8	0.021	18.0
further polar [b]					0.000	0.0	0.001	2.9	0.000	0.0	0.000	0.0	0.012	10.6
M800H10 and/or unknown					0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
further medium polar [c]					0.000	0.4	0.000	0.8	0.000	0.0	0.000	0.0	0.000	0.0
further non-polar [d]					0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0	0.000	0.0
aqueous extract					0.002	2.4	0.001	3.3	0.038	10.7	0.021	4.8	0.009	7.4
RRR					0.004	4.0	0.002	12.9	0.056	15.6	0.060	13.6	0.052	44.7

n. a. - not sampled/analysed

[a] added from combined methanol and combined aqueous extract;

[b] "polar" with retention times between 0 and 20 minutes

[c] "medium polar" with retention times between 20 and 75 minutes;

[d] "non-polar" with retention times above 75 minutes

[e] re-calculated in consideration of the molecular mass of TFA

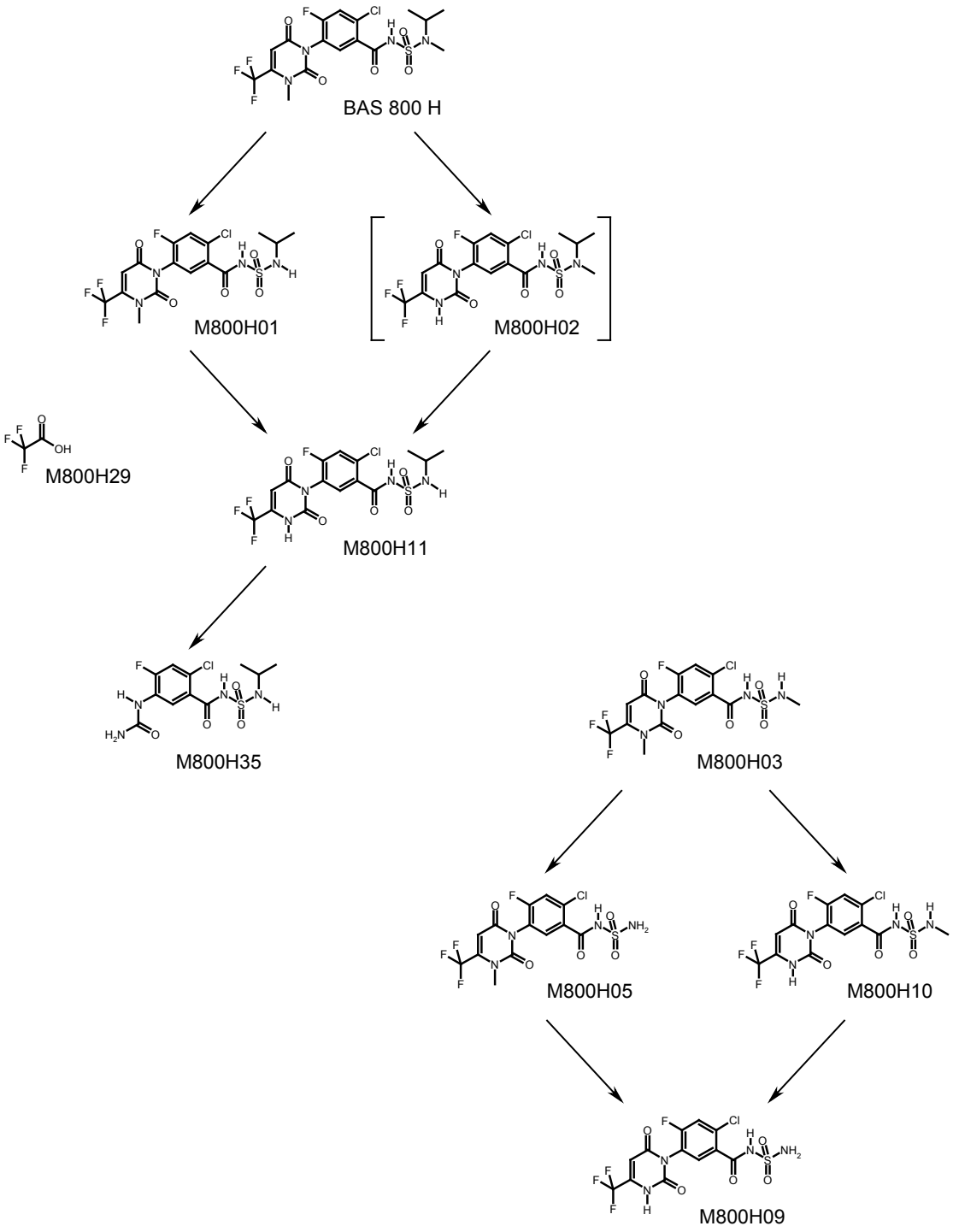


Figure 10 Proposed Metabolic Profile of saflufenacil in Rotational Crops

Field rotational crop studies were conducted in representative rotational crops (radish, lettuce, and wheat) in NAFTA Growing Regions 2 (GA, three trials) and 10 (CA, three trials) (Norris F.A., Saha M. 2007.)

Saflufenacil (70% WG) was applied as a single pre-emergence application to the soil (at the time of planting of the primary crop, wheat) at 0.148–0.154 kg ai/ha. The applications were made in 197–224 L/ha water using ground equipment. An adjuvant was included in the spray mixture together with ammonium sulphate liquid fertilizer. At 4, 6 and 9 months after treatment, the primary crop was

destroyed (mowed) and the representative rotational crops were planted at a number of time intervals post-treatment (days after treatment; DAT): 119-125, 180-183, and 270-274 DAT.

The rotational wheat RAC samples were harvested at commercial maturity; 59-147 days after planting (DAP) for forage and hay (BBCH 39-59) and 121-223 days after planting for grain and straw (maturity). The rotational radish RAC samples (tops and root) were harvested 34-169 days after planting (BBCH 45-49). The rotational leaf lettuce RAC samples (leaves) were harvested 39-187 days after planting (BBCH 45-49).

Rotational crop RAC samples were analysed for residues of saflufenacil using BASF Analytical Method No. D0603. Residues were extracted with methanol/water, concentrated to an aqueous solution and liquid-partitioned with acetate/cyclohexane/TFA. The organic phase is evaporated to dryness, resuspended in methanol/water and subjected to HPLC-MS/MS analysis. MS/MS detection in the positive ionization mode was used to monitor ion transitions from *m/z* 501→349 for Saflufenacil, *m/z* 473→335 for M800H11, *m/z* 353→232 for M800H35. The validated limit of quantitation is 0.01 mg/kg each for parent Saflufenacil and its metabolites M800H11 and M800H35, except for wheat forage, hay and straw, for which the LOQ is 0.025 mg/kg each.

The residues of saflufenacil, M800H11 and M800H35 were below the LOQ in all samples of wheat (forage, hay, grain and straw), radish (tops and root), and lettuce (leaves) harvested from plant-back intervals of 119-125, 180-183, and 270-274 days.

METHODS OF RESIDUE ANALYSIS

Efficiency of extraction

The extractability and accountability of various metabolites and the residues of parent Saflufenacil were investigated applying solvent systems were acetonitrile/water 70:30 (v:v), methanol/water 70:30 (v:v) and methanol and water used sequentially (Thiaener J., Hafemann C. 2007). The relative quantities of the analytes defined for the plant residue method of saflufenacil (M800H11, M800H35 and saflufenacil) after the extraction with the different solvent systems were compared (Nejad H., Hafemann C. 2008). The plant samples used were soya bean forage, pod and straw after pre-emergence treatment with ^{14}C-phenyl ring labelled saflufenacil obtained from a soya bean metabolism study.

The total radioactive residue (TRR) of the samples was measured within the metabolism study in soya beans. These TRR values were the basis for calculation of extractability and quantities of Saflufenacil and the metabolites M800H11 and M800H35. The soya bean samples were extracted according to BASF method No. D0603. Appropriate aliquots of liquid samples were mixed with scintillator and two or three replicates were measured in a liquid scintillation counter with internal quench correction. The results were expressed in disintegrations per minute (dpm). Extracts and reference items were analysed by High Performance Liquid Chromatography. Co-chromatography was performed in order to identify the metabolites M800H11 and M800H35 in selected extracts. Appropriate aliquots of extracts were spiked with aliquots of the metabolites and the mixture was submitted to radio-HPLC.

The results of the individual extraction procedures are summarized in Tables 43–45.

Table 42 Extractability of radioactive residue in soya bean samples with different solvents

Solvent	Forage (40 DAT [a])		Pod (95 DAT [a])		Straw (95 DAT [a])	
	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Acetonitrile/Water						
TRR calc. [b]	0.081		0.179		0.431	
Acetonitrile/ Water Extract [c]	0.071	82.30	0.104	57.14	0.285	74.56
Residues	0.016	19.08	0.082	44.86	0.094	24.53
Sum		101.38		102.00		99.09
Methanol/Water						
TRR calc. [b]	0.081		0.179		0.431	
Methanol/Water Extract [d]	0.063	73.66	0.043	23.71	0.265	69.27

Solvent	Forage (40 DAT [a])		Pod (95 DAT [a])		Straw (95 DAT [a])	
	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Residues	0.020	22.97	0.137	75.23	0.098	25.56
Sum		96.63		98.94		94.83
Methanol + Water sequentially						
TRR calc. [b]	0.081		0.179		0.431	
Methanol Extract	0.065		0.027		0.253	
Water Extract	0.014		0.064		0.091	
Methanol + Water Extract	0.079	91.32	0.091	50.11	0.344	89.90
Residues	0.010	11.40	0.100	54. 75	0.033	8.72
Sum		102.72		104.87		98.62

[a] DAT - days after treatment

[b] TRR was taken from the metabolism study II A 6.2.1/2 and was calculated as sum of extractable and non-extractable residues

[c] Acetonitrile/ water 70/30 (v/v)

[d] Methanol/ water 70/30 (v/v)

Table 43 Quantities of saflufenacil and its metabolites M800H11 and M800H35 in Extracts of Soya bean Matrices after Pre-emergence Treatment with ^{14}C-saflufenacil (phenyl label)

	Acetonitrile/Water			Methanol/Water			Methanol and Water Pooled sample		
Designation	[%ROI]	[mg/kg]	[% TRR]	[%ROI]	[mg/kg]	[% TRR]	[%ROI]	[mg/kg]	[% TRR]
Soya bean Forage Extracts									
ERR		0.071	82.3		0.063	73.66		0.079	91.32
ERR concentrated		0.066	76.33		0.060	70.19		0.074	86.55
M800H35	9.64	0.006	7.36	8.85	0.005	6.21	12.76	0.010	11.05
M800H11	3.76	0.002	2.87	5.90	0.004	4.14	4.48	0.003	3.88
Saflufenacil	26.6	0.017	20.31	22.75	0.014	15.97	18.09	0.013	15.65
Soya bean Pod Extracts									
ERR		0.104	57.14		0.043	23.71		0.091	50.11
ERR concentrated		0.104	57.23		0.039	21.62		0.088	48.47
M800H35	21.80	0.023	12.48	22.66	0.009	4.9	19.01	0.017	9.22
M800H11	16.89	0.018	9.67	14.39	0.006	3.11	13.51	0.012	6.55
Saflufenacil	2.55	0.003	1.46	5.58	0.002	1.21	6.12	0.005	2.97
Soya bean Straw Extracts									
ERR		0.285	74.56		0.265	69.27		0.344	89.90
ERR concentrated		0.250	65.42		0.242	63.26		0.313	82.02
M800H35	22.95	0.057	15.01	21.83	0.053	13.81	21.31	0.067	17.48
M800H11	25.58	0.064	16.73	26.20	0.063	16.58	25.56	0.080	20.96
Saflufenacil	2.31	0.006	1.51	2.67	0.006	1.69	2.90	0.009	2.38

ERR: Extractable Radioactive Residues

ROI: region of interest

Table 44 Comparison of extraction results from the extractability experiment (from the extractability and accountability study) with the results obtained from the soya bean metabolism study

	Results metabolism study		Results from extractability experiment					
	MeOH + water		MeOH + water		MeOH/water		ACN/water	
Matrix	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]	[mg/kg]	[% TRR]
Forage	0.074	91.8	0.079	91.3	0.063	73.7	0.071	82.3
	0.019	0.005	0.004	0.014	0.004	0.005	0.013	0.003
Pod	0.111	62.1	0.091	50.1	0.043	23.7	0.104	57.1
	Pod	0.003	0.016	0.023	0.002	0.006	0.009	0.005
Straw	0.369	85.5	0.344	89.9	0.263	69.3	0.285	74.6
	0.011	0.107	0.067	0.006	0.063	0.053	0.009	0.080

Analytical methods

Analytical residue methods developed for the determination of residues of Saflufenacil in target crops and animal products (meat, fat, liver, kidney and milk) are summarized in Table 45.

Table 45 Summary table of analytical methods

Matrix	Analyte(s) (purpose of the method)	Method	LOQ	Reference
PLANT				
Wheat grain Garbanzo bean Soya bean seed Orange fruit Peach fruit Wheat hay Corn oil	Saflufenacil M800H11 M800H35 (enforcement and data generation)	HPLC-MS/MS	0.01 mg/kg (portions for human consumption) 0.01 mg/kg (portions for feed items)	Method No. D0603/02 Method validation (Nejasd H, 2007)
Wheat grain Orange fruit Wheat hay Corn oil	Saflufenacil M800H11 M800H35 (enforcement and data generation)	HPLC-MS/MS	0.01 mg/kg (portions for human consumption) 0.01 mg/kg (portions for feed items)	Method No D0603/02 Independent Lab validation (Perez R., Perez S., 2007)
ANIMAL				
Liver Kidney Muscle Fat Milk Cream Skimmed milk Egg	Saflufenacil	HPLC-MS/MS	0.01 mg/kg	Method No L0073/01 Method validation (Grosshans F., Blumenstiel S., 2007)
Liver Kidney Muscle Fat Milk Cream	Saflufenacil	HPLC-MS/MS	0.01 mg/kg	Method No L0073/01 Independent Lab validation Rawle N.

A study was conducted to evaluate the capability of the FDA multi-residue methods to analyse for residues of saflufenacil, M800H11 and M800H35 (Perez R., Tarkalanov N. 2008).

The study specifically evaluated the usefulness of the multi-residue methods described in the FDA Pesticide Analytical Manual (PAM) – Volume I, Third Edition, Jan. 1994: Multi-residue Methods, Protocols B, C, D, E and F for measuring residues of saflufenacil, M800H11 and M800H35. Protocols B, C, D, E and F were tested as per protocol guidelines. The tests indicated that the FDA multiresidue method is not suitable for the determination of the residues of targeted analytes.

BASF Method D0603/02 was developed for the analysis of residues in saflufenacil and its metabolites M800H11 and M800H35 in plant matrices. Residues are extracted from crop matrices (except oil) with methanol-water (70:30, v/v). Residues of saflufenacil and its metabolites are extracted from oil matrices with acetonitrile. The residues are determined using LC/MS/MS.

Table 46 Summary of recoveries with method D0603/02: saflufenacil and metabolites in plant

Matrix	Analyte	No. of tests	Fortification level [mg/kg]	1. Transition *			2. Transition **		
				mean [%]	SD [+/-]	CV [%]	mean [%]	SD [+/-]	CV [%]
Wheat grain	Saflufenacil	5	0.01	93	8	9	91	6	7
		5	0.1	91	4	4	90	6	7

Matrix	Analyte	No. of tests	Fortification level [mg/kg]	1. Transition *			2. Transition **		
				mean [%]	SD [+/-]	CV [%]	mean [%]	SD [+/-]	CV [%]
	M800H11	5	0.01	80	8	11	84	6	8
		5	0.1	73	4	6	68	9	13
	M800H35	5	0.01	83	8	10	85	10	11
		5	0.1	83	1	1	89	6	7
Garbanzo bean	Saflufenacil	5	0.01	85	5	6	82	5	6
		5	0.1	77	5	6	44	4	5
	M800H11	5	0.01	81	8	10	83	7	9
		5	0.1	79	4	5	87	4	5
	M800H35	5	0.01	79	7	9	78	11	14
		5	0.1	84	6	8	85	5	6
Soya bean seed	Saflufenacil	5	0.01	74	9	13	66	6	9
		5	0.1	118	10	8	116	10	9
	M800H11	5	0.01	83	6	7	92	8	8
		5	0.1	113	5	4	114	8	7
	M800H35	5	0.01	110	6	6	119	9	7
		5	0.1	110	7	6	112	5	5
Orange fruit	Saflufenacil	5	0.01	76	7	9	84	7	8
		5	0.1	90	11	12	87	7	8
	M800H11	5	0.01	109	8	7	64	4	6
		5	0.1	101	10	10	54	2	3
	M800H35	5	0.01	110	10	10	108	7	7
		5	0.1	95	9	9	94	6	7
Peach fruit	Saflufenacil	5	0.01	90	7	8	87	6	7
		5	0.1	96	10	10	98	10	10
	M800H11	5	0.01	98	9	9	87	8	9
		5	0.1	107	12	11	110	8	8
	M800H35	5	0.01	89	12	14	91	14	15
		5	0.1	98	4	4	94	4	4
Wheat hay	Saflufenacil	5	0.025	79	7	9	69	4	6
		5	0.25	108	5	5	108	3	3
	M800H11	5	0.025	93	12	13	93	6	6
		5	0.25	102	6	5	104	5	4
	M800H35	5	0.025	110	6	5	117	4	3
		5	0.25	104	7	7	110	3	3
Corn oil	Saflufenacil	5	0.01	88	12	14	76	11	14
		5	0.1	84	9	11	82	11	14
	M800H11	5	0.01	83	9	11	87	11	12
		5	0.1	87	3	4	94	11	12
	M800H35	5	0.01	81	10	12	79	10	12
		5	0.1	91	10	11	88	9	11

*1. Transition (for quant.) Saflufenacil: 501 → 349

**2. transition (for confirm.)501 → 459; M800H11:473 → 431; 473 → 335

M800H35: 353 → 232; 353 → 215

Good linearity was observed in the range of 0.05 to 0.5 ng/mL for all three analytes. The method determines saflufenacil and its metabolites M800H11 and M800H35 in plant matrices. There were no known interferences from plant components or from reagents, solvents and glassware used. The LOQ for residues of saflufenacil is 0.01 mg/kg for each analyte in/on food matrices (human consumption) and 0.025 mg/kg each in/on feed matrices (animal consumption).

The method was independently validated using wheat grain, wheat hay, orange fruit and corn oil as the experimental matrices. The method performance parameters had been confirmed by the validation study.

Animal matrices

Applying BASF Method No. L0073/01, the saflufenacil is extracted with acetonitrile. An aliquot of the extract is partitioned with dichloromethane. An aliquot of the organic phase is evaporated to

dryness and dissolved in a mixture of methanol and water. The final determination is performed by HPLC-MS/MS (Blumenstiel S., Grosshans F. 2007; Grosshans F. Blumenstiel S. 2007)

Table 47 Summary of recoveries with method L0073/01: saflufenacil in animal matrices

Matrix	Analyte	No. of tests	Fortification level [mg/kg]	1. Transition *			2. Transition **		
				mean [%]	SD [+/-]	CV [%]	mean [%]	SD [+/-]	CV [%]
Liver	Saflufenacil	5	0.01	78.2	7.1	9.1	78.6	6.9	8.8
		5	0.1	80.6	5.3	6.6	77.8	6.0	7.7
Kidney	Saflufenacil	5	0.01	94.4	3.1	3.3	94.6	3.0	3.2
		5	0.1	87.6	1.7	1.9	90.1	3.3	3.6
Muscle	Saflufenacil	5	0.01	74.3	2.2	2.9	73.0	3.0	4.1
		5	0.1	92.0	3.1	3.3	91.9	1.6	1.7
Fat	Saflufenacil	5	0.01	87.9	4.5	5.1	89.6	3.1	3.4
		5	0.1	93.8	2.1	2.2	92.1	1.3	1.4
Milk	Saflufenacil	5	0.01	79.5	2.8	3.6	76.0	3.8	5.0
		5	0.1	89.4	3.2	3.6	87.8	3.7	4.2
Cream	Saflufenacil	5	0.01	84.9	2.4	2.8	88.1	1.5	1.7
		5	0.1	93.6	1.7	1.9	93.5	1.6	1.8
Skimmed milk	Saflufenacil	5	0.01	80.3	3.8	4.7	83.5	3.7	4.4
		5	0.1	87.2	2.9	3.3	90.7	3.1	3.4
Egg	Saflufenacil	5	0.01	87.0	4.1	4.7	87.2	6.4	7.4
		5	0.1	87.9	2.3	2.6	88.9	2.3	2.6

*1. Transition (for quant.) Saflufenacil: 501 → 349 **2. transition (for confirm.) 501 → 459

The response was linear in the range of 0.01 to 0.25 ng/mL. The limit of quantitation was defined by the lowest fortification level successfully tested, which was 0.01 mg/kg in all matrices.

The method was independently validated (Rawle N. 2007) in liver, kidney, muscle, fat as well as milk and cream.

Table 48 ILV results of method L0073/01: saflufenacil in animal matrices

Matrix	Analyte	No. of tests	Fortification level [mg/kg]	Transition 501 → 349		
				mean [%]	SD [+/-]	CV [%]
Liver	Saflufenacil	5	0.01	98.0	3.1	3.1
		5	0.1	102.2	6.0	5.8
Kidney	Saflufenacil	5	0.01	80.4	13.5	16.8
		5	0.1	101.8	9.2	9.0
Muscle	Saflufenacil	5	0.01	97.2	3.2	3.3
		5	0.1	106.0	10.7	10.1
Fat	Saflufenacil	5	0.01	86.4	3.9	4.5
		5	0.1	102.0	2.9	2.9
Milk	Saflufenacil	5	0.01	88.6	13.7	15.4
		5	0.1	83.8	11.1	13.3
Cream	Saflufenacil	5	0.01	105.0	8.1	7.7
		5	0.1	98.2	7.3	7.5

The limit of quantitation was defined by the lowest fortification level successfully tested, which was 0.01 mg/kg in all matrices.

Stability of residues in stored analytical samples

The stability of residues in stored samples was tested by conducting storage stability studies using spiked samples of plant and animal origin.

Storage stability

Stability of residues was studied as part of the study on metabolism in corn (Hoefs R. *et al*. 2007) soya bean (Rabe U., Glaessgen W.E. 2007(a)), and tomato (Hafemann C., Kloeppner U. 2007(a)),

All investigations were performed within six months after sampling. All samples were stored in a freezer (-18 °C or below) directly after sampling until used.

No significant changes of the HPLC patterns were observed in various corn matrices. The composition of the residues in the plant materials remained stable for a period of approximately 16 to 21 months. The extracts were stored for a period of approximately 10 to 13 months.

Subsamples of soya bean stem and seeds were extracted about two weeks, subsamples of pods and leaves about three weeks after sampling. Aliquots of extracts were analysed by HPLC one to two weeks after extraction (methanol extracts) and two to three weeks after extraction (aqueous extracts) or within three to four weeks after extraction (methanol extracts) and three to four weeks after extraction (aqueous extracts). Metabolites M800H01 and M800H02 were identified by HPLC co-chromatography within four weeks after extraction. No noticeable change of the metabolic patterns was observed during co-chromatographic investigations. All extracts were stored frozen (-18 °C or below) between creation, initial analysis and reanalysis. To investigate the storage stability of the plant matrices, subsamples of seeds and leaves were re-extracted 23 weeks after sampling and the samples analysed within 8 days. The extracts showed a similar chromatographic pattern as those initially analysed.

For all tomato matrices no significant changes of the HPLC patterns were observed. The residues in the stored extracts were stable over a period of approximately 9 to 10 months under the chosen conditions. The composition of the residues in the plant materials remained stable over a period of approximately 10 to 11 months. All tomato plant matrices were extracted within 10–55 days after sampling. The metabolite profiles used for quantification of metabolites were obtained by HPLC analysis not later than 3-22 days after extraction. The maximum time period between sampling and HPLC analysis (metabolite profile used for quantification) was 59 days.

Hence, it was concluded that the results of the reported metabolism studies were not influenced by storage effects and that the data accurately reflect the metabolite pattern in all sample materials collected.

The untreated control plant samples were obtained from crop field trial studies. For stored-fortified samples, the plant matrix surface was spiked, using a micro-pipette, with 0.02 mL of a standard of saflufenacil, M800H11 or M800H35 in methanol (concentration, 5 µg/mL each) for a fortification level of 1 mg/kg for each analyte (Nejad H. 2008). The samples were fortified separately for the parent compound and metabolites M800H11 or M800H35. All spiked samples and controls were immediately stored in a freezer (<-5 °C) where they remained until analysis.

The samples were analysed according to method D0603/02 which determines saflufenacil and its metabolites M800H11 and M800H35 by means of LC-MS/MS with external standardization and a limit of quantitation of 0.01 mg/kg each. The mean recoveries were between 71 and 144% for saflufenacil**,** between 65 and 134% for M800H11 and between 70 and 140% for M800H35.

Table 49 Storage stability results of saflufenacil in plant matrices

Mean Recovery of saflufenacil (%)										
Day	A: mean in stored samples, % of nominal				B: mean procedural, in freshly spiked sample					
	A	B	A	B	A	B	A	B	A	B
	Corn forage		Corn grain		Corn stover		Garbanzo bean, seed		Orange, fruit	
0	-	117	-	107	-	126	-	89	-	99
44	135	117	88	107	116	126	63	89	93	99
130	98	100	82	105	98	101	114	108	86	76
214	86	82	81	91	70	77	104	93	74	79
410	109	99	95	96	92	97	91	89	97	102
548	78	93	96	104	69	88	88	82	68	81
	Orange, juice		Orange, oil		Orange, pulp		Raisin		Radish root	
0	-	98	-	110	-	99	-	104	-	93
44	86	98	91	110	97	99	71	104	98	93
130	81	83	85	80	99	104	109	110	100	87
214	86	80	78	78	81	79	74	80	81	75

Mean Recovery of saflufenacil (%)										
Day	A: mean in stored samples, % of nominal				B: mean procedural, in freshly spiked sample					
	A	B	A	B	A	B	A	B	A	B
	Corn forage		Corn grain		Corn stover		Garbanzo bean, seed		Orange, fruit	
410*	107	110	108	110	99	92	102	110	105	117
548	76	82	138	121	88	87	86	83	79	85
	Soya bean, forage		Soya bean, hay		Soya bean, seed					
0	-	111	-	110	-	124				
44	85	111	107	110	97	124				
130	109	105	98	101	98	112				
214	88	80	87	89	71	88				
410	97	106	103	100	98	98				
548	78	84	91	81	75	81				

* in case of raisin 422 days

Table 50 Storage stability results of M800H11 in plant matrices

Mean Recovery of M800H11 (%)										
Day	A: mean in stored samples, % of nominal				B: mean procedural, in freshly spiked sample					
	A	B	A	B	A	B	A	B	A	B
	Corn forage		Corn grain		Corn stover		Garbanzo bean, seed		Orange, fruit	
0	-	99	-	79	-	116	-	87	-	93
44	90	99	70	79	112	116	109	87	89	93
130	110	96	59	93	110	104	114	103	87	91
214	82	80	56	70	76	93	85	93	78	72
410	86	93	72	81	89	100	77	102	93	110
548	75	90	66	79	77	91	70	87	87	80
	Orange, juice		Orange, oil		Orange, pulp		Raisin		Radish root	
0	-	89	-	92	-	94	-	91	-	98
44	84	89	83	92	91	94	84	91	106	98
130	81	82	100	79	106	94	83	105	87	90
214	88	82	77	75	86	86	70	80	81	86
410*	100	99	88	93	106	102	91	105	95	114
548	89	102	104	115	76	92	79	80	75	104
	Soya bean, forage		Soya bean, hay		Soya bean, seed					
0	-	97	-	105	-	105				
44	105	97	99	105	118	105				
130	106	91	103	96	89	110				
214	76	79	87	82	80	88				
410	89	116	93	106	66	96				
548	80	91	82	72	68	85				

* in case of raisin 422 days

Table 51 Storage stability results of M800H35 in plant matrices

Mean Recovery of M800H35 (%)										
Day	A: mean in stored samples, % of nominal				B: mean procedural, in freshly spiked sample					
	A	B	A	B	A	B	A	B	A	B
	Corn forage		Corn grain		Corn stover		Garbanzo bean, seed		Orange, fruit	
0	-	104	-	106	-	126	-	87	-	105
44	98	104	84	10	112	126	97	87	93	105
130	85	98	95	99	110	96	117	108	93	104
214	89	92	82	92	97	98	98	97	87	78
410	93	94	83	92	84	103	73	95	116	106
548	71	76	72	92	86	82	86	87	73	78

Mean Recovery of M800H35 (%)										
Day	A: mean in stored samples, % of nominal				B: mean procedural, in freshly spiked sample					
	A	B	A	B	A	B	A	B	A	B
	Orange, juice		Orange, oil		Orange, pulp		Raisin		Radish root	
0	-	87	-	94	-	100	-	94	-	92
44	95	87	93	94	98	100	85	94	87	92
130	91	91	86	81	104	101	86	101	83	91
214	87	91	89	83	95	102	80	92	90	81
410*	111	105	142	94	108	100	90	96	96	102
548	61	90	84	103	75	74	68	82	67	91
553	76	100	-	-	-	-	-	-	-	-
	Soya bean, forage		Soya bean, hay		Soya bean, seed					
0	-	96	-	106	-	117				
44	109	96	112	106	110	117				
130	104	98	117	107	113	129				
214	99	85	84	93	87	98				
410	96	108	87	109	99	110				
548	79	88	84	78	77	82				

* in case of raisin 422 days

Storage stability tests of saflufenacil in milk and bovine tissues such as muscle, liver, kidney and fat were conducted (Rawle N.W. 2007). In addition, the stability in the dosing solution was tested.

During the study, the specimens were stored at approximately -18 °C or lower. BASF Analytical Method No. L0073/01 was used to determine residues of saflufenacil in matrices of animal origin. The storage stability test conducted at 0.01 mg/kg and 0.1 mg/kg spike levels simultaneously with the analyses of samples, just covered the period of storage for samples from sampling to extraction. Samples taken from the control caw feeding study was used for the storage stability tests. The stability of resides in sample extracts and dosing solutions was also tested and no degradation was found.

Table 52 Storage stability results of saflufenacil in milk and cow tissues

Matrix	Storage stability test interval (days)	Max storage of samples (days)	Recovery in stored samples (%)	Recovery in freshly spiked samples (%)
Milk	51	47	77 67	77 80
Muscle	31	29	104 93	111 100
Liver	32	30	68 90	101 91
Kidney	32	31	93 87	112 106
Fat	35	34	88 95	100 100

USE PATTERN

Saflufenacil provides very effective contact and residual control of broad leaf weeds and is used in many crops in pre-emergence, pre-plant burn down, post-emergence directed sprays burn down, or pre-harvest desiccation. It is rapidly absorbed through the foliage of plants. Within a few hours following application, the foliage of susceptible weeds shows signs of desiccation, and in subsequent days necrosis and death of the plant.

The compound is registered in Argentina, Canada, Colombia, Mexico and USA.

Formulations containing saflufenacil, alone or co-formulated with other compounds are registered for use on a wide variety of crops in 13 countries.

The tables below contain the following abbreviations:

F = outdoor or field use, G = glasshouse, P = protected, I = indoor application

p.e. = pre-emergence application

Information given on active substance (ai) refers to saflufenacil only

ai = active substance

Broadcast = Broadcast, banded or spot spray

Pre-seed = Pre-seed spraying

NA = not applicable

[a] ground application

[b] spot treatment

[c] aerial treatment

Table 53 Registered uses based on the labels provided to the Meeting

Crop	Country	Application							PHI [day]
		Form. Type	Method	No	Interval [days]	Volume [L/ha]	Rate kg ai/ha	Max rate kg/ha/season	
Apple	Argentina	WG	Spray, p.e.	2	20	100–200	0.025	0.05	7
Banana	Columbia	WG	Spray, p.e.	1		100-150	0.028–0.039	0.039	n.a.
Barley	Argentina	WG	Spraying	1	n.a.	100–150	0.025	0.05	n.a.
Barley	Canada	SG	Spraying	2	20	100 – 200	0.025–0.050	0.050	60
Barley	Canada	WG	Spraying	1	n.a.	50–100	0.018–0.050	0.050	60
Barley	US	SC	Spraying	1	n.a.	28[c], 47[a]	0.025–0.050	0.150	30
Canary seed	Canada	WG	Spraying	1	n.a.	50–100	0.018–0.050	0.050	60
Canary seed	US	SC	Spraying	1	n.a.	28[c], 47[a]	0.025–0.050	0.150	30
Canola (rapeseed)	USA	SC	Desiccation	1		28.0 – 47.0[c] 94.0[a]	0.025-0.05	0.05	3
Chickpea	Canada	WG	p.e.	1		50-100	0.018–0 05	0.05	60
Chickpea	USA	SC	Pre-plant pre emergence	≥ 1	14	28[c], 47[a]	0.025	0.05	65
Citrus	Mexico	WG	Spray, p.e.	3	30		0.025–0.05	0.15	7
Citrus	US	WG	Broadcast, banded or spot spray p.e	1-3	21	> 94[(a)] 1000[(b)]	0.05	0.15	0
Coffee	Columbia	WG	Post e	1	n.a.	100–150	0.028–0.039	0.039	n.a.
Common beans, dry	Canada	SC	Desiccation	1	n.a.	200	0.025–0.050	0.05	2
Common beans, dry	Canada	WG	Desiccation	1	n.a.	50[c], 200[a]	0.025 0.05	0.05	2
Corn	Argentina	WG	Spraying	1	n.a.	100–150	0.025	0.05	n.a.
Corn	Columbia	WG	Spraying	≥ 1		150	0.116	0.116	n.a.
Corn	Mexico	WG	Spraying	≥ 1			0.05–0.13	0.13	
Corn	Mexico	WG	Spraying	1	n.a.		0.02–0.05	0.05	
Corn	USA	WG	Spraying			28[c], 47[a]	0.025	0.025	n.a.
Corn (field)	Canada	SG	Spraying	≥ 1		100–200	0.050–0.100	0.100	60
Corn (field)	Canada	WG	Spraying	1	n.a.	50-100	0.018–0 050	0.050	60
Corn (sweet)	Canada	WG	Spraying	1	n.a.	50-100	0.018–0 050	0.050	60
Corn, field (grain, silage)	USA	SC	Spraying	2	30	28[c], 47[a]	0.050–0.130	0.150	80
Corn, field (grain, silage)	USA	EC	Spraying			> 28.0	0.05–0.08	0.13	n.a.
Corn, field (grain, silage)	USA	EC	Spraying			13–25	0.05–0.08	0.13	n.a.
Corn, popcorn	USA	SCSC	Spraying	≥ 1		28[c]	0.065–0.100	0.150	80
Corn, popcorn	USA	EC	Spraying			> 28.0	0.05–0.08	0.13	n.a.
Cotton	US	SC	Desiccation	≥ 1	5-7	> 28.0[a] 47.0	0.013-0.05	0.05	5
Cotton	US	SC	Pre-plant	≥ 1	14	> 28[a] >47.0	0.025–0.050	0.05	
Dry beans	USA	SC	spray	≥ 1		28[c], 47[a]	0.025–0.05	0.05	2
Edible bean	USA	SC	Spray ground or	≥ 1	14	28[c], 47[a]	0.02–0.05	0.1	65

Crop	Country	Application							PHI [day]
		Form. Type	Method	No	Interval [days]	Volume [L/ha]	Rate kg ai/ha	Max rate kg/ha/season	
			aerial						
Field pea	USA	SC	Spray	≥ 1	14	28[c], 47[a]	0.02–0.05	0.1	65
Grapevines	USA	WG	p.e	1-3	21	> 94[a], 1000[b]	0.025	0.075	0
Lemon	Argentina	WG	Spray p.e.	2	20	100–200	0.025	0.05	n.a.
Lentils	Canada	WG	Pre-seed	1		50-100	0.18	0.18	60
Lentils	Canada	WG	Spray	1		50[c], 200[a]	0.025 0.05	0.05	3
Lentils	USA	SC	Spray	1	14	28[c], 47[a]	0.025	0.1	65
Mandarin	Argentina	WG	Spray p.e.	2	20	100–200	0.025	0.05	n.a.
Millet	USA	WG	Spraying	2		28[c]	0.025–0.050	0.150	30
Nuts	USA	WG	P. e.	1-3	21	> 94[a] 1000[b]	0.05	0.15	7
Oats	Canada	WG	Spraying	1		50–100	0.018–0.050	0.050	60
Oats	USA	SC	Spraying	≥ 1		28[c], 47[a]	0.025–0.050	0.150	30
Orange	Argentina	WG	Spray p.e	2	20	100–200	0.025	0.05	n.a.
Pear	Argentina	WG	Spray, p.e	2	20	100–200	0.025	0.05	n.a.
Peas, field dry	Canada	WG	Pre-seed, p.e.	1	n.a.	50–100	0.018–0.05	0.05	60
Peas, field dry	Canada	WG	Desiccation	1	n.a.	50[c], 200[a]	0.025 0.05	0.05	3
Peas, field dry	USA	WG	Desiccation	≥ 1		28[c], 47[a]	0.025–0.05	0.05	3
Peas, field dry	USA	SC	Desiccation	≥ 1		28[c], 47[a]	0.025–0.05	0.05	3
Peas, field dry, chickpea,	USA	WG	Pre-plant p.e.	1		28[c], 47[a]	0.0185		n.a
Pome fruit	US	WG	Broadcast,	1-3	21	> 94[a], 1000[b]	0.05	0.15	0
Rice	Columbia	WG	Spraying	1	n.a.	100–150	0.028–0.039	0.039	n.a.
Rye	USA	SC	Spraying	1	n.a.	28[c], 47[a]	0.025–0.050	0.150	30
Sorghum	Argentina	WG	Spraying	2	20	100–150	0.025	0.05	n.a.
Sorghum	USA	SC	Spraying	2	30	28[c], 47[a]	0.050–0.100	0.150	70
Soya bean	Argentina	WG	Pre-plant	2	20	100–150	0.025	0.05	n.a.
Soya beans	Canada	SC	Pre-plant	1	n.a.	100–200	0.025	0.025	60
Soya beans	Canada	SC	Desiccation	1	n.a.	200	0.025–0.05	0.05	3
Soya beans	Canada	WG	Pre-seed, p.e.	1	n.a.	50–100	0.018	0.018	60
Soya beans	Canada	WG	Ground or aerial	1		50[c], 200[a]	0.025–0.05	0.05	3
Soya beans	USA	WG	Pre-plant p.e	1		28[c], 47[a]	0.0246	0.0246	n.a.
Soya beans	USA	SC	Desiccation	≥ 1		28[c], 47[a]	0.025–0.05	0.05	3
Soya beans	USA	SC	Pre-plant p.e	≥ 1		28[c], 47[a]	0.025–0.05	0.1	65
Stone fruit	US	WG	Broadcast, p.e.	1-3	21	> 94[a], 1000[b]	0.05	0.15	0
Sunflower	Canada	WG	Desiccation	1	n.a.	50[a], 200	0.025–0.050	0.05	7
Sunflower	US	SC	Desiccation	≥ 1		28-47[a] 94.0	0.025–0.050	0.1	7
Sweet corn	Canada	SG	p.e.	1		100-120	0.050–0.100	0.100	60
Sweet corn	USA	SC	p.e.	≥ 1		28[c], 47[a]	0.065–0.100	0.150	80
Triticale	USA	SC	Spraying	≥ 1		28[c], 47[a]	0.025–0.050	0.150	30
Wheat	Argentina	WG	Spraying	1	n.a.	100–150	0.025	0.05	n.a.
Wheat	USA	SC	Spraying	1–2	nm	28[c], 47[a]	0.025–0.050	0.150	30
Wheat (spring, winter, durum)	Canada	WG	Spraying			50–100	0.018–0 050	0.050	60
Wheat, spring, winter, durum)	Canada	SB	Spraying	1	n.a.	100–200	0.025–0.050	0.050	60

RESIDUES RESULTING FROM SUPERVISED TRIALS

Residue data were submitted by the manufacturer from supervised trials conducted on citrus fruits, pome fruits, stone fruits, berries and small fruits, assorted tropical and sub-tropical fruits-inedible peel, fruiting vegetables, legume vegetables, pulses, root and tuber vegetables, cereals, grasses for sugar or syrup production, tree nuts, oilseeds, seeds for beverages and sweets. The trials were generally conducted at maximum GAP and well documented.

Samples were stored and analysed within the period tested for storage stability of residues. The residues of parent saflufenacil, M800H11 and M800H35 were determined in all samples with method D0603/02 or equivalent. The LOQ for each compound was 0.01 mg/kg, unless otherwise stated. The performance of the methods was verified with concurrent recovery studies.

In cases where all samples contained residues below the LOQ, only the summary of the trials results is given. In the Summary tables the number of trials provided samples is given under column **N**, and number of samples analysed is given under column **n**.

Citrus fruits

In 2006/07, 23 trials were conducted on sweet orange, lemon and grapefruit in 5 states of the USA. Saflufenacil was applied in WG formulation three times as broadcast floor application at a rate of 50 g ai/ha in a spray volume of 183–339 L/ha with a retreatment interval of 20–22 days in compliance with US GAP. Fruit specimens were taken directly after the third application (PHI 0 days) and in two decline trials 7, 14 and 21 days thereafter.

The samples were analysed according to method D0603 which determines saflufenacil and its metabolites M800H11 and M800H35 by means of LC-MS/MS with a limit of quantitation of 0.01 mg/kg each. The mean recovery was 75% for saflufenacil, 91% for M800H11 and 80% for M800H35. Samples were stored for a maximum of 15 months (Jordan J.M., Saha M. 2007).

In 2008, a study was conducted in Brazil comprising three trials in orange applying saflufenaci**l** three times at a rate of 49 g ai/ha in a spray volume of 200 L/ha as a weed post-emergence directed jet. Citrus fruit were taken 7 days after the last application. The samples were analysed according to SOP-PA.0298 based on method D0603/02 which determines saflufenacil and its metabolites M800H11 and M800H35 by means of LC-MS/MS with external standardization and a limit of quantitation of 0.01 mg/kg each. The mean recovery was 101% for Saflufenacil, 85% for M800H11 and 87% for M800H35. In citrus fruit specimens, residues of parent Saflufenacil and its metabolites M800H11 and M800H35 were found to be below their calculated limit of detection (0.002 mg/kg each) (Jones B., Souza C. 2008(a)).

Table 54 Summary of residues in citrus

Portion analysed	Year	N	n	DALA [a]	Residues (mg/kg)		
					Saflufenacil	M800H11	M800H35
Sweet orange [c]	2006/07	12[b]	24	0	< 0.01	< 0.01	< 0.01
		2	4	7	< 0.01	< 0.01	< 0.01
		2	4	14	< 0.01	< 0.01	< 0.01
		2	4	21	< 0.01	< 0.01	< 0.01
Lemon [c]		5	10	0	< 0.01	< 0.01	< 0.01
Grapefruit [c]		6	12	0	< 0.01	< 0.01	< 0.01
Orange [d]	2008	3	3	7	< 0.002	< 0.002	< 0.002

[a] days after last application

[b] The number of trials include the 2 trials with decline studies

[c] Trials conducted in USA

[d] Trials conducted in Brazil

N: Number of trials

n: number of samples analysed

Pome fruits

In 2006, a study was conducted in the USA comprising 25 trials in pome fruit out of which 15 trials were done in apple and 10 in pears. Saflufenacil was applied in WG formulation three times as broadcast floor application at a rate of 50 g ai/ha in a spray volume of 190–360 L/ha, complying to US GAP. The first application took place at dormancy, 2 ± 1 weeks before bud break. The second application was done 19–22 days before harvest, the last application on the day of harvest. Fruit

specimens were taken directly after the third application, in the decline trials (one each for apple and pear) also 7 and 14 days later.

The samples were analysed according to method D0603. The mean recovery was 81% and 88% (apple/pear) for saflufenacil, 99% for M800H11 and 99% and 81% for M800H35 (Jordan J.M. 2007).

In 2008, a study was conducted in Brazil comprising three trials in apple applying saflufenacil in WG formulation three times at a rate of 49 g ai/ha in a spray volume of 200 L/h. The applications were done as post-emergency treatments for weeds and took place at the apple growth stages 72–75, 75–78 and 86–87 (BBCH). Apple fruit were taken at the intended PHI of 15 days after the last application.

The samples were analysed according to SOP-PA.0298 based on method D0603/02 which determines saflufenacil and its metabolites M800H11 and M800H35 by means of LC-MS/MS with external standardization and a limit of quantitation of 0.01 mg/kg each. The mean recovery was 87% for saflufenacil and 88% for both M800H11 and M800H35. In apple fruit sampled after 15 days (PHI), residues of parent saflufenacil and of the metabolites M800H11 and M800H35 were their calculated limit of detection of 0.002 mg/kg each (Jones B., Souza C. 2008(b)).

Table 55 Summary of residues in pome fruit

Portion analysed	Year	N	n	DALA	Residues (mg/kg)		
					Saflufenacil	M800H11	M800H35
Apple fruit [a]	2006	15	30	0	< 0.01	< 0.01	< 0.01
		1	2	7	< 0.01	< 0.01	< 0.01
		1	2	14	< 0.01	< 0.01	< 0.01
Pear fruit[1]		5	10	0	< 0.01	< 0.01	< 0.01
		1	2	7	< 0.01	< 0.01	< 0.01
		1	2	14	< 0.01	< 0.01	< 0.01
Apple fruit [b]	2008	3	3	15	nd	nd	nd

[a] US trials

[b]. Brazilian trials,

nd: < 0.002 mg/kg

Stone fruits

In 2006/07, a study was conducted in nine states of the USA comprising 29 trials in stone fruit out of which six trials were done in cherry (3 tart and 3 sweet), 13 in peach and 10 in plum. Saflufenacil in WG formulation was applied three times as broadcast floor application at a rate of 50 g ai/ha in a spray volume of 187–340 L/ha according to US GAP. The first application took place at dormancy, 2 ± 1 weeks before bud break. The second application was done 20–24 days before harvest, the last application on the day of harvest. Fruit specimens were taken directly after the third application as well as about 7, 14 and 21 days later (Jordan J.M., Stewart J. 2007)

The samples were analysed according to method D0603. The mean recovery was 85% for saflufenacil, 77% for M800H11 and 71% for M800H35.

Table 56 Summary of residues in stone fruit

Portion analysed	Year		n	DALA	Residues (mg/kg)		
					Saflufenacil	M800H11	M800H35
Cherry, tart	2006/07	3	6	0-21	< 0.01	< 0.01	< 0.01
Cherry, sweet		3	6		< 0.01	< 0.01	< 0.01
Peach		13	26		< 0.01	< 0.01	< 0.01
Plum		10	20		< 0.01	< 0.01	< 0.01

n = number of samples analysed

Berries and other small fruits

In 2006, a study was conducted in the US comprising 12 trials in grape. Saflufenacil in WG formulations applied three times as broadcast floor application at a rate of 25 g ai/ha in a spray volume of 18–340 L/ha. The first application took place at dormancy, 2 ± 1 weeks before bud break. The second application was done 20–21 days before harvest, the last application on the day of harvest. Fruit specimens were taken directly after the third application and in one decline trial about 14 days thereafter (Jordan J.M. 2007a).

The samples were analysed according to method D0603. The mean recovery was 90% for saflufenacil, 102% for M800H11 and 101% for M800H35

In 2008, a study was conducted in Brazil comprising two trials in grape applying BAS 800 01 H twice at a rate of 24.5 g ai/ha as broadcast floor application in a spray volume of 200 L/ha. Grape fruit were taken 17 days after the last application (Jones B., Souza C. 2008(c)).

In grape fruit specimens sampled after 17 days, residues of parent compound and of the metabolites M800H11 and M800H35 were found to be below their calculated limits of detection (0.001 mg/kg for parent, 0.002 mg/kg each for the metabolites).

Table 57 Summary of residues in grape

Portion analysed	Year	N	n	DALA	Residues (mg/kg)		
					Saflufenacil	M800H11	M800H35
Grape [a]	2006	12 1	24 2	0 14	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
Grape [b]	2008	2	2	17	nd	nd	nd

[a] US trials

[b] Brazilian trials, nd < 0.001-0.002 mg/kg

Assorted tropical and sub-tropical fruits–inedible peel

Banana

In 2008, a study was conducted in Brazil comprising two trials in banana applying saflufenacil in WG formulation three times at a rate of 49 g ai/ha as a weed post-emergence directed jet to weed in a spray volume of 200 L/ha. Banana fruit were taken at the intended PHI of 30 days after the last application. The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 88% for the parent compound and M800H11 and 83% for M800H35 (Jones B., Souza C. 2008(e).

In 2009, a study was conducted in Brazil comprising two trials in banana applying saflufenacil five times at a rate of 74.9 g ai/ha in a spray volume of 200 L/ha. Banana fruit were taken directly after the application and one day later (Jones B., Santiago L. 2010).

In banana fruits, residues of parent were below its calculated limit of detection (0.002 mg/kg) or below quantitation (0.01 mg/kg). Both the metabolites M800H11 and M800H35 were below their limits of detection (0.003 and 0.001 mg/kg, respectively).

In 2008, a study was conducted in Costa Rica (2 trials), Colombia (1 trial), Ecuador (3 trials), Guatemala (1 trial), Honduras (2 trials), and Panama (1 trial) comprising ten trials in banana. Applications of saflufenacil directed to the base were performed five times at rates between 72 and 80 g ai/ha in a spray volume of 191–213 L/ha and retreatment intervals of 20 ± 5 days. Banana fruit were taken directly after the application and one day later. The samples were analysed according to method D0603/02. The mean recovery was 97% for saflufenacil, 92% for M800H11 and 93% for M800H35. In banana fruit specimens, residues of total Saflufenacil were found to be below their limit of quantitation (0.01 mg/kg each) and 0.03 mg/kg of the sum (Jordan J.M. 2010).

Table 58 Summary of residues in banana

Portion analysed	Year	N	n	DALA [a]	Residues (mg/kg)		
					Saflufenacil	M800H11	M800H35
Banana [a]	2008	2	2	30	nd / < 0.01	nd < 0.003	Nd < 0.001
Banana [a]	2009	2	2	0	nd	nd	nd
			2	1	nd	nd	nd
Banana [b]	2010	1	1	0	< 0.01	< 0.01	< 0.01
			1	1	< 0.01	< 0.01	< 0.01
Banana [c]	2010	2	2	0	< 0.01	< 0.01	< 0.01
			2	1	< 0.01	< 0.01	< 0.01
Banana [d]	2010	1	1	0	< 0.01	< 0.01	< 0.01
				1	< 0.01	< 0.01	< 0.01
Banana [e]	2010	3	3	0	< 0.01	< 0.01	< 0.01
				1	< 0.01	< 0.01	< 0.01
Banana [f]	2010	1	1	0	< 0.01	< 0.01	< 0.01
				1	< 0.01	< 0.01	< 0.01
Banana [g]	2010	2	2	0	< 0.01	< 0.01	< 0.01
				1	< 0.01	< 0.01	< 0.01

[a] Brazil
[b] Columbia
[c] Costa Rica
[d] Panama
[e] Ecuador
[f] Guatemala
[g] Honduras

Mango

In 2008, a study was conducted in Brazil comprising two trials in mango applying saflufenacil three times at a rate of 49 g ai/ha as a weed post-emergence directed jet to weeds in a spray volume of 200 L/ha. Mango fruit were taken at the intended PHI which is 15 days after the last application (± 1 day) (Jones B., Souza C. 2008(e)).

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 91% for parent compound, 96% for M800H11 and 104% for M800H35. In mango fruit specimens sampled after about 15 days, residues of parent Saflufenacil and of the metabolite M800H35 were found to be below their calculated limit of detection (0.002 and 0.003 mg/kg, respectively). Metabolite M800H11 was below the limit of quantitation of 0.01 mg/kg.

In 2008, a study was conducted in Brazil comprising two trials in mango applying BAS 800 01 H three times at a rate of 49 g ai/ha as a weed post-emergence directed jet in a spray volume of 200 L/ha. Mango fruit were taken at the intended PHI which is 15 days after the last application (± 1 day) (Jones B. 2010).

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 91% for parent compound, 102% for M800H11 and 104% for M800H35. No residue was detected above LOQ (0.01 mg/kg).

Table 59 Summary of residues in mango

Portion analysed	Year	N	n	DALA [1)]	Growth stage	Residues (mg/kg)		
						Saflufenacil	M800H11	M800H35
Mango fruit	2008	2	2	14–15	BBCH 85-91	nd < 0.002	< 0.01	nd < 0.003
Mango fruit	2008		2	15	BBCH 83-89	nd < 0.002	nd < 0.003	nd < 0.003

Sweet corn

Five residue trials in sweet corn were conducted in USA with saflufenacil incorporated into soil before pre-planting or applied pre-emergence directed to soil once at 0.15 kg/ha. The residues of parent compound M800H11 and M800H35 were below the LOQ of 0.01 mg/kg.

Table 60 Summary of residues in sweet corn

Portion analysed	N	n	PHI	Residues (mg/kg)		
				Saflufenacil	M800H11	M800H35
Sweet corn, k + cwhr	5	18	81-111	< 0.01	< 0.01	< 0.01

K + cwhr - kernel + cob with husk removed

Legume vegetables and pulses

Beans (dry)

Field trial data have been generated for saflufenacil on bean (10 trials) during the 2009 growing season. At each test location, one untreated control and one treated plot were established. The treated plots received a single late season pre-harvest desiccation application of saflufenacil (70% WG, formulation code BAS 800 00 H) at 0.050 kg ai/ha. The applications were made with ground equipment using approximately 152-285 L/ha. Samples of mature dried bean seed were harvested at a 2-day pre-harvest interval (PHI). At one trial additional treated samples were collected at 0, 1, 7 and 10 days after the pesticide application, in addition to the targeted 2-day PHI (Norris F.A. 2010(b)).

The samples were analysed according to method D0603. The mean recoveries averaged at 86% for Saflufenacil, at 81% for M800H11 and at 80% for M800H35.

In 2008, a study was conducted in Brazil comprising five trials in bean applying saflufenacil twice at a rate of 98 g ai/ha in a spray volume of 200 L/ha. The first application was done pre-emergence on the day of sowing; the second took place before harvest as culture desiccant (growth stage 77–97). The dry bean seeds were taken at the intended PHI of 7 days after the last application, and in three trials at harvest intervals of 0, 3, 10 and 14 days (Jones B., Souza C. 2008(g))

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 90% for saflufenacil, 84% for M800H11 and 101% for M800H35. At the intended PHI of 7 days, parent saflufenacil was found below the limit of quantitation of 0.01 mg/kg in bean seed. The metabolites M800H11 and M800H35 were below their calculated limits of detection (0.002 and 0.001 mg/kg).

Table 61 Detailed residue results of saflufenacil in bean from trials in the USA, Canada and Brazil

Country Trial No.	Formulation, Appl. rate (g ai/ha)	Timing	PHI (days)	Residues found [a] (mg/kg)			
				Matrix	BAS 800 H	M800 H11	M800 H35
Missouri R090350	BAS 800 00 H 1 × 50	late season	2 2	dried seed dried seed	0.01 0.01	< 0.01 < 0.01	< 0.01 < 0.01
North Dakota R090351	BAS 800 00 H 1 × 50	late season	2 2	dried seed dried seed	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
Iowa R090352	BAS 800 00 H 1 × 50	late season	2 2	dried seed dried seed	0.06[b] 0.21[b]	< 0.01[b] < 0.01[b]	< 0.01[b] < 0.01
Wisconsin R090353	BAS 800 00 H 1 × 50	late season	2 2	dried seed dried seed	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
North Dakota R090354	BAS 800 00 H 1 × 50	late season	2 2	dried seed dried seed	0.03[b] 0.06[b]	< 0.01[b] < 0.01[b]	< 0.01 < 0.01[b]
Alberta R090355	BAS 800 00 H 1 × 50	late season	2 2	dried seed dried seed	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
Kansas R090356	BAS 800 00 H 1 × 50	late season	2 2	dried seed dried seed	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
Utah R090357	BAS 800 00 H 1 × 50	late season	2 2	dried seed dried seed	0.08[b] 0.23[b]	< 0.01[b] < 0.01[b]	< 0.01 < 0.01

Country Trial No.	Formulation, Appl. rate (g ai/ha)	Timing	PHI (days)	Residues found [a] (mg/kg)			
				Matrix	BAS 800 H	M800 H11	M800 H35
California R090358	BAS 800 00 H 1 × 50	late season	2 2	dried seed dried seed	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
Idaho R090359	BAS 800 00 H 1 × 50	late season	0 0 1 1 2 2 7 7 10 10	dried seed dried seed dried seed dried seed dried seed dried seed dried seed dried seed dried seed dried seed	0.02 < 0.01[b] 0.03 0.03 0.15[b] 0.04 0.02 0.03 0.02 0.03	< 0.01 < 0.01[b] < 0.01 < 0.01 < 0.01[b] < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01[b] < 0.01 < 0.01 < 0.01[b] < 0.01 < 0.01 < 0.01 < 0.01 < 0.01
Brazil	2 x 98	late season	0[c]	dried seed	< 0.01– 0.01	nd / < 0.01	nd
			3[c]	dried seed	< 0.01– 0.01	nd / < 0.01	nd
			7[d]	dried seed	< 0.01	nd	nd
			10[c]	dried seed	< 0.01	< 0.01	nd
			14[c]	dried seed	nd– < 0.01	nd / < 0.01	nd

[a] Saflufenacil, M800H11 and M800H35 residues are expressed in terms of each analyte

[b] result of multiple analyses of individual field sample

[c] Range of residues in samples derived from three trials

[d] Range of residues in samples derived from five trials

Peas

A total of 24 field trials were conducted during the 2006 and 2007 growing seasons in 18 states USA and Canada: 13 trials on peas and 11 trials on chick pea (garbanzo beans). The treatments were as single broadcast, pre-plant incorporated (PPI) or pre-emergence (PRE) application of WG formulation at 0.10 kg ai/ha using approximately 147–289 L/ha water. There were one or two treated plots at one site (Jordan J. 2007).

The samples were analysed according to method D0603. The mean recoveries were between 69 and 115% for saflufenacil, between 70 and 101% for M800H11 and between 66 and 100% for M800H35. The residues were below the LOQ in all matrices tested.

Table 62 Summary of residues in dried pea samples derived from single pre-plant or pre-emergence application of saflufenacil

Portion analysed		N	n	DALA[a]	Residues (mg/kg)		
					Saflufenacil	M800H11	M800H35
Pea	succulent seed with pod	24	28	63-81	< 0.01	< 0.01	< 0.01
	succulent seed without pod	24	28	63-81	< 0.01	< 0.01	< 0.01
	dried seed	9	18	82-117	< 0.01	< 0.01	< 0.01
Chick pea (Garbanzo bean)	dried seed	11	22	90-148	< 0.01	< 0.01	< 0.01

[a] US and Canadian trials;

Nine field trial data were performed for saflufenacil on peas during the 2009 growing season in the US and Canada. At each test location, one untreated control and one treated plot were established. The treated plots received a single late season pre-harvest application of saflufenacil (70% WG, formulation code BAS 800 00 H) at 0.050 kg ai/ha. The applications were made with ground equipment using approximately 182–306 L/ha. Samples of dried seed and vines were harvested at a 2–4 day pre-harvest interval (PHI). At one trial additional treated samples were

collected at 0, 1, 7 and 10 days after the last application, in addition to the targeted 3-day PHI, to evaluate residue decline.

The pesticide applications corresponded to maximum GAP **(**Norris F.A. 2010(a)).

The samples were analysed according to method D0603. The mean recoveries for Saflufenacil were 92% in seed and 74% in vines, for M800H11 99% in seed and 88% in vines and for M800H35 90% in seed and 80% in vines.

Table 63 Results of supervised trials conducted with late season pre-harvest application of saflufenacil in pea in the US and Canada

Country Trial No.	Formulation, Appl. rate (g ai/ha)	Timing	PHI (days)	Residues found [a] (mg/kg)			
				Matrix	saflufenacil	M800 H11	M800 H35
North Dakota R090341	BAS 800 00 H 1 × 50	BBCH 92	3 3	dried seed dried seed	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
Wisconsin R090342	BAS 800 00 H 1 × 50	mature	4 4	dried seed dried seed	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
Idaho R090343	BAS 800 00 H 1 × 50	BBCH 89	3 3	dried seed dried seed	0.03 0.01	< 0.01 < 0.01	< 0.01 < 0.01
North Dakota R090344	BAS 800 00 H 1 × 50	90% mature	0 0 1 1 3 3 7 7 10 10	dried seed dried seed dried seed dried seed dried seed dried seed dried seed dried seed dried seed dried seed	0.04 0.05 0.04 0.04 0.03 0.03 0.03 0.02 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01
Oregon R090345	BAS 800 00 H 1 × 50	BBCH 87	3 3	dried seed dried seed	< 0.01 < 0.01	< 0.01[b] < 0.01[b]	< 0.01[b] < 0.01[b]
Alberta R090346	BAS 800 00 H 1 × 50	BBCH 88	3 3	dried seed dried seed	< 0.01 < 0.01	< 0.01[b] < 0.01[b]	< 0.01[b] < 0.01[b]
Sasketchewan R090347	BAS 800 00 H 1 × 50	BBCH 87	2 2	dried seed dried seed	< 0.01 < 0.01	< 0.01[b] < 0.01[b]	< 0.01[b] < 0.01[b]
Sasketchewan R090348	BAS 800 00 H 1 × 50	BBCH 86	2 2	dried seed dried seed	0.03 0.05	< 0.01[b] < 0.01[b]	< 0.01[b] < 0.01[b]
Manitoba R090349	BAS 800 00 H 1 × 50	BBCH 82	4 4	dried seed dried seed	0.01 0.01	< 0.01 < 0.01	< 0.01 < 0.01

[a] Saflufenacil, M800H11 and M800H35 residues are expressed in terms of each analyte

Combined residues of saflufenacil (parent + M800H11 + M800H35), expressed as parent equivalents. To calculate the combined residues, values for the individual metabolites were converted to parent equivalents using a MWCF (1.06 x for M800H11, and 1.42 x for M800H35). For calculation, seed residue values of < 0.01 mg/kg (<LOQ) were considered to be 0.01 mg/kg, and vine residue values of < 0.025 mg/kg (<LOQ) were considered to be 0.025 mg/kg.

[b] result of multiple analyses of individual field sample

Soya bean

Fifteen field trial data were performed for saflufenacil on soya bean during the 2006 growing season. At each test location, one untreated control and one or two treated plots were established. The treated plots received a single broadcast, pre-plant incorporated (PPI) or pre-emergence (PRE) application of saflufenacil (70% WG, formulation code BAS 800 00 H) at 0.10 kg ai/ha. The applications were made with ground equipment using approximately 147–289 L/ha. (US GAP: > 1 Pre-plant or pre-emergence application at 14-day intervals at 0.025 kg ai/ha and seasonal maximum rate of 0.1 kg/ha with PHI of 65 days (Jordan J. 2007(a)).

The soya bean immature RAC samples (succulent seed with pod and succulent seed without pod) were harvested at 62–119 days after treatment, targeting growth stage BBCH 73 to 77. Soya bean forage and hay samples were harvested at the same time the succulent pods were collected. Jordan J. 2007)

The samples were analysed according to method D0603. The mean recoveries were between 67 and 102% for Saflufenacil, between 72 and 97% for M800H11 and between 65 and 81% for M800H35.

Table 64 Summary of residues in succulent soya bean, forage, hay and dried seed

Portion analysed	N	n	DALA [1)]	Residues (mg/kg)		
				Saflufenacil	M800H11	M800H35
succulent seed with pod	15	42	62-126	< 0.01	< 0.01	< 0.01
succulent seed without pod	15	42	62-126	< 0.01	< 0.01	< 0.01
dried seed	15	30	82-162	< 0.01	< 0.01	< 0.01

Field trial data have been generated for Saflufenacil on soya bean (20 trials) during the 2009 growing season. At each test location, one untreated control and one or two treated plots were established. The treated plots received a single late-season, broadcast application of the 70% water-dispersible granule (WG) formulation of saflufenacil applied as a harvest aid / desiccant at 0.05 kg ai/ha. In addition, at three sites, a comparison plot was treated in the same manner with a single late-season, broadcast application of the suspension concentrate (SC) formulation of saflufenacil (BAS 800 04 H) applied as a desiccant also at 0.05 kg ai/ha. The applications were made using ground equipment with 130–354 L/ha of water spray volumes. Samples of *mature soya bean* raw agricultural commodity (RAC) dried seed were harvested at a 2–4 day pre-harvest interval (PHI). At two trials, including one at which both formulations were tested, additional treated samples were collected at 0, 1, 7 and 10 days after the last application, in addition to the targeted 2-day PHI, to evaluate residue decline. (Norris F. A. 2010(c))

The samples were analysed according to method D0603. The mean recoveries at the LOQ and 100× higher were 86% and 74% for Saflufenacil, between 96% and 71% for M800H11 and between 81% and 67% for M800H35.

In 2008, a study was conducted in Brazil comprising five trials in soya bean applying BAS 800 01 H twice: the first application took place on the day of the plantation at a rate of 49 g ai/ha. The second application at a rate of 98 g ai/ha was done pre-harvest as desiccant of the crop. In both cases the spray volume was 200 L/ha. Soya bean seed was taken at the intended PHI of 7 days after the last application, in three trials also after 0, 3, 10 and 14 days. (Jones B., Souza C. 2008(h)).

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 99% for Saflufenacil, 87% for M800H11 and 96% for M800H35. At the intended PHI of 7 days, parent Saflufenacil was found below the limit of detection (0.002 mg/kg) or the limit of quantitation (0.01 mg/kg). The metabolites M800H11 and M800H35 were below their calculated limits of detection (0.003 mg/kg each).

Table 65 Detailed residue results of saflufenacil in soya bean from trials in the Canada, Brazil and USA

Crop	Country Trial No.	Appl. rate (g ai/ha)	Timing	PHI (days)	Matrix	Residues found * (mg/kg)		
						Saflufenacil	M800 H11	M800 H35
soya bean	S. Carolina R090360	 1 × 50	late season	3 3	dried seed dried seed	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
soya bean	Georgia R090361	 1 × 50	late season	0 0 1 1 3 3 7 7 10 10	dried seed dried seed dried seed dried seed dried seed dried seed dried seed dried seed dried seed dried seed	0.01 0.01 < 0.01 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 0.02	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01

Crop	Country Trial No.	Appl. rate (g ai/ha)	Timing	PHI (days)	Matrix	Residues found * (mg/kg)		
						Saflufenacil	M800 H11	M800 H35
		1 × 50	late season	0	dried seed	0.01	< 0.01	< 0.01
				0	dried seed	0.01	< 0.01	< 0.01
				1	dried seed	< 0.01	< 0.01	< 0.01
				1	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
				7	dried seed	< 0.01	< 0.01	< 0.01
				7	dried seed	< 0.01	< 0.01	< 0.01
				10	dried seed	< 0.01	< 0.01	< 0.01
				10	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Missouri R090362	1 × 50	late season	2	dried seed	< 0.01	< 0.01	< 0.01
				2	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Arkansas R090363	1 × 50	late season	3	dried seed	0.05	< 0.01	< 0.01
				3	dried seed	0.05	< 0.01	< 0.01
		1 × 50	late season	3	dried seed	0.02	< 0.01	< 0.01
				3	dried seed	0.02	< 0.01	< 0.01
soya bean	Mississippi R090364	1 × 50	late season	0	dried seed	< 0.01	< 0.01	< 0.01
				0	dried seed	< 0.01	< 0.01	< 0.01
				1	dried seed	< 0.01	< 0.01	< 0.01
				1	dried seed	0.02	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
				7	dried seed	< 0.01	< 0.01	< 0.01
				7	dried seed	< 0.01	< 0.01	< 0.01
				10	dried seed	< 0.01	< 0.01	< 0.01
				10	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Missouri R090365	1 × 50	late season	2	dried seed	< 0.01	< 0.01	< 0.01
				2	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Missouri R090366	1 × 50	late season	2	dried seed	< 0.01	< 0.01	< 0.01
				2	dried seed	< 0.01	< 0.01	< 0.01
soya bean	North Dakota R090367	1 × 50	late season	3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
		1 × 50	late season	3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
soya bean	North Dakota R090368	1 × 50	late season	3	dried seed	0.01*	< 0.01	< 0.01
				3	dried seed	0.01*	< 0.01	< 0.01
soya bean	Minnesota R090369	1 × 50	late season	3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Minnesota R090370	1 × 50	late season	3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Kansas R090371	1 × 50	late season	2	dried seed	< 0.01	< 0.01	< 0.01
				2	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Ohio R090372	1 × 50	late season	3	dried seed	0.02*	< 0.01	< 0.01
				3	dried seed	0.02*	< 0.01	< 0.01
soya bean	Illinois R090373	1 × 50	late season	3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Iowa R090374	1 × 50	late season	3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Illinois R090375	1 × 50	late season	3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Wisconsin R090376	1 × 50	late season	3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Wisconsin R090377	1 × 50	late season	3	dried seed	< 0.01	< 0.01	< 0.01
				3	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Kansas R090378	1 × 50	late season	4	dried seed	< 0.01	< 0.01	< 0.01
				4	dried seed	< 0.01	< 0.01	< 0.01
soya bean	Ontario R090379	1 × 50	late season	2	dried seed	0.01	< 0.01	< 0.01
				2	dried seed	0.02	< 0.01	< 0.01
soya bean	Brazil G080103	2 appl.	85-90	0	seed	0.03	nd	nd
				3	seed	< 0.01	nd	nd

Crop	Country Trial No.	Appl. rate (g ai/ha)	Timing	PHI (days)	Matrix	Residues found * (mg/kg)		
						Saflufenacil	M800 H11	M800 H35
		49 and 98		7	seed	nd	nd	nd
				10	seed	nd	nd	nd
				14	seed	nd	nd	nd
soya bean	Brazil G080104	2 appl. 49 and 98	88	7	seed	nd	nd	nd
soya bean	Brazil G080105	2 appl. 49 and 98	88-89	0	seed	0.02	nd	nd
				3	seed	0.01	nd	nd
				7	seed	< 0.01	nd	nd
				10	seed	< 0.01	nd	nd
				14	seed	nd	nd	nd
soya bean	Brazil G080106	2 appl. 49 and 98	88	7	seed	nd	nd	nd
soya bean	Brazil G080107	2 appl. 49 and 98	85-89	0	seed	0.01	nd	nd
				3	seed	nd	nd	nd
				7	seed	nd	nd	nd
				10	seed	nd	nd	nd
				14	seed	nd	nd	nd

* result of multiple analyses of individual field sample

Root and Tuber vegetables

Potato

In 2008, a study was conducted in Brazil comprising four trials in potato applying saflufenacil in WG formulation once at a rate of 98 g ai/ha as pre-harvest desiccant in a spray volume of 200 L/ha. Potato tubers were taken at the intended PHI of 7 days after the last application, in two trials also after 0, 3, 10 and 14 days (Jones B., Souza C. 2008(f)).

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 95% for Saflufenacil, 79% for M800H11 and 89% for M800H35

In potato tuber, parent Saflufenacil and its metabolite M800H35 were not detected above their calculated limits of detection (0.009 and 0.001 mg/kg, respectively) throughout the study. Metabolite M800H11 was either below its limit of detection of 0.0003 mg/kg or below the LOQ of 0.01 mg/kg.

Table 66 Summary of residues in potato

Portion analysed	Year	N	n	DALA[a]	Growth stage	Residues (mg/kg)		
						Saflufenacil	M800H11	M800H35
Potato tuber	2008	4	2	0	BBCH 45-79	nd	nd / < 0.01	nd
			2	3		nd	nd	nd
			4	7		nd	nd / < 0.01	nd
			2	10		nd	nd	nd
			2	14		nd	nd / < 0.01	nd

[a] days after last application

nd not detected

Cereals

Field trial data have been generated for saflufenacil on the representative crops wheat (25 trials), field and sweet corn (15 + 5 trials), grain sorghum (9 trials), rice (6 trials) and barley (6 trials). A total of 66 field trials were conducted on cereal grains during the 2006-2007 growing seasons.

Saflufenacil was applied as single broadcast pre-plant incorporated (PPI) or pre-emergence (PRE) application to the soil surface at 0.142–0.158 kg ai/ha. The pre-plant incorporated applications were made before planting and were incorporated into the soil. The pre-emergence sprays were made after planting but before crop emergence. All applications were made in 95–346 L/ha using ground equipment. The cereal RAC samples were harvested at commercial maturity. (Johnston R.L. 2008)

Table 67 Summary of use conditions applied in residue trials conducted with WG formulation

Crop	Country	No of trials	GAP	Application				PHI (actual sampling) [days]
				Method	Rate [kg ai/ha]	Spray conc. [kg ai/hL]	No	
barley	US/Canada	6	PHI 30 d	PPI or PRE	0.150	0.043–0.158	1	n.a. (grain 81-100)
Maize[a]	US/Canada	20	max GAP	PPI or PRE	0.150	0.043–0.158	1	n.a. (grain 118-158)
maize	Brazil	2	No GAP	at planting	0.098	0.049	1	n.a.
rice	US/Canada	6	No GAP	PPI or PRE	0.150	0.043–0.158	1	n.a. (grain 121-149)
rice	Brazil	4	GAP	1) at planting 2) post emergence	1) 0.098 2) 0.147	1) 0.049 2) 0.074	2	60 (40-80)
sorghum	US/Canada	9	GAP	PPI or PRE	0.150	0.043–0.158	1	n.a. (grain 68-150)
wheat	US/Canada	25	PHI 30 d	PPI or PRE	0.150	0.043–0.158	1	n.a. (grain 76-280)
wheat	Brazil	2	No GAP	at planting	0.098	0.049	1	n.a.

[a] 15 trials on field corn and 5 trials on sweet corn; PPI - pre-plant incorporated

PRE - pre-emergence

n.a. - not applicable

The samples were analysed according to method D0603. The mean recovery in wheat was between 69 and 97% for Saflufenacil, between 70 and 99% for M800H11 and between 64 and 97% for M800H35 (Johnston R.L. 2008).

In 2008, a study was conducted in Brazil comprising two trials in wheat applying saflufenacil once at a rate of 49 g ai/ha at planting in a spray volume of 200 L/ha. Wheat grain specimens were taken at normal harvest maturity (Jones B., Souza C. 2008(i))

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 94% for both Saflufenacil and M800H11 and 81% for M800H35.

Summary of results is given in Table 79.

Barley

Six field trials were conducted on barley during 2006-2007 growing seasons. Saflufenacil was applied as single broadcast pre-plant incorporated (PPI) or pre-emergence (PRE) application to the soil surface at 0.142–0.158 kg ai/ha. The pre-plant incorporated applications were made before planting and were incorporated into the soil. The pre-emergence sprays were made after planting but before crop emergence. All applications were made in 95–346 L/ha using ground equipment. The cereal RAC samples were harvested at commercial maturity (Johnston R.L. 2008).

The samples were analysed according to method D0603. The mean recovery in barley matrices was at 95% for Saflufenacil, at 81% for M800H11 and at 91% for M800H35. No residues could be detected in any of the samples.

Sorghum

Nine field trials were condcted on grain sorghum during the 2006–2007 growing seasons. Saflufenacil was applied as single broadcast pre-plant incorporated (PPI) or pre-emergence (PRE) application to the soil surface at 0.142–0.158 kg ai/ha. The pre-plant incorporated applications were

made before planting and were incorporated into the soil. The pre-emergence sprays were made after planting but before crop emergence. All applications were made in 95–346 L/ha using ground equipment. The cereal RAC samples were harvested at commercial maturity (Johnston R.L. 2008).

The samples were analysed according to method D0603. The mean recovery in sorghum matrices was between 63 and 113% for saflufenacil, between 70 and 85% for M800H11 and between 68 and 104% for M800H35. No residues could be detected in any of the samples.

Table 68 Summary results of analyses of barley, sorghum and wheat samples for saflufenacil residues

Portion analysed	N	n	DLA	Residues (mg/kg)		
				Saflufenacil	M800H11	M800H35
Wheat grain [a]	25	62	90-280	< 0.01	< 0.01	< 0.01
Wheat grain [b]	2	2	n.a.	nd–< 0.01	nd	nd
Sorghum, grain, matured [a]	9	18	n.a.	< 0.01	< 0.01	< 0.01
Barley, grain, matured [a]	6	12	81–99	< 0.01	< 0.01	< 0.01

[a] Trials in Canada and USA

[b] Trials in Brazil

Maize

Field trial data have been generated for Saflufenacil on field and sweet corn (15 + 5 trials), during the 2006-2007 growing seasons.

Saflufenacil was applied as single broadcast pre-plant incorporated (PPI) or pre-emergence (PRE) application to the soil surface at 0.142–0.158 kg ai/ha. The pre-plant incorporated applications were made before planting and were incorporated into the soil. The pre-emergence sprays were made after planting but before crop emergence. All applications were made in 95–346 L/ha using ground equipment. The cereal RAC samples were harvested at commercial maturity (Johnston R.L. 2008).

The samples were analysed according to method D0603. The mean recovery in maize matrices was between 71 and 105% for Saflufenacil, between 74 and 95% for M800H11 and between 73 and 104% for M800H35. No residues could be detected in any of the samples.

In 2008, a study was conducted in Brazil comprising two trials in corn applying saflufenacil once at a rate of 98 g ai/ha at planting in a spray volume of 200 L/ha. Corn grain specimens were taken at normal harvest maturity (Jones B. 2008(b)).

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 95% for Saflufenacil, 87% for M800H11 and 92% for M800H35.

Residues of parent saflufenacil and its metabolites M800H11 and M800H35 were below their limits of detection (0.002 mg/kg each) in mature corn grain samples.

Table 69 Summary of residues in maize

Portion analysed	N	n	DLA	Residues (mg/kg)		
				Saflufenacil	M800H11	M800H35
Maize (corn), grain	15	30	120-158	< 0.01	< 0.01	< 0.01
Maize (corn), grain[2]	2	2	n.a.	nd	nd	nd

k+cwhr - kernel + cob with husk removed; nd: < 0.002 mg/kg

[a] Trials in Canada and USA

[b] Trials in Brazil

Rice

Six field trials were conducted on dry-land rice during the 2006–2007 growing seasons. Saflufenacil was applied as single broadcast pre-plant incorporated (PPI) or pre-emergence (PRE) application to the soil surface at 0.142–0.158 kg ai/ha. The pre-plant incorporated applications were made before

planting and were incorporated into the soil. The pre-emergence sprays were made after planting but before crop emergence. All applications were made in 95–346 L/ha using ground equipment. The cereal RAC samples were harvested at commercial maturity (Johnston R.L. 2008).

The samples were analysed according to method D0603. The mean recovery in rice matrices was between 63 and 97% for saflufenacil, between 67 and 82% for M800H11 and between 76 and 98% for M800H35.

In 2008, a study was conducted in Brazil with four trials in rice applying saflufenacil two times: the first application took place on the day of the plantation at a rate of 98 g ai/ha. The second application at a rate of 147 g ai/ha was done post outgrowth, 90 to 130 days after the first treatment. In both cases the spray volume was 200 L/ha. Rice grain samples were taken 40 to 80 days after the last application. Specimens of whole grain and grain without hulls were analysed (Jones B., Souza C. 2008(j)).

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 95% for Saflufenacil, 81% for M800H11 and 96% for M800H35. None of the samples contained any detectable residues.

Table 70 Summary of residues in rice

Portion analysed	Year	N	n	DALAa	Residues (mg/kg)		
					Saflufenacil	M800H11	M800H35
Rice grain [b]	2006-7	6	12	121–146	< 0.01	< 0.01	< 0.01
whole grain [c]	2008	4	2	40	nd	nd	nd
			2	50	nd–< 0.01	nd–< 0.01	nd
			4	60	nd–< 0.01	nd	nd
			2	70	nd	nd	nd
			2	80	nd	nd	nd
grain w/o hull [c]			2	40	nd	nd–< 0.01	nd
			2	50	nd	nd	nd
			4	60	nd	nd–< 0.01	nd
			2	80	nd	nd–0.03	nd–< 0.01

[a] days after last application

[b] US trials

[c] Brazilian trials

nd not detected

Grasses for sugar or syrup production

Sugarcane

In 2008, a study was conducted in Brazil with five trials in sugar cane applying saflufenacil once at a rate of 98 g ai/ha as pre-harvest desiccant in a spray volume of 200 L/ha. Sugar cane stalks were taken after 7 and 10 days, in two trials also after 0, 14 and 21 days.

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 83% for saflufenacil, 82% for M800H11 and 87% for M800H35 (Jones B., Souza C. 2008(l)).

Table 71 Summary of residues in sugar cane

Portion analysed	Year	N	n	DALA [a]	Residues (mg/kg)		
					Saflufenacil	M800H11	M800H35
Sugarcane stalks	2008	5	2	0	nd / < 0.01	nd < 0.0009	nd: < 0.0003
			5	7	nd / < 0.01	nd < 0.0009	nd: < 0.0003
			2	10	< 0.01	nd < 0.0009	nd: < 0.0003
			5	14	nd / < 0.01	nd < 0.0009	nd: < 0.0003
			2	21	nd	nd < 0.0009	nd: < 0.0003

[a] days after last application

Tree nuts

In 2006, a study was conducted in the US comprising 10 trials in tree nuts out of which five trials were done in almonds and five in pecan nuts. Saflufenacil was applied three times as directed to weeds/soil broadcast application at a rate of 50 g ai/ha in a spray volume of 182–287 L/ha. The first application took place at dormancy, 2 ± 1 weeks before bud break. The second application was done 20–24 days before harvest, the last application on the day of harvest. US GAP permits up to 3 treatments at 0.05 kg ai/ha rate (annual maximum of 0.15 kg ai/ha) with 7-day PHI.

Nutmeat specimens (in case of almond also hulls) were taken about 7 and 14 days after the third application, in one decline trial (almond) also 0, 21 and 28 days later (Jordan J.M., Nejad H. 2007)

The samples were analysed according to method D0603. The mean recovery was 85% and 114% (almond/pecan) for Saflufenacil, 90% and 108% for M800H11 and 80% and 94% for M800H35.

Almond and pecan nutmeat collected about 7 and 14 days after the last application did not contain any residue of Saflufenacil or its metabolites M800H11 and M800H35 above the limit of quantitation.

Table 72 Summary of residues in tree nuts

Portion analysed	Year	N	n	DALA [a]	Residues (mg/kg)		
					Saflufenacil	M800H11	M800H35
almond nutmeat	2006	5	2	0	< 0.01	< 0.01	< 0.01
			10	7	< 0.01	< 0.01	< 0.01
			10	14	< 0.01	< 0.01	< 0.01
			2	21	< 0.01	< 0.01	< 0.01
			2	28	< 0.01	< 0.01	< 0.01
pecan nutmeat		5	10	7-8	< 0.01	< 0.01	< 0.01
				13-14	< 0.01	< 0.01	< 0.01

[a] days after last application

Oilseeds

Cotton

In 2007, a study was conducted in the US with 12 trials in cotton applying saflufenacil once as at-planting pre-emergence broadcast spray to soil. Two different application rates were compared: in variant 2, 24–36 g ai/ha were applied, in variant 3 the twofold amount with 49–72 g ai/ha. The spray volume was between 190 and 265 L/ha. Cotton seed samples were taken at 141–186 days after treatment. Undelinted cotton seed and in some trials also gin by-products were collected at normal maturity (White M.T., Nejad H. 2008).

The samples were analysed according to method D0603. The mean recovery was 98% and 92% (undelinted seed/ gin by-products) for Saflufenacil, 101% and 93% for M800H11 and 101% and 81% for M800H35.

Table 73 Summary of residues in cotton

Appl. rate (g ai/ha)	Portion analysed	N	n	DALA [a]	Residues (mg/kg)		
					Saflufenacil	M800H11	M800H35
24–36	undelinted seed	12	24	141–186	< 0.01	< 0.01	< 0.01
49–72	undelinted seed		22	141–186	< 0.01	< 0.01	< 0.01

[a] days after last application

nd not detected

In 2009, a study was conducted in the US with 12 trials in cotton applying saflufenacil with a single late-season, broadcast application as a harvest aid / desiccant at a rate of 50 g ai/ha in a spray volume of about 290–380 L/ha. (GAP: 1 × 50 g late season, 290-380 L/ha, PHI 5 days).

Cotton seed and gin by-products samples were taken at the PHI of 5 days, in one trial also after 1, 3, 5, 10 and 15 days (Culligan J.F. 2010).

In 2008, a study was conducted in Brazil with four trials in cotton applying saflufenacil three times: the first application took place on the day of the plantation and the second post outgrowth, both at a rate of 49 g ai/ha. The third application was done pre-harvest as desiccant at a rate of 98 g ai/ha. In all cases the spray volume was 200 L/ha. Cotton seed samples were taken at the PHI of 7 days, in two trials also after 0, 3, 10 and 14 days (Jones B. 2008(a)).

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 93% for Saflufenacil, 95% for M800H11 and 104% for M800H35.

Table 74 Results of supervised trials on cotton following desiccant use of saflufenacil in WG formulation

Country Trial No.	Formulation, Appl. rate (g ai/ha)	GS [a]	PHI (days)	Residues found (mg/kg)			
				Matrix	saflufenacil	M800H11	M800H35
Georgia R090329	BAS 800 00 H 1 × 50	97	5 5	seed seed	< 0.01 < 0.01	< 0.01 < 0.01	< 0.01 < 0.01
Arkansas R090330	BAS 800 00 H 1 × 50	99	5 5	seed seed	0.02 0.02	< 0.01 < 0.01	< 0.01 < 0.01
Arkansas R090331	BAS 800 00 H 1 × 50	99	5 5	seed seed	0.03 0.02	< 0.01 < 0.01	< 0.01 < 0.01
Arkansas R090332	BAS 800 00 H 1 × 50	99	5 5	seed seed	0.07 0.08	< 0.01 < 0.01	< 0.01 < 0.01
Oklahoma R090333	BAS 800 00 H 1 × 50	98	5 5	seed seed	0.02 0.03	< 0.01 < 0.01	< 0.01 < 0.01
Texas R090334	BAS 800 00 H 1 × 50	97	5 5	seed seed	0.03 0.03	< 0.01 < 0.01	< 0.01 < 0.01
Texas R090335	BAS 800 00 H 1 × 50	96	5 5	seed seed	0.03 0.03	< 0.01 < 0.01	< 0.01 < 0.01
Texas R090336	BAS 800 00 H 1 × 50	96	5 5	seed seed	0.03 0.02	< 0.01 < 0.01	< 0.01 < 0.01
California R090337 Texas R090338	BAS 800 00 H 1 × 50 BAS 800 00 H 1 × 50	94 96	5 5 1 1 3 3 5 5 10 10 15 15	seed seed seed seed seed seed seed seed seed seed seed seed	0.07 0.12 0.07 0.08 0.01 < 0.01 0.03 0.03 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01
California R090339	BAS 800 00 H 1 × 50	94	5 5	seed seed	0.09 0.12	< 0.01 < 0.01	< 0.01 < 0.01
Texas R090340	BAS 800 00 H 1 × 50	94	5 5	seed seed	0.03 0.02	< 0.01 < 0.01	< 0.01 < 0.01
Brazil G080109	BAS 800 01 F 3 appl. 49, 49, 98	93- 95	0 3 7 10 14	seed seed seed seed seed	0.06 0.09 0.02 0.04 0.02	nd nd nd nd nd	nd nd nd nd nd
Brazil G080110	BAS 800 01 F 3 appl. 49, 49, 98	89	0 3 7 10 14	seed seed seed seed seed	0.34 0.25 0.09 0.04 0.02	nd nd nd nd nd	nd nd 0.01 < 0.01 < 0.01

Country Trial No.	Formulation, Appl. rate (g ai/ha)	GS [a]	PHI (days)	Residues found (mg/kg)			
				Matrix	saflufenacil	M800H11	M800H35
Brazil G080111	BAS 800 01 F 3 appl. 49, 49, 98	94	7	seed	0.02	nd	nd
Brazil G080112	BAS 800 01 F 3 appl. 49, 49, 98	89	7	seed	< 0.01	nd	nd

*Mean of multiple analyses of the same field sample

Rape seed

Field trial data had been generated for saflufenacil on oilseed rape (canola varieties only, 16 trials) during the 2009 growing season in the US and Canada. Each trial location consisted of one untreated and one treated plot. Each treated plot received a single late-season, broadcast application of the 70% water-dispersible granule (WG) formulation of saflufenacil applied as a harvest aid / desiccant at 0.049–0.051 kg ai/ha.

In addition, at three trial sites, a bridging comparison plot was treated in the same manner with a single late-season, broadcast application of the 342 g/L suspension concentrate (SC) formulation of saflufenacil (BAS 800 04 H) applied as a harvest aid /desiccant at 0.046–0.052 kg ai/ha. The applications were made using ground equipment with 132–305 L/ha spray volumes.

Samples of mature rape seed dried seed were harvested at a 2–3 day pre-harvest interval (PHI). The US GAP permits one application at 0.053–0.178 kg ai/ha maximum seasonal rate of 0.05 kg ai/ha, allow up to 7 days for optimum desiccation effect depending on environmental conditions. At two trials, additional treated samples were collected at 0, 1, 7 and 10 days after treatment, in addition to the targeted 3 ± 1 day PHI, to evaluate residue decline (Norris F.A. 2010(d).

The samples were analysed according to method D0603/02. The mean recoveries at 0.01 and 1.0 mg/kg were 90 and 70% for Saflufenacil, 71 and 59% for M800H11 and 78 and 60% for M800H35.

Residues of parent saflufenacil ranged from 0.011 to 0.329 mg/kg, M800H11 residues were < 0.01–0.029 mg/kg, and M800H35 residues were < 0.01 mg/kg in/on 32 treated dried rape seed samples harvested 2–3 days after a single broadcast foliar application of saflufenacil (70% WG, BAS 800 00 H) applied as a harvest aid/desiccant targeting 0.050 kg ai/ha. Combined residues of saflufenacil in/on dried seed ranged from 0.031 to 0.352 mg/kg.

In the three trials testing the SC formulation, residues of parent saflufenacil ranged from 0.019 to 0.482 mg/kg, M800H11 residues were < 0.01–0.055 mg/kg, and M800H35 residues were < 0.01 mg/kg in/on six treated dried rape seed samples harvested 3 days after a single broadcast foliar application of saflufenacil (342 g/L SC, BAS 800 04 H) applied as a harvest aid/desiccant targeting 0.050 kg ai/ha. Combined residues of saflufenacil in/on dried seed ranged from 0.039 to 0.547 mg/kg. The bridging trials comparing the two formulations (WG vs. SC) demonstrated that there was no observable difference in residues in canola treated with the two formulations.

Table 75 Results of supervised trials conducted in rape seed in the US and Canada

Country Trial No.	Formulation, Appl. rate (g ai/ha)	Timing	PHI (days)	Matrix	Residues found * (mg/kg)		
					Saflufenacil	M800 H11	M800 H35
Georgia R090380	BAS 800 00 H 1 × 50	89	3 3	Dried seed	0.049 0.039	< 0.01 < 0.01	< 0.01 < 0.01
Michigan R090381	BAS 800 00 H 1 × 50	89	0 0 1 1 3	Dried seed	0.123 0.163 0.142 0.072 0.048	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01

Country Trial No.	Formulation, Appl. rate (g ai/ha)	Timing	PHI (days)	Matrix	Residues found * (mg/kg)		
					Saflufenacil	M800 H11	M800 H35
			3 7 7 10 10		0.040 0.021 0.018 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01
Nebraska R090382	BAS 800 00 H 1 × 50	90% ripe	3 3	Dried seed	0.011 0.023	< 0.01 < 0.01	< 0.01 < 0.01
Idaho R090383	BAS 800 00 H 1 × 50 BAS 800 04 H 1 x 46	90% ripe	3 3 3 3	Dried seed	0.329 0.250 0.482 0.375	0.014 0.029 0.055 0.043	< 0.01 < 0.01 < 0.01 < 0.01
Idaho R090384	BAS 800 00 H 1 × 50	89	0 0 1 1 3 3 7 7 10 10	Dried seed	0.057 0.045 0.076 0.134 0.087 0.105 0.185 0.150 0.100 0.091	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01
Manitoba R090385	BAS 800 00 H 1 × 50	89	3 3	Dried seed	0.106 0.090	< 0.01 < 0.01	< 0.01 < 0.01
Manitoba R090386	BAS 800 00 H 1 × 50	89	3 3	Dried seed	0.087 0.112	< 0.01 < 0.01	< 0.01 < 0.01
Saskatchewan R090387	BAS 800 00 H 1 × 50	89	2 2	Dried seed	0.068 0.053	0.01 0.01	0.01 0.01
Saskatchewan R090388	BAS 800 00 H 1 × 50	89	2 2	Dried seed	0.117 0.119	0.01 0.01	0.01 0.01
Saskatchewan R090389	BAS 800 00 H 1 × 50	89	3 3	Dried seed	0.045 0.087	0.01 0.01	0.01 0.01
Saskatchewan R090390	BAS 800 00 H 1 × 50	89	3 3	Dried seed	0.082 0.057	0.012 0.01	0.01 0.01
Alberta R090391	BAS 800 00 H 1 × 50 BAS 800 04 H 1 x 46	88	3 3 3 3	Dried seed	0.049 0.070 0.054 0.046	0.01 0.01 0.01 0.01	0.01 0.01 0.01 0.01
Alberta R090392	BAS 800 00 H 1 × 50 BAS 800 04 H 1 x 46	88	3 3 3 3	Dried seed	0.021 0.022 0.019 0.021	0.01 0.01 0.01 0.01	0.01 0.01 0.01 0.01
Alberta R090393	BAS 800 00 H 1 × 50	82-83	3 3	Dried seed	0.066 0.070	0.01 0.01	0.01 0.01
Alberta R090394	BAS 800 00 H 1 × 50	82-83	3 3	Dried seed	0.053 0.058	0.01 0.01	0.01 0.01
Alberta R090395	BAS 800 00 H 1 × 50	88	3 3	Dried seed	0.045 0.044	0.01 0.01	0.01 0.01

Sunflower

In 2007, a study was conducted in the US with eight trials in sunflower applying BAS 800 00 H in two late-season, over-the-top broadcast applications at a rate of 0.05 kg ai/ha and a retreatment interval of 7 days. Commercially mature sunflower seed samples were harvested about 7 and about 14 days after the last application (DALA). In one trial, additional samples were collected at 3, 10, and 20 days after the last application to examine residue decline (Johnston R.L., Saha M. 2008).

The samples were analysed according to method D0603. The mean recovery was 90% for Saflufenacil, 97% for both M800H11 and M800H35.

In 2008, a study was conducted in Brazil comprising four trials in sunflower applying BAS 800 01 H once at a rate of 98 g ai/ha as pre-harvest desiccant in a spray volume of 200 L/ha. Sunflower seed were taken 7 (PHI) and 10 days after the last application, in two trials also after 0, 3 and 14 days (Jones B., Micheleto P. 2008).

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 88% for Saflufenacil, 86% for M800H11 and 85% for M800H35.

Table 76 Results of supervised trials conducted on sunflower with WG formulations in the USA, Canada and Brazil

Crop	Country Trial No.	Formulation, Appl. rate (g ai/ha)	PHI (days)	Residues found (mg/kg)			
				Matrix	Saflufenacil	M800H11	M800H35
Sun-flower	Kansas R070224	BAS 800 00 H 2 x 50	7 7 14 14	seed seed seed seed	0.1346 0.1904 0.2438 0.1141	0.0166 0.0228 0.0281 0.0260	< 0.01 < 0.01 < 0.01 < 0.01
Sun-flower	Wisconsin R070225	BAS 800 00 H 2 x 50	8 8 15 15	seed seed seed seed	0.0866 0.0904 0.0867 0.0701	0.0261 0.0231 0.0355 0.0300	< 0.01 < 0.01 < 0.01 < 0.01
Sun-flower	Michigan R070226	BAS 800 00 H 2 x 50	6 6 14 14	seed seed seed seed	0.0516 0.0608 0.0648 0.0723	0.1343 0.1574 0.3258 0.3346	< 0.01 < 0.01 < 0.01 < 0.01
Sun-flower	North Dakota R070227	BAS 800 00 H 2 x 50	7 7 14 14	seed seed seed seed	0.1517 0.1520 0.0367 0.0874	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01
Sun-flower	North Dakota R070228	BAS 800 00 H 2 x 50	7 7 14 14	seed seed seed seed	0.3691 0.5048 0.4573 0.3175	0.0389 0.0664 0.0881 0.0704	< 0.01 < 0.01 < 0.01 < 0.01
Sun-flower	Kansas R070229	BAS 800 00 H 2 x 50	3 3 6 6 10 10 14 14 20 20	seed seed seed seed seed seed seed seed seed seed	0.1019 0.0964 0.0484 0.0803 0.0764 0.0803 0.0652 0.0506 0.0399 0.0374	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01
Sun-flower	Saskat-chewan R070230	BAS 800 00 H 2 x 50	6 6 13 13	seed seed seed seed	0.1270 0.2524 0.0587 0.1606	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01
Sun-flower	North Dakota R070231	BAS 800 00 H 2 x 50	7 7 14 14	seed seed seed seed	0.0306 0.0866 0.0152 0.0437	< 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01
Sun-flower	Brazil G080066	BAS 800 01 F 1 x 98	0 3 7 10 14	seed seed seed seed seed	0.03 < 0.01 < 0.01 0.02 0.01	nd nd nd < 0.01 < 0.01	nd nd nd nd nd
Sun-flower	Brazil G080067	BAS 800 01 F 1 x 98	7 10	seed seed	< 0.01 0.02	nd nd	nd nd
Sun flower	Brazil G080069	BAS 800 01 F 1 x 98	7 10	seed seed	0.04 0.08	< 0.01 0.02	nd < 0.01

Crop	Country Trial No.	Formulation, Appl. rate (g ai/ha)	PHI (days)	Residues found (mg/kg)			
				Matrix	Saflufenacil	M800H11	M800H35
Sun-flower	Brazil G080070	BAS 800 01 F 1 x 98	0	seed	0.05	nd	nd
			3	seed	0.08	nd	nd
			7	seed	0.07	nd	nd
			10	seed	0.09	nd	nd
			14	seed	0.05	nd	nd

Seed for beverages and sweets

Coffee

In 2008, a study was conducted in Brazil comprising three trials in coffee applying BAS 800 01 H three times at a rate of 49 g ai/ha as a weed post-emergence directed jet in a spray volume of 200 L/ha. Coffee grains were taken 7 days after the last application (Jones B., Souza C. 2008(k)).

The samples were analysed according to SOP-PA.0298 based on method D0603/02. The mean recovery was 97% for saflufenacil, 96% for M800H11 and 86% for M800H35.

In 2008, a study was conducted in Costa Rica (2 sites), Colombia (2 sites) and Mexico (1 site) comprising five trials in coffee. Applications of saflufenacil directed to the base of the plants were performed four times at rates between 98 and 104 g ai/ha in a spray volume of 193–209 L/ha and retreatment intervals of 30 ± 5 days. Samples of commercially mature coffee beans (red coffee cherries) were harvested at a 0-day or 1-day pre-harvest interval (PHI) and processed according to typical commercial practices to produce the coffee raw agricultural commodity (RAC), green bean (Jordan J.M. 2010(b)).

The samples were analysed according to method D0603/02. The mean recovery was 109% for saflufenacil, 97% for M800H11 and 76% for M800H35.

Table 77 Results of supervised trials conducted in coffee applying a WG formulation in Brazil, Columbia, Costa Rica and Mexico

Trial No.	Appl. rate (g ai/ha)	GS [1)]	PHI (days)	Residues found (mg/kg)			
				Matrix	Saflufenacil	M800H11	M800H35
G080114[a]	3 x 49	89	7	Green bean	< 0.01	< 0.01	< 0.01
G080115 [a]	3 x 49	89	7	Green bean	< 0.01	nd	< 0.01
G080227 [a]	3 x 49	86	7	Green bean	nd	nd	< 0.01
R080665[b]	4 x 100	n.r.	0	Green bean	< 0.01	< 0.01	< 0.01
R080666			1	Green bean	< 0.01	< 0.01	< 0.01
R080667 [c]	4 x 100	n.r.	0	Green bean	< 0.01	< 0.01	< 0.01
R080668[c]			1	Green bean	< 0.01	< 0.01	< 0.01
R080669[d]	4 x 100	n.r.	0	Green bean	< 0.01	< 0.01	< 0.01
			1	Green bean	< 0.01	< 0.01	< 0.01

[a] Brazil (3)

[b] Columbia (2)

[c] Costa Rica (2)

[d] Mexico (1)

Legume animal feed

Pea vines

At a PHI of 3 days, the results of all these nine trials (18 values for Saflufenacil, M800H11 and M800H35 each) were between the LOQ of 0.27 mg/kg and 4.88 mg/kg for the total residue (sum of parent Saflufenacil, M800H11 and M800H35) in pea vines.

Table 78 Residues in pea vines from supervised trials conducted in the US and Canada

Country Trial No.	Formulation, Appl. rate (g ai/ha)	Timing	PHI (days)	Residues found (mg/kg)			
				Matrix	Saflufenacil	M800H11	M800H35
North Dakota R090341	BAS 800 00 H 1 × 50	BBCH 92	3 3	vines vines	1.56 1.89	< 0.025 < 0.025	0.06 0.05
Wisconsin R090342	BAS 800 00 H 1 × 50	mature	4 4	vines vines	0.36 0.41	< 0.025 < 0.025	0.07 0.07
Idaho R090343	BAS 800 00 H 1 × 50	BBCH 89	3 3	vines vines	1.96 2.27	< 0.025 < 0.025	0.13 0.12
North Dakota R090344	BAS 800 00 H 1 × 50	90% mature	0 0 1 1 3 3 7 7 10 10	vines vines vines vines vines vines vines vines vines vines	3.10 4.4 2.50 2.99 2.39 1.67 0.91 1.39 0.84 0.54	< 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025	< 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025
Oregon R090345	BAS 800 00 H 1 × 50	BBCH 87	3 3	vines vines	0.10 0.09	< 0.025 < 0.025	0.11 0.11
Alberta R090346	BAS 800 00 H 1 × 50	BBCH 88	3 3	vines vines	4.83 3.67	< 0.025 < 0.025	< 0.025 < 0.025
Saskatchewan R090347	BAS 800 00 H 1 × 50	BBCH 87	2 2	vines vines	4.54 4.58	< 0.025 < 0.025	< 0.025 < 0.025
Saskatchewan R090348	BAS 800 00 H 1 × 50	BBCH 86	2 2	vines vines	3.73 4.29	< 0.025 < 0.025	< 0.025 0.03
Manitoba R090349	BAS 800 00 H 1 × 50	BBCH 82	4 4	vines vines	1.29 1.28	< 0.025 < 0.025	0.06 0.06

Soya beans

In soya beans 15 trials were conducted in the US testing a pre-plant incorporated (PPI) or pre-emergence (PRE) application at 0.10 kg ai/ha. The residues in soya bean forage and hay were all below the LOQ of < 0.025 mg/kg for individual residue components.

Table 79 Summary of residues in soya bean

Portion analysed	N	n	DAT [a]	Residues (mg/kg)		
				Saflufenacil	M800H11	M800H35
forage	15	42	62-126	< 0.025	< 0.025	< 0.025
hay				< 0.025	< 0.025	< 0.025

[a] DALA Days after treatment

Straw, fodder and forage of spring and winter wheat, sorghum

The results of all trials (62 values each in cereal straw, 104 values each for wheat forage and hay) were below the LOQ of 0.025 mg/kg for all residue components. All sorghum samples contained non-detectable residues, except one which contained 0.04 mg/kg M800H35.

Table 80 Summary of residues in wheat

Portion analysed	N	n	DAT	Residues (mg/kg)		
			days	Saflufenacil	M800H11	M800H35
Wheat forage	25	104	34-231	< 0.025	< 0.025	< 0.025
Wheat hay	25	104	41-184	< 0.025	< 0.025	< 0.025
Wheat straw	25	62	103-280	< 0.025	< 0.025	< 0.025
Sorghum, forage	9	36	69-116	< 0.025	< 0.025	< 0.025
Sorghum, stover	9	18	103-050	< 0.025	< 0.025	< 0.025–< 0.04

Corn/maize

The results of 15 field trials on field corn indicated that the residues were below the LOQ of 0.025 mg/kg for each residue component in corn forage sampled 86–114 days and corn stover sampled 120–158 days after the single pre-plant treatment at max GAP.

Table 81 Summary of residues in maize

Portion analysed	N	n	DLA	Residues (mg/kg)		
				Saflufenacil	M800H11	M800H35
Maize (corn), forage	20	60	63-134	< 0.025	< 0.025	< 0.025
Maize (corn), stover	20	30	136-153	< 0.025	< 0.025	< 0.025

k+cwhr - kernel + cob with husk removed

Miscellaneous fodder and forage crops

Almond hull

The results of five field trials on almond indicated that the residues were below the LOQ of 0.025 mg/kg for each residue component in almond hulls sampled 7–28 days after the last of 3 treatments at max GAP.

Cotton gin by-product

Table 82 Residues in cotton gin by-product from supervised trials conducted in the US

Crop	Country Trial No.	Formulation, Appl. rate (g ai/ha)	GS [1)]	PHI (days)	Residues found (mg/kg)			
					Matrix	Saflufenacil	M800H11	M800H35
cotton	Georgia R090329	BAS 800 00 H 1 × 50	97	5 5	gin by-prod. gin by-prod.	0.10 0.08	< 0.025 < 0.025	< 0.025 < 0.025
cotton	Oklahoma R090333	BAS 800 00 H 1 × 50	98	5 5	gin by-prod. gin by-prod.	0.15 0.23	< 0.025 < 0.025	< 0.025 < 0.025
cotton	Texas R090334	BAS 800 00 H 1 × 50	97	5 5	gin by-prod. gin by-prod.	0.14 0.29*	< 0.025 < 0.025	< 0.025 < 0.025
cotton	Texas R090335	BAS 800 00 H 1 × 50	96	5 5	gin by-prod. gin by-prod.	0.15 0.21	< 0.025 < 0.025	< 0.025 < 0.025
cotton	California R090337	BAS 800 00 H 1 × 50	94	5 5	gin by-prod. gin by-prod.	1.91* 2.25	< 0.025 < 0.025	< 0.025 < 0.025
cotton	Texas R090338	BAS 800 00 H 1 × 50	96	1 1 3 3 5 5 10 10 15 15	gin by-prod. gin by-prod. gin by-prod. gin by-prod. gin by-prod. gin by-prod. gin by-prod. gin by-prod. gin by-prod. gin by-prod.	0.61 0.77 0.13 0.12 0.15 0.18 0.25 0.18 0.16 0.15	< 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025	< 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025 < 0.025
cotton	California R090339	BAS 800 00 H 1 × 50	94	5 5	gin by-prod. gin by-prod.	1.94* 1.74*	< 0.025 < 0.025	< 0.025 < 0.025

[a] BBCH Growth stage

* Residues were determined with multiple analyses as performed from individual samples

FATE OF RESIDUES IN STORAGE AND PROCESSING

In processing

Soya bean

A soya bean processing study was conducted to determine the potential for concentration of residues of Saflufenacil in soya bean processed fractions. In one trial conducted in Arkansas during the 2006 growing season, BAS 800 00 H was applied as a single broadcast pre-emergence application, 1 day after planting of soya bean, at a rate of 0.100 kg ai/ha/season or at an exaggerated rate of 0.300 kg ai/ha/season.

Commercially mature, soya bean RAC samples were harvested at normal maturity, 125 days after the pre-emergence application (126 days after planting). A single treated bulk seed sample was later processed into soya bean aspirated grain fractions RAC samples and duplicate exaggeratedly treated bulk seed samples were later separately processed into soya bean processed commodities (Norris F.A., Gooding R.F. 2007(a)).

Following a single pre-emergence application of Saflufenacil at 0.300 kg ai/ha), combined residues of Saflufenacil were below the combined LOQ (< 0.03 mg/kg; < 0.01 mg/kg for each analyte) in two soya bean seed RAC samples harvested 125 days after treatment.

Soya bean processing studies were conducted to determine the potential for concentration of residues of saflufenacil (Saflufenacil) in the processed fractions of soya bean and to determine the magnitude of the residue of saflufenacil in/on aspirated grain fractions RAC samples. In two field trials conducted during the 2009 growing season in the USA. Saflufenacil (formulation, BAS 800 00 H; 70% WG) was applied as a single late-season, broadcast application to soya bean as a harvest aid / desiccant at an exaggerated rate of 0.252–0.253 kg ai/ha (5× the maximum proposed label rate).

Table 83 Saflufenacil residues in processed soya bean samples

Trial Location	Total Rate (kg ai/ha)	Processed Commodity	PHI	Residues (mg/kg)			
				Saflufenacil [a]	M800H11 [a]	M800H35 [a]	Processing factor for parent [c]
Tift, GA 2009	0.252	Seed (RAC)	3	0.04*	< 0.01	< 0.01	-
		Hulls		0.28	< 0.01	< 0.01	7.0
		Meal		0.02*	< 0.01	< 0.01	0.5
		RBD oil		< 0.01	< 0.01	< 0.01	0.3
		Flour		0.02	< 0.01	< 0.01	0.5
		Milk		< 0.01	< 0.01	< 0.01	0.3
		Tofu		< 0.01	< 0.01	< 0.01	0.3
Jefferson, IA 2009	0.253	Seed (RAC)	3	0.06*	< 0.01	< 0.01	-
		Hulls		0.53	< 0.01	< 0.01	8.8
		Meal		0.05*	< 0.01	< 0.01	0.8
		RBD oil		< 0.01	< 0.01	< 0.01	0.2
		Flour		0.11	< 0.01	< 0.01	1.8
		Milk		< 0.01	< 0.01	< 0.01	0.2
		Tofu		< 0.01	< 0.01	< 0.01	0.2

[a] All analytes are reported in terms of themselves

[b] The total of saflufenacil + M800H11 + M800H35 (values "< 0.01" are set to "0.01" for calculating purposes)

[c] The processing factor is calculated by dividing the residue in the processed fraction by the residue in the seed RAC

* Mean of two analyses of the same sample

Sunflower

A sunflower processing study was conducted to determine the potential for concentration of residues of saflufenacil in sunflower processed fractions.

In one trial conducted in Minnesota during the 2006 growing season, saflufenacil was applied as two late-season broadcast applications to sunflower at 0.257 kg ai/ha/application, with a retreatment interval of 6 days, for a total exaggerated rate of 0.513 kg ai/ha/season. The applications, which were initiated 13 days prior to mature dry seed harvest, were made with ground equipment using approx. 190 L/ha of water. An adjuvant was included in the spray mixture for each application.

The samples were analysed according to method D0603. The limit of quantitation was 0.01 mg/kg for saflufenacil, M800H11 and M800H35, and the recoveries at 0.01–25 mg/kg were 77–107%, 88–105%, and 72–122%, respectively (Norris F.A., Saha M. 2007(a)).

Saflufenacil residues were 0.30 and 0.32 mg/kg in/on two treated sunflower seed samples harvested at the 7-day PHI.

The two treated bulk sunflower samples were separately processed using simulated commercial processing procedures. Combined residues in the two treated meal samples derived from the treated sunflower seed RAC samples were 0.21 and 0.22 mg/kg, and the residues were below the LOQ in the two treated refined oil samples.

Table 84 Saflufenacil residues in sunflower processed fractions

Trial Location	Total Rate (kg ai/ha)	Processed Commodity	PHI	Residues [a] (mg/kg)			
				BAS 800 H	M800H11	M800H35	Processing Factor [b] for parent
Clay, MN 2006	0.513	Seed RAC	7	0.28-0.30	< 0.01	< 0.01	-
		Meal	7	0.22	< 0.01	< 0.01	0.8
		Refined oil	7	< 0.01	< 0.01	< 0.01	< 0.03

[a] All residues are expressed as parent equivalents. The LOQ is 0.01 mg/kg each for BAS 800 H, M800H11 and M800H35 in/on sunflower commodities.

[b] Calculated by dividing the residues in the processed fraction by the residues in the sunflower RAC.

A comparison of the residues in the RAC with those in each processed fraction indicated that combined residues of saflufenacil do not concentrate in sunflower processed fractions (sunflower meal and refined oil).

Cottton

Following the pre-emergence broadcast spray of saflufenacil to the soil surface at 0.051 kg ai/ha at-planting, the residues in cotton seed were below the LOQ of 0.01 mg/kg. The bulk seed cotton samples were processed into cotton processed commodities according to simulated commercial procedures. The residues of saflufenacil M800H11 and M800H35 were < 0.01 mg/kg in two treated samples as well as in each of hull, meal and refined oil (White M.T., Nejad H, 2008a).

Oranges

In one trial conducted in Florida during the 2006 growing season, saflufenacil was applied as three broadcast orchard floor applications at 0.249–0.252 kg ai/ha/application, with a 20–21 day retreatment interval, for a total exaggerated rate of 0.75 kg ai/ha/season. The applications were made in 277–281 L/ha using ground equipment and an adjuvant was included in the spray mixture together with ammonium sulphate liquid fertilizer.

Commercially mature orange RAC samples (whole fruit) were harvested immediately after the last application (0-day PHI) (Jordan J.M., Saha M. 2007(a)).

The samples were analysed according to method D0603. Concurrent recoveries of Saflufenacil, M800H11 and M800H35 from control orange fruit and oil samples fortified at 0.01 and 0.1 mg/kg were 63–67%, 69–123%, and 67–107%, respectively.

Following the last of three broadcast applications of saflufenacil combined residues of Saflufenacil were < LOQ (< 0.01 mg/kg each for parent, M800H11 and M800H35) in/on two treated

orange RAC samples (fruit) collected at the 0-day PHI. As quantifiable residues were not found in the whole fruit treated at the exaggerated rate, or in any of the whole fruit collected from the citrus crop field trials treated at the proposed rate, analysis of the dried pulp and juice was not required and was not conducted. Residues in citrus oil were determined because of the 1000x theoretical concentration factor for this commodity. Residues of each analyte were < 0.01 mg/kg in the two citrus oil samples derived from the orange fruit samples. A comparison of the residues in the RAC with those in each processed fraction indicated that combined residues of Saflufenacil do not concentrate in the citrus oil.

Apple

An apple processing study was conducted to determine the potential for concentration of residues of Saflufenacil in apple processed fractions. In one trial conducted in New York during the 2006 growing season, BAS 800 00 H was applied as three broadcast orchard floor applications at 0.246–0.251 kg ai/ha/application, for a total exaggerated rate of 0.749 kg ai/ha/season. The sprays were made at dormancy (2 ± 1 weeks prior to bud break) 179 days prior to harvest, 21 days before harvest, and on the day of harvest with ground equipment using 230–235 L/ha. An adjuvant was included in the spray mixture together with ammonium sulphate liquid fertilizer.

Commercially mature, apple RAC samples (fruit) were harvested immediately after the last application (0-day PHI) (Jordan J.M. 2007(c)).

The samples were analysed according to method D0603. Concurrent recoveries of saflufenacil, M800H11 and M800H35 fortified in two control apple fruit samples at 0.01 and 0.1 mg/kg were 104 and 82%, 104 and 86%, and 78 and 92%, respectively.

Following the last of three broadcast foliar applications of Saflufenacil (70% WG) at 0.246–0.251 kg ai/ha/application, totalling 0.749 kg ai/ha/season, combined residues of saflufenacil were below the limit of quantitation (< 0.01 mg/kg for each analyte, parent, M800H11, and M800H35) in/on two treated apple RAC samples harvested at the 0-day PHI.

Plum

In one trial conducted in California during the 2006 growing season, saflufenacil was applied as three broadcast orchard floor applications beginning at dormancy (2 ± 1 weeks prior to bud break) at 0.173 kg ai/ha followed by applications made 20 days before harvest and on the day of harvest at 0.254–0.257 kg ai/ha/application, for a total exaggerated rate of 0.68 kg ai/ha/season. The applications were made in 277–286 l water/ha using ground equipment and an adjuvant was included in the spray mixture together with ammonium sulphate liquid fertilizer.

After the last of three broadcast orchard floor applications of saflufenacil, combined residues of Saflufenacil were below the limit of quantitation (< 0.03 mg/kg) in/on two treated plum RAC samples (fruit) harvested at the 0-day PHI (Jordan J.M., Stewart J.M. 2007).

After the last of three broadcast orchard floor applications of Saflufenacil, combined residues of Saflufenacil were below the limit of quantitation (< 0.03 mg/kg) in/on two treated plum RAC samples (fruit) harvested at the 0-day PHI. LOQ 0.01

Cereals

Winter wheat

After a single broadcast pre-emergence application of saflufenacil at 0.247 kg ai/ha to winter wheat, combined residues of Saflufenacil were below the combined LOQ (< 0.03 mg/kg) in/on one treated wheat RAC sample (grain) harvested at maturity, 280 days after planting (< 0.01 mg/kg each for parent, M800H11 and M800H35).

Field corn

After a single broadcast pre-emergence application of saflufenacil at 0.303 kg ai/ha to field corn, combined residues of saflufenacil were below the combined LOQ (< 0.03 mg/kg) in/on one treated

wheat RAC sample (grain) harvested at maturity, 154 days after planting (< 0.01 mg/kg each for parent, M800H11 and M800H35).

Sweet sorghum

After a single broadcast pre-emergence application of saflufenacil at 0.100 kg ai/ha to sweet sorghum, combined residues of saflufenacil were below the combined LOQ (< 0.075 mg/kg) in/on one treated sweet sorghum RAC sample (stalk) harvested at commercial maturity, 104 days after planting (< 0.025 mg/kg each for parent, M800H11 and M800H35).

Rice

After a single broadcast pre-emergence application of saflufenacil at 0.214–0.240 kg ai/ha to field corn, combined residues of saflufenacil were below the combined LOQ (< 0.03 mg/kg) in/on two treated rice RAC samples (grain) harvested at maturity, 151 days after planting (< 0.01 mg/kg each for parent, M800H11 and M800H35) (Johnston R.L., Saha M. 2007).

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

Lactating dairy cows

The saflufenacil was administered orally to 14 lactating cows over a period of 28 days at the target nominal dose levels of 0.1 ppm feed (1×), 0.3 ppm (3×) and 1.0 ppm (10×). The actual dose levels of 0.15 ppm (1×), 0.48 ppm (3×) and 1.7 ppm (10×) were calculated based on actual feed intake. 3 animals formed the control, 1× and 2× groups. Three animals from each group was sacrificed within one day after the last dose. Two out of five animals dosed at 10× level were sacrificed 65 h and 185 h after the last dose (Rawle N.W. 2007(a)).

Milk was collected twice a day and pooled. The sampling days were 3, -1, 1, 3, 6, 9, 12, 15, 18, 21, 24, 28/29, 30, and 35. Skim milk and cream were analysed from day 22. The muscle, liver, kidney and fat tissues were collected at the time of sacrifice.

Analytical Method No. L0073/01 was used to determine residues of saflufenacil in matrices of animal origin (milk, skim milk, cream, muscle, kidney, liver, fat). The final determination is performed by HPLC-MS/MS. The limit of quantification (LOQ) of the method is 0.01 mg/kg for all matrices. During the study, the specimens were stored at approximately -18 °C or lower. The storage stability test covers the period of storage for samples from the dairy cattle feeding study.

No residues above the LOQ were detected in milk and cream at any of the dosing levels.

Table 85 Residues of saflufenacil in tissues and milk of dairy cow

Treatment Group	Group Mean (and Maximum Individual) Residues in Tissue for saflufenacil (mg/kg)			
	Muscle	Liver	Kidney	Fat
1 (0×, control)	< 0.01 (< 0.01)	< 0.01 (< 0.01)	< 0.01 (< 0.01)	< 0.01 (< 0.01)
2 (1×, 0.1 mg/kg)	< 0.01 (< 0.01)	0.21 (0.26)	< 0.01 (< 0.01)	< 0.01 (< 0.01)
3 (3×, 0.3 mg/kg)	< 0.01 (< 0.01)	0.77 (0.88)	0.02 (0.02)	< 0.01 (< 0.01)
4 (10×, 1.0 mg/kg)	< 0.01 (< 0.01)	2.61 (3.49)	0.04 (0.04)	< 0.01 (< 0.01)
4 (10×, 1.0 mg/kg) 2 days withdrawal	< 0.01	1.66	0.03	< 0.01
4 (10×, 1.0 mg/kg) 5 days withdrawal	< 0.01	0.34	< 0.01	< 0.01

Laying hens

The calculated feed burden for poultry based on feed items with highest residues resulted in 0.038 mg/kg total dry matter feed. Thus, the trigger value of 0.1 mg/kg dry matter feed for conducting a farm animal feeding study was not reached.

In addition, it can be concluded from the data of the hen metabolism study that there are no residues to expect in any of the edible hen matrices assuming a hen feeding level of 0.07 mg/kg dry matter feed. This feeding level would be lower by a factor of more than 300 compared to the feeding level of 12.6–12.7 mg/kg in the hen metabolism study.

Therefore, by extrapolation from the residue levels in the metabolism study the residues in a hen feeding study would be far below the LOQ of 0.01 mg/kg of the residue analytical method for any of the edible hen matrices even at a 10x feeding level. Thus a hen feeding study has not been conducted.

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

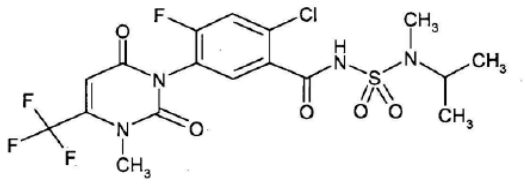
No data were available.

APRAISAL

Saflufenacil is a new herbicide applied for contact and residual control of broad leaf weeds and is used in many crops in pre- and post-emergence, or desiccation. It is evaluated by the JMPR for the first time.

The Meeting received information from the manufacturer on metabolism in animals, plants, soil and water, analytical methods, effect of storage and processing and animal transfer studies. Residue data derived from supervised trials on a variety of crops, including fruits, tree nuts, potatoes, legume vegetables, cereals, oil seeds, coffee, sugar cane and follow up crops were also submitted.

The IUPAC name of saflufenacil is N'-[2-chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)benzoyl]-N-isopropyl-N-methylsulfamide



Metabolism

The metabolism and distribution of saflufenacil in plants and animals were investigated using the active substance radio labelled in the phenyl ring and the uracil ring.

The following abbreviations are used for the metabolites discussed:

Metabolite Code	Chemical Name
M800H01	N'-[2-chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)benzoyl]-N-isopropylsulfamide
M800H02	N'-[2-chloro-5-(2,6-dioxo-4-(trifluoromethyl)-3,6-dihydropyrimidin-1(2H)-yl)-4-fluorobenzoyl]-N-isopropyl-N-methylsulfamide
M800H03	N'-[2-chloro-5-(2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)-4-fluorobenzoyl]-N-isopropyl-N-methylsulfamide
M800H04	(2E)-3-{4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino)

Metabolite Code	Chemical Name
	carbonyl]phenyl)amino]carbonyl(methylamino)}-4,4,4-trifluorobut-2-enoic acid
M800H05	N'-[2-chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)benzoyl]-sulfamide
M800H07	N-{4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino)carbonyl]phenyl}-N'-methylurea
M800H08	N'-[2-chloro-4-fluoro-5-(3-methyl-2,6-dioxo-4-(trifluoromethyl)tetrahydro-1(2H)-pyrimidinyl)benzoyl]-N-isopropyl-N-methylsulfamide
M800H09	N'-[2-chloro-5-(2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)-4-fluorobenzoyl]-sulfamide
M800H10	N'-[2-chloro-5-(2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)-4-fluorobenzoyl]-N-methylsulfamide
M800H11	N'-[2-chloro-5-(2,6-dioxo-4-(trifluoromethyl)-3,6-dihydro-1(2H)-pyrimidinyl)-4-fluorobenzoyl]-N-isopropylsulfamide
M800H15	N-{4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino)carbonyl]phenyl}-4-4-4-trifluoro-3,3-dihydroxybutanamide
M800H17	N-{4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino)carbonyl]phenyl}-N-(methylamino)carbonyl-4,4,4-trifluoro-3-oxo-butanamide
M800H18	N-{4-chloro-2-fluoro-5-[({[isopropylamino]sulfonyl}amino)carbonyl]phenyl}-N'-methylurea
M800H22	3-[({4-chloro-2-fluoro-5-[({[isopropyl(methyl)amino]sulfonyl}amino)carbonyl]anilino}carbonyl)(methyl)amino]-4,4,4-trifluorobutanoic acid
M800H26	N-Methyl-2,2,2-trifluoroacetamide
M800H29 (TFA)	Trifluoroacetic acid (or its Na salt)
M800H31	3-[carboxy(methyl)amino]-4,4,4-trifluorobutanoic acid
M800H33	Trifluoroacetone
M800H34	N-{4-chloro-2-fluoro-5-[([aminosulfonyl]amino)carbonyl]phenyl}-N'-methylurea
M800H35	N-[4-chloro-2-fluoro-5-({[(isopropylamino)sulfonyl]amino} carbonyl)phenyl]urea
M800H36	Not IUPAC classified due to ambiguous hydroxyl position
M800H37	N-{4-chloro-2-fluoro-5-[({[ethyl(methyl)amino]sulfonyl}amino)carbonyl]phenyl}-N'-methylurea

Animal metabolism

Animal metabolism studies were conducted with saflufenacil on lactating goats and laying hens. The metabolism in rats performed as part of toxicological studies is reported under toxicology.

Lactating goats

Two-year old lactating goats dosed with [phenyl-U-^{14}C] saflufenacil were administered 18.4 mg/day, equivalent to 13.9 ppm in the feed. The animal dosed with [uracil-4-^{14}C] saflufenacil received a dose of 17.8 mg/day, equivalent to 13.4 ppm in the feed.

Production of urine and faeces was recorded once daily and production of milk twice daily (in the afternoon and in the morning before dosing). Animals were sacrificed within 24 h of the last dose. Liver, kidney, blood, adipose tissue, muscle, GI tract with contents and bile were collected. The total recovery of radioactivity was found to be 91.83% in the phenyl-label group and 89.89% in the uracil-label group.

Radioactivity in milk amounted to 0.001–0.005% and 0.002–0.009% of the radioactivity administered for the phenyl-labelled and the uracil-labelled [^{14}C]saflufenacil, respectively. Concentrations of radioactivity in milk stayed relatively constant after three application days ranging from 0.004–0.019 mg eq/kg and 0.006–0.024 mg eq/kg for the phenyl-labelled and the uracil-labelled [^{14}C]saflufenacil, respectively.

At sacrifice, highest concentrations of radioactivity were found in liver and bile. Residue concentrations of phenyl-labelled and uracil-labelled [^{14}C]saflufenacil in liver and bile samples were 0.962 and 3.832 mg eq/kg, and 0.634 and 1.461 mg eq/kg, respectively. In adipose tissue and muscle, 0.010 mg eq/kg and 0.017 mg eq/kg, as well as 0.008 mg eq/kg and 0.011 mg eq/kg were found for the phenyl-labelled and the uracil-labelled [^{14}C]saflufenacil, respectively.

Saflufenacil was transformed to a number of metabolites after administration to the goats. Following the application of phenyl and uracil labelled compound the TRR was 0.008 mg/kg and 0.011 mg/kg in muscle, 0.01 mg/kg and 0.017 mg/kg in fat, 0.13 mg/kg and 0.17 mg/kg in kidney, 0.962 mg/kg and 3.832 mg/kg in liver, 0.006 mg/kg and 0.012 mg/kg in milk, respectively. The unchanged parent compound was found as the predominant compound in muscle (44.2% and 56.7%), fat (44.1% and 65.1%), kidney (73.8% and 71.3%), liver (80.2% and 75.7%) whilst in milk its proportion was somewhat lower (47% and 25.4%) following the dosing with phenyl and uracil labelled compounds, respectively. In addition, metabolites M800H01, M800H03, M800H04 and M800H10 were present in few percentages, except M800H10 in milk (39–40%).

The metabolism of the active substance saflufenacil in lactating goats is characterized by several dealkylation steps (phase I reactions), which occurred at two sites of the molecule: N-demethylation at the N-isopropyl-N-methylsulfamide side chain resulting in metabolite M800H01, and N-demethylation at the uracil ring producing M800H02. Both demethylation reactions formed metabolite M800H11. Elimination of the N-isopropyl group converted the parent compound to M800H03. This reaction furthermore transformed metabolite M800H01 to M800H05, and metabolite M800H02 to M800H10. The metabolites M800H05 and M800H10 could also be formed by the respective demethylation of metabolite M800H03. An additional transformation was hydrolytic opening of the uracil ring of saflufenacil to form metabolite M800H04. Degradation of the resulting side chain generated metabolite M800H07 with its N-methyl-amide group. This metabolite was only detected with the phenyl label. The metabolites are rapidly excreted, along with parent, and do not readily accumulate in tissues or milk. The residues in edible tissues and milk were low. All relevant metabolites were identified and a comprehensive metabolic pathway was elucidated.

Laying hens

Phenyl-U-[^{14}C] saflufenacil or uracil-[^{14}C] saflufenacil was administered orally by gavage once a day to two groups of eight laying hens for 10 consecutive days at a nominal rate of 12 mg/kg feed. The total recovery of radioactivity was found to be 88.76% in the phenyl-[^{14}C]-label group and 83.67% in the uracil-[^{14}C]-label group.

The eggs were collected in the afternoon after administration and in the morning before the administration. The radioactivity was determined in liver, adipose tissue, blood, muscles (leg and chest muscles), gastrointestinal tract (skin and contents). All samples were extracted and analysed within approximately four months after sampling. The extractability of radioactivity from all matrices was greater than 80%. The metabolic fate of approximately 75–80% of the total administered radioactivity considering both labels of saflufenacil could be elucidated.

Excreta contained 85.14% of the phenyl-labelled [^{14}C]saflufenacil administered (uracil-[^{14}C]label: 78.10%). Radioactivity recovered from excreta and cage wash amounted to 88.07% (phenyl-[^{14}C]-label) and 82.96% (uracil-[^{14}C]-label) of the total radioactivity administered.

In eggs, 0.029% (phenyl-[^{14}C]-label) and 0.046% (uracil-[^{14}C]-label) of the total radioactivity administered were found. With both labels, egg concentrations increased continuously up to day 6 and remained unchanged (0.01–0.012 mg/kg for phenyl and 0.016–0.018 mg/kg for uracil labels) until day 10, indicating that a steady state was reached.

At sacrifice, 23 h after the last administration, highest organ concentrations of radioactivity were found in liver (phenyl-[^{14}C]-label: 0.062 mg/kg; uracil-[^{14}C]-label: 0.060 mg/kg,). Residue concentrations of phenyl and uracil labelled [^{14}C]-material in muscles (0.011 mg/kg, 0.011 mg/kg), adipose tissue (0.011 mg/kg, 0.011 mg/kg), eggs (0.012 mg/kg, 0.018 mg/kg) in fat (0.011 mg/kg, 0.011 mg/kg) and in liver (0.062 mg/kg, 0.06 mg/kg) respectively.

The parent compound was the major residue (in muscle 54.7% of TRR, 0.006 mg/kg), fat (26.1%, 0.002 mg/kg) and liver (47.4%, 0.029 mg/kg). In eggs M800H10 amounted to 67.6% of TRR corresponding to 0.008 mg/kg (saflufenacil 20.8%, 0.002 mg/kg). Altogether, < 1% of the total radioactivity administered could be found in the tissues and organs analysed for both radiolabels.

The metabolic reactions are in good accordance with the metabolism of saflufenacil in rats and in lactating goats and hens.

Plant metabolism

Metabolism of saflufenacil was studied in maize, soya beans and tomatoes applying phenyl and uracil labelled compounds.

Maize

Maize plants were grown in soil treated once at a nominal application rate of 200 g ai/ha directly on the bare soil after sowing (pre-emergence treatment). Forage samples were taken 42 and 101/102 days after treatment (DAT) (at the growth stages BBCH 18 and 85). Maize husks, cob, grain and straw (stover) were harvested at 133 days after treatment (BBCH 89).

The highest level of total radioactive residues (TRR) for the phenyl label was detected in maize husks (0.215 mg/kg), followed by stover (0.096 mg/kg). Lower residue levels were found in maize forage 42 DAT (0.018 mg/kg), forage 101 DAT (0.029 mg/kg), cob (0.016 mg/kg) and grain (0.020 mg/kg). In the case of the uracil label, the highest amount of TRR was detected in corn straw (stover) (0.553 mg/kg). Maize husks contained 0.226 mg/kg, forage sampled 102 DAT contained 0.149 mg/kg and maize forage 42 DAT contained 0.039 mg/kg. In maize grain and cob, 0.049 mg/kg and 0.065 mg/kg were found, respectively. Extractability of radioactive residues with methanol and water ranged from 60 to 96% of the TRR), with the exception of cob and grain (phenyl label, ~ 19% TRR each).

In the experiments with the phenyl label, metabolites M800H09, M800H34 and M800H10 were the major components in the matrices sampled at harvest and in maize forage 101 DAT (up to 21.4% TRR). In maize forage sampled 42 DAT (phenyl label), the main components were M800H09, M800H10, M800H01, M800H03 and M800H05 (11% to 20% TRR). At harvest the parent saflufenacil was non-detectable in maize grain, cob and straw (< 0.0005) and present in husk in traces (0.0001 mg/kg), the metabolite M800H11 was found in portions of 1.6% to 4.6% TRR (< 0.0005–0.004 mg/kg).

In the case of the uracil label, the polar metabolite M800H29 (trifluoroacetic acid) was the predominant constituent of the methanol extracts of all plant matrices investigated (64% to 88% TRR, grain: 30.5% TRR, 0.004 mg/kg). Since the potentially corresponding [^{14}C]phenyl-labelled metabolites as counter parts of M800H29 were not detected at adequate quantities, the occurrence of TFA could be explained by the uptake of this metabolite or a respective precursor molecule from the soil. The parent saflufenacil was not detectable in maize grain and any of the other samples and metabolite M800H11 was present at ≤ 0.5% of TRR.

Saflufenacil is metabolized in maize plants by the following main transformation reactions: N-demethylation at the uracil ring; stepwise degradation (N-dealkylation) of the N-methyl-N-isopropyl group to NH_2 forming a sulfonamide group and hydrolytic cleavage of the uracil ring generating a urea side chain.

Soya beans

Pre-emergence treatment

Soya bean plants were grown in soil treated once at a nominal application rate of 150 g ai/ha directly on the bare soil after sowing (pre-emergence treatment). Soya bean forage samples were taken at 39/40 DAT (days after treatment). Soya bean beans, pods (hull), and straw were harvested at 95 DAT.

Following the application of phenyl and uracil labelled compounds the TRR expressed as mg/kg were in forage (0.086, 0.38), bean (0.038, 0.22), pod (0.18, 2.0) and straw (0.43, 1.2), respectively. The extractable radioactive residues ranged from 60% to 98% of TRR.

In soya bean forage sampled 39 DAT (phenyl label), the parent compound was present at 23.5% TRR (0.019 mg/kg). The parent compound and the metabolites M800H01, M800H03, M800H05 and M800H37 were found in portions of up to 6.5% TRR in the other matrices. M800H11 and M800H35 were found up to 13% of TRR in forage, bean and pod and 24.9% and 15.6% of TRR in straw. The corresponding concentrations expressed as mg/kg were in forage (0.005, 0.004), bean (0.001), pod (0.016, 0.023) and straw (0.11, 0.067), respectively. The parent saflufenacil was present in matured beans at 0.002 mg/kg.

In the case of the uracil label, the polar metabolite M800H29 was the predominant constituent of the extracts of all plant matrices investigated (85.2% in forage 65.4% in beans, 75.9% in pods and 69.2% in straw.

Pre-harvest (late season) use

Soya bean leaves, stems, pods and seeds were harvested at 7 days after the foliar application of [^{14}C]uracil labelled saflufenacil at a rate of 100 g ai/ha. The TRR were 0.419 mg/kg in stem, 1.86 mg/kg in pod, 0.043 mg/kg in seed and 17.9 mg/kg in leaves. The extractable radioactive residues ranged between 75.6% and 97.6% of TRR.

The unchanged parent compound was identified with 73% and 76% of the TRR in the extracts of stem and pod, with 64% TRR in leaves and with 26% of the TRR in seed (0.011 mg/kg). Four metabolites were identified in soya bean matrices. The most abundant metabolite identified in all soya bean matrices was M800H02 (5% to 26% of the TRR). The metabolites M800H01 and M800H03 were mainly detected in soya bean leaves (9% to 14% TRR) and in minor portions in soya bean pod (< 1% to 3% TRR). The metabolite M800H11 was detected in all matrices (3% to 10% TRR).

Tomatoes

The metabolism study was conducted with phenyl- and uracil- labelled saflufenacil applied on bare soil before planting of tomato plants at a nominal application rate of 100 g ai/ha. Tomato plants were sampled 68 and 113 days after application. Mature tomato fruits were harvested 113 days after treatment.

The total radioactive residues in tomato plants sampled 68 days after treatment accounted for 0.089 mg/kg (phenyl label) and 0.131 mg/kg (uracil label). In tomato plants at harvest (113 DAT), the radioactive residues were 0.113 mg/kg for the phenyl label and 0.138 mg/kg for the uracil label. In tomato fruits (113 DAT), the residue levels were significantly lower, accounting for 0.015 mg/kg (phenyl label) and 0.037 mg/kg (uracil label). Extractability of radioactive residues with methanol and water was good and generally amounted to 80–100% of the TRR.

In the methanol extract of tomato plants sampled at day 68 (phenyl label), the unchanged parent compound was the most abundant component, accounting for 29% TRR. Major metabolites were M800H07 (14% TRR) and M800H11 (13% TRR). Other metabolites were detected at minor

quantities below 7% TRR: M800H01, M800H02, M800H09, M800H10 and M800H35. The methanol extract of tomato plants at harvest (phenyl label) contained the parent compound at a significantly lower concentration (11% TRR). The following metabolites were identified as minor metabolites at 6% TRR or below: M800H01, M800H02, M800H07, M800H09, M800H10, M800H11 and M800H35. The harvested tomato fruits contained the parent compound in traces < 0.0005 mg/kg, all metabolites were non-detectable.

Following the treatment with uracil labelled saflufenacil, the tomato plants contained the parent compound, M800H10 and M800H11 metabolites in ≤ 8.5% of TRR and M800H29 was the major residue component (82.2% and 51.7% of TRR at days 68 and 113, respectively). The fruit contained only M800H29 in detectable amounts (0.004 mg/kg). The parent saflufenacil amounted to 0.7% of TRR (< 0.0005 mg/kg). The formation of natural sugar compounds after complete breakdown of the test substance was proven for tomato fruit.

In summary, the metabolite pathway of saflufenacil in animals and plant materials is qualitatively similar. The metabolism of the active substance saflufenacil is characterized by several dealkylation steps (phase I reactions), which occurred at two sites of the molecule: N-demethylation at the N-isopropyl-N-methylsulfamide side chain resulting in metabolite M800H01, and N-demethylation at the uracil ring producing M800H02. Both demethylation reactions formed metabolite M800H11. Elimination of the N-isopropyl group converted the parent compound to M800H03. This reaction furthermore transformed metabolite M800H01 to M800H05, and metabolite M800H02 to M800H10. The metabolites M800H05 and M800H10 could also be formed by the respective demethylation of metabolite M800H03. An additional transformation was hydrolytic opening of the uracil ring of saflufenacil to form metabolite M800H04.

In the case of the uracil label, the polar metabolite M800H29 (trifluoroacetic acid) was the predominant constituent of the methanol extracts of plant matrices investigated. The occurrence of TFA was explained by the uptake of this metabolite or a respective precursor molecule from the soil.

Environmental fate

The fate and behaviour of saflufenacil and its metabolites in the environment was investigated under various conditions using the uracil ring- and phenyl ring labelled saflufenacil.

Aerobic degradation

The aerobic degradation of [^{14}C]uracil and phenyl-labelled saflufenacil was studied on sandy loam, silty clay loam, silt loam, and loamy sand soils treated approximately at the proposed maximum use rate of 400 g ai/ha. Following the application of uracil labelled saflufenacil M800H01, M800H02, M800H08, M800H22, M800H26 and M800H31 were identified. Their proportion ranged during the study. M800H02 occurred in largest proportion amounting to 26.4% of total administered radioactivity (TAR) by the end of the study (334 days).

In case of phenyl label, M800H01, M800H02, M800H07, M800H08 and M800H22 were identified. The M800H08 was present in largest proportion in the four soils (14.5–55% of TAR).

The average aerobic degradation DT_{50} values for saflufenacil approximately ranged from 4 days to 22 days in the four soils.

Field trials conducted at various location of USA revealed that the major route of dissipation of saflufenacil in bare soil was degradation by aerobic processes. The DT_{50} and DT_{90} values ranged between 1.36–32.2 days and 4.52–118 days, respectively.

Different metabolites were present at very low concentrations or were not detectable at all. The rate of mineralisation is low and up to 15% of the applied test material is converted to carbon dioxide and other organic volatiles within 365 days. Soil bound residues increased with time during test period.

Photolysis on soil surface

Photolysis of U-[^{14}C]phenyl label] saflufenacil in a light/dark experiment and [^{14}C] uracil and U-[^{14}C] phenyl label] saflufenacil in a continuous irradiation experiment was studied using a loamy sand soil.

In the light/dark experiment saflufenacil in the dark control samples accounted for approximately 97.7% at 0 DAT and decreased to 65.2% TAR at 30 DAT. From the irradiated samples, saflufenacil accounted for approximately 97.7% at 0 DAT and decreased to 43.1% TAR after 30 days of light/dark irradiation. Under the conditions of the study which were similar to the real field situation, there were no major degradation products from the irradiated samples, for either label, which were greater than 10% TAR at any time during the experiment. There were 10 minor products (< 10% TAR) observed.

In the continuous irradiation experiment saflufenacil accounted for approximately 96.43–97.80% at 0 DAT and decreased to 70.21–73.25% TAR at 15 DAT (in the dark control samples of both labels). For the irradiated samples of both labels, saflufenacil accounted for approximately 96.43–97.80% at 0 DAT and decreased to 50.64–58.03% TAR after 15 days of continuous irradiation. The only one major transformation product was an unidentified and unstable product that degraded quickly to M800H01. Minor amounts of M800H01, M800H07, M800H08 and M800H17 were also tentatively identified by HPLC.

Under the dark conditions, saflufenacil undergoes microbial reactions similar to those in aerobic soil metabolism. Saflufenacil was mainly converted to M800H08 and M800H07, as seen in the aerobic soil metabolism study. In addition, the loss of the methyl group on the sulfonylurea side chain of parent to form M800H01 was also observed. There was one major degradation product from the dark samples, and seven other minor products, none of which exceeded 5% TAR at any time during the experimental period. The major dark control product was identified as M800H08.

The DT_{50} for true phototransformation could be calculated as 66 days for the phenyl labelled saflufenacil in the light/dark cycle and 43 and 41 days for the phenyl and uracil labels, respectively, for continuous irradiation.

Saflufenacil undergoes photolysis on soil mainly via demethylation at the sulfonylurea side chain of parent to form M800H01, followed by the demethylation of the uracil ring and the cleavage of the sulfamide side chain. Photolysis also resulted in the opening and fragmentation of the uracil ring to form M800H07. Ultimately all the products could be further degraded to CO_2, but CO_2 production was less than 3% for any of the experiments.

Degradation in aquatic system

The hydrolysis of U-[^{14}C phenyl label] saflufenacil and [^{14}C uracil label] saflufenacil was investigated in dark at 25 °C in 0.01 N sterile buffer solutions at pH 5 (acetate), pH 7 (TRIS) and pH 9 (TRIS).

Saflufenacil was stable to hydrolysis in buffer at pH 5, and no half-life was determined. It degraded slowly in buffer at pH 7 reaching an average of 89% TAR and 94% TAR at 30 DAT for the phenyl and uracil label treatments, respectively. At pH 8 the degradation was rapid.

The photolysis of [^{14}C]saflufenacil (phenyl and uracil label) was conducted in aqueous buffer (pH 5, 0.01 M) and natural water (pH 7.1) at 22 ± 1 °C. The treated solutions (10 mg/kg saflufenacil) were continuously exposed to artificial sunlight (filtered Xenon lamp) for about 20 days for the photolysis conducted in aqueous buffer and 21 days for the natural water.

Saflufenacil degraded rapidly under photolytic conditions with half-lives of 26.8–35.2 and 9.7–9.8 days from the pH5 buffer and the natural water, respectively. Saflufenacil is fairly stable in both pH5 buffer and the natural water in the dark, although trifluoroacetone (M800H33) and M800H07 were found in the latter.

From the pH 5 buffer there are several minor photoproducts formed from both the phenyl and uracil labels; however, only one of them exceeds 10% TAR, but only after 20 days of constant irradiation. This unknown was < 10% TAR in the natural water. In the natural water, there are two

major photoproducts formed from the uracil label and identified as trifluoroacetic acid (M800H29) and M800H33 and several other minor photoproducts (none of them exceeds 10% TAR) from both labels.

Saflufenacil degrades in water under photolytic conditions by the opening of the uracil ring followed by the fragmentation of the uracil ring to form M800H04, M800H15, M800H07, M800H33, and M800H29. Hydroxylation of the trifluoromethyl group and the cleavage of the sulfonylurea side chain result in other minor degradation products.

Crop rotation studies

Studies with labelled saflufenacil

The metabolism of saflufenacil was investigated in rotational crops after one single application of the test substance in the EC formulation at a nominal application rate of 150 g ai/ha. Treatment was performed with either [phenyl-U-^{14}C]- or [^{14}C]-[uracil-4-^{14}C]-saflufenacil by spraying onto bare loamy sand soil. After soil aging periods of 30, 58, 120 and 365 days and ploughing saflufenacil, lettuce, white radish and spring wheat were planted/sowed and cultivated under natural climatic conditions.

Plant samples were harvested at maturity, and additional wheat forage samples were taken 48 to 68 day after planting (DAP). Soil samples were taken after ploughing and after harvest of the mature crops for each plant-back interval.

The total radioactive residues (calculated as the sum of extractable and non-extractable residues, ERR + RRR) in lettuce head (phenyl label) were below or equal to 0.010 mg/kg for all plant-back intervals. In the case of the uracil label, the TRR in lettuce head reached values between 0.078 mg/kg and 0.092 mg/kg after plant-back intervals of 30, 58 and 120 days, and only 0.002 mg/kg after 365 days of soil aging.

The TRR levels in white radish root did not exceed 0.005 mg/kg for all plant-back intervals in the case of the phenyl label. For the uracil label, the TRR in white radish root accounted for 0.034 to 0.038 mg/kg after soil aging periods of 30 and 58 days and for 0.008 to 0.010 mg/kg after the longer plant-back intervals.

In white radish top, higher TRR levels of 0.025 mg/kg (30 DAP), 0.014 mg/kg (58 and 120 DAP) and 0.007 mg/kg (365 DAP) were found for the phenyl label. In the case of the uracil label, the TRR in white radish top were also higher compared to root, accounting for 0.167 and 0.205 mg/kg after 30 and 58 days, and reaching lower levels of 0.046 and 0.087 mg/kg after 120 days and 365 days of soil aging, respectively.

The highest residue levels were detected in spring wheat chaff after a plant-back interval of 30 days (0.383 mg/kg for the phenyl label, 1.604 mg/kg for the uracil label). After longer periods of soil aging (120 and 365 days), the residues in wheat chaff were lower (0.068 and 0.114 mg/kg for the phenyl label, 0.629 mg/kg and 0.439 mg/kg for the uracil label, respectively).

The residue levels in wheat straw (0.089 to 0.125 mg/kg for the phenyl label, 0.196 to 0.356 mg/kg for the uracil label) and forage (decreasing with time from 0.048 to 0.011 mg/kg for the phenyl label and from 0.183 to 0.017 mg/kg for the uracil label) were generally lower compared to chaff.

In spring wheat grain, TRR levels of 0.017 mg/kg (30 DAP), 0.006 mg/kg (120 DAP) and 0.044 mg/kg (365 DAP) were found for the phenyl label. In the case of the uracil label, the residues in grain accounted for 0.370 mg/kg (30 DAP), 0.094 mg/kg (120 DAP) and 0.116 mg/kg (365 DAP).

In summary, the predominant metabolites in the case of the phenyl label were M800H35, M800H05, M800H01, M800H11 and M800H10 (and/or an unknown medium polar component), representing stepwise degradation of the molecule by N-dealkylation reactions and by hydrolytic cleavage of the uracil ring generating an urea side chain. For the [^{14}C]uracil label, M800H29 as trifluoroacetic acid was the predominant metabolite. Since [^{14}C]phenyl-labelled metabolites as counter

parts have not been detected at corresponding quantities, the occurrence of TFA could be explained by uptake of this metabolite or a respective precursor molecule from the soil. Most of the metabolites were found at low levels (< 0.1 mg/kg), except for metabolite M800H35 in spring wheat chaff (0.162 mg/kg at 30 DAP, phenyl label) and metabolite M800H29 in spring wheat chaff (0.32 mg/kg at 30 DAP, uracil label; 0.12 mg/kg at 120 DAP, uracil label). The unchanged parent compound was not detectable in wheat grain (< 0.000 mg/kg) and detected at very low quantities (≤ 5% TRR) in other matrices, except for lettuce head (13.7%, 0.001 mg/kg at30 DAP) and white radish top (13.8%, 0.004 mg/kg at 30 DAP) and 8.4% (0.001 mg/kg at 120 DAP) when phenyl labelled saflufenacil was applied.

Field studies

In 2006–2007 six trials (two for each representative crop) were conducted in representative rotational crops (radish, lettuce, and wheat) in the USA.

Saflufenacil (70% WG) was applied as a single pre-emergence application to the soil (at the time of sowing wheat as primary crop) at 0.148–0.154 kg ai/ha. At 4, 6 and 9 months after treatment, the primary crop was destroyed (removed) and the representative rotational crops were planted at a number of time intervals post-treatment.

The residues of saflufenacil, M800H11 and M800H35 were below 0.01 mg/kg (LOQ) in all samples of wheat (forage, hay, grain and straw), radish (tops and root), and lettuce (leaves) harvested from plant-back intervals of 119–125, 180–183, and 270–274 days.

The results of the studies indicate that no detectable residue deriving from the use of saflufenacil can be expected in follow-up crops.

Analytical methods

Information was available on efficiency of extraction, analytical methods for saflufenacil and its metabolites (M800H11 and M800H35) in plants and parent saflufenacil in animal commodities.

Efficiency of extraction

A study was designed to investigate the influence of different solvent mixtures on the extractability and accountability of plant matrices.

The solvent systems were used sequentially: acetonitrile/water 70:30 (v/v), methanol/water 70:30 (v:v), methanol and water. The plant samples used were soya bean forage, pod and straw after pre-emergence treatment with [^{14}C]saflufenacil (phenyl ring labelled) obtained from a soya bean metabolism study.

The extractability behaviour was comparable when using mixtures of acetonitrile/water or methanol/water or methanol and water sequentially on different soya bean matrices like forage, pod and straw. The extraction efficiency was highest for forage and straw using methanol and water sequentially.

The relative quantities of the specified analytes (saflufenacil, M800H11 and M800H35) determined by the residue analytical method were very similar after HPLC analysis of the different extracts obtained after extraction with acetonitrile/water or methanol/water mixtures or with methanol and water applied sequentially.

The results indicate that methanol/water, or acetonitrile/water, were the most suitable solvent systems for extraction and characterization. These systems released most of the total radioactive residues, and residues of concern, and the quantitative results were comparable with those obtained in the original metabolism study.

The use of acetonitrile was shown in the livestock metabolism studies to be suitable for extraction of saflufenacil residues of in animal matrices. Multiple extractions did not contribute significantly to the extraction of the parent saflufenacil.

Analytical methods used in supervised trials

BASF Method D0603/02 was developed for the analysis of residues of saflufenacil and its metabolites M800H11 and M800H35 in plant matrices.

Residues of saflufenacil and its metabolites are extracted from crop matrices (except oil) with methanol-water (70:30, v/v). The oil matrices are extracted with acetonitrile. The residues are determined using LC/MS/MS.

For quantitation ion, the mean recoveries of saflufenacil, and its metabolites, M800H11 and M800H35 in different plant matrices were generally between 70 and 120% within each fortification level. Standard deviations of the recovery were generally less than 15% for quantitation ion.

Good linearity was observed in the range of 0.05 to 0.5 ng/mL for all three analytes. The LOQ for saflufenacil residues is 0.01 mg/kg for each analyte in/on food matrices and 0.025 mg/kg each in/on feed matrices. The mean recoveries obtained at 0.01 mg/kg (LOQ) and 0.1 mg/kg level ranged from 74.3% to 93.6%. The relative standard deviation (RSD) ranged between 1.9% and 9.1%.

Method No L0073/01 was developed and validated for the determination of saflufenacil in liver, kidney, muscle, fat, milk, cream, skimmed milk and eggs. The sample materials are extracted with acetonitrile, partitioned into dichloromethane, evaporated and dissolved in methanol/water mixture.

The final determination is performed by HPLC-MS/MS. The recovery of saflufenacil tested at 0.01 and 0.1 mg/kg level ranged between 74–95% for both transition ions. The reproducibility of the procedure was good (RSD < 10%). The LOQ was 0.01 mg/kg for all matrices.

A study was conducted to evaluate the capability of the FDA multi-residue methods to analyse for residues of saflufenacil, M800H11 and M800H35, but the tests indicated that the method is not suitable for the determination of the targeted residues.

In conclusion, suitable analytical methods are available for the determination of parent saflufenacil and its metabolites (M800H11 and M800H35) in plant matrices and for the parent saflufenacil in animal tissues and milk.

Stability of pesticide residues in stored analytical samples

The stability of residues in samples stored at ≤ -18 ºC was tested as part of the metabolism studies on maize, soya beans and tomatoes by comparing the HPLC chromatographic patterns during the studies. No significant change of the metabolic patterns was observed during co-chromatographic investigations. The composition of the residues in the plant materials remained stable for a period of approximately 16 to 21 months. The extracts were stored for a period of approximately 10 to 13 months.

The stability of residues in stored samples was tested by conducting storage stability studies using spiked samples of plant and animal origin.

Samples of maize (grain, forage and stover), soya beans (seed, forage and hay), oranges (fruit, pulp, juice and oil), radish roots, raisins and garbanzo beans (seeds), spiked separately with saflufenacil, M800H11 or M800H35 at a level of 1.0 mg/kg for each analyte, were stored at < -5 °C for a duration of 548–553 days. Under these conditions, residues of parent and the metabolites appeared to be stable in each crop matrix tested. The data indicate that residues of saflufenacil and its metabolites at < -5 °C are stable for at least 18 months in maize (grain, forage and stover), soya beans (seeds, forage and hay), oranges (fruit, pulp, juice and oil), radish roots, raisins and chick peas .

Storage stability of saflufenacil at -18 ^{o}C in milk and bovine tissues such as muscle, liver, kidney and fat was tested at 0.01 and 0.1 mg/kg level. In addition, the stability in the dosing solution was tested. The study, covering the period between sampling and extraction, showed that saflufenacil was stable in milk, muscle, liver, kidney and fat. No decline in concentration of saflufenacil in the extracts and dosing solutions was observed.

Definition of the residue

Residues in animal matrices

Animal metabolism studies were conducted with saflufenacil on lactating goats and laying hens. In these studies, it was found that saflufenacil was transformed to a number of metabolites. All relevant metabolites were identified. The unchanged parent compound was the predominant residue component in the cases of administration of phenyl-labelled saflufenacil in muscle and fat (0.004 mg/kg; 44% of TRR), milk (0.003 mg/kg; 47% of TRR), kidney (0.096 mg/kg; 74 % of TRR) and liver (0.77 mg/kg; 80% of TRR). Following the administration of uracil-labelled saflufenacil the parent saflufenacil was also present in largest proportion in muscle, fat, kidney and liver (57–76% of TRR). In milk the M800H10 was present at highest concentration (0.005 mg/kg) and the parent saflufenacil was second at 0.003 mg/kg level.

Metabolites M800H04 and M800H10 detected at quantities above 10% TRR within the animal metabolism studies conducted at highly exaggerated dose levels, are not considered relevant, because they would not be detectable in food items of animal origin when considering realistic feeding levels resulting from good agricultural practice.

The definition of residues in animal commodities for both enforcement and risk assessment purposes is: saflufenacil

The log P_{ow} of the parent compound is 2.6. The residues were present in fat and muscle at about the same concentration indicating that the residue is not fat soluble.

Residues in plant matrices

Metabolism studies in maize, soya beans and tomatoes were conducted to determine the metabolic fate of saflufenacil in plants after pre-emergence and pre-plant application as well as pre-harvest use for crop desiccation use.

Pre-plant, pre-emergence directed application to bare soil or to weeds in plantations of orchards and vineyards:

Following the application of labelled saflufenacil at exaggerated rates (2–4×) directly on the bare soil after sowing/planting the residues of saflufenacil were generally low. The parent saflufenacil was not detectable (< 0.0005 mg/kg) in maize cob, grain and stover, and it was present at 0.001 mg/kg level in husk and forage at day 133. M800H11 was present in maize forage at 0.002 mg/kg at days 42 and 102, and in husk and stover at 0.003–0.004 mg/kg level. M800H35 could not be identified during the study.

In tomato fruits at harvest the parent saflufenacil, M800H11 and M800H35 were not present in detectable amounts (< 0.0005 mg/kg). The parent saflufenacil was the predominant residue in tomato plants 8.5–11% of TRR, while M800H11 and M800H35 residues were present in 5.8–5.9% of TRR.

In soya beans, the parent saflufenacil was the predominant residue in forage at day 39, but M800H11 and M800H35 were present in larger proportion in pod (9–13% of TRR) and straw (25–16% of TRR) at 95-day samples. The seed did not contain any detectable residues.

The results of supervised trials provide additional information on the levels of residues in food commodities. Samples of oranges, apples, cherries, peaches, plums, grapes, bananas, mangoes and sweet corn, cereal grains, potato sugar cane, tree nuts and coffee beans, maize forage and stover and almond hull derived from treatments according to GAP no residues were detectable at any pre-harvest intervals.

Pre-harvest (desiccant harvesting aid) applications:

In a soya beans metabolism study, with application at seven days before harvest, the parent saflufenacil was the predominant residue in soya bean leaves, stem and pod (64–76% of TRR) and in

seed (26% of TRR, 0.011 mg/kg). M800H11 was present in much lower proportion (2.7–10% of TRR, 0.004 mg/kg)

In supervised trials the metabolites M800H11 and M800H35 were not found above LOQ, in any of the succulent or dried bean, dried pea, soya bean, cotton seed, and cotton gin by-product samples regardless of the PHI. In canola seed the M800H35 residues were below the LOQ of 0.01 mg/kg in all samples. M800H11 residues were < 0.01 in 12 samples. Where M800H11 was detectable in 0.01–0.055 mg/kg concentration range, it amounted to 4.3% and 53% of the parent saflufenacil (ranging between 0.021–0.48mg/kg).

In sunflower seeds M800H35 was not detected in any of the samples taken between 3 and 20 days after last application. At day 7 only one sample contained detectable M800H11 residue (0.066 mg/kg) amounting to 13% of the parent saflufenacil (0.50 mg/kg) being in the same sample. In other two samples taken at 14 day the M800H11 were present in concentrations amounting to 19% and 22% of the parent compound except one trial where it was present five times higher concentration than the parent compound (0.065 mg/kg).

The Meeting noted that the majority of the commodities treated directly or grown in treated soil did not contain detectable residues at all. The metabolite M800H11 occurred at or below 53% of the parent compound. M800H35 was present in detectable amount only in desiccated pea vine samples.

Taking into account that the residues of parent saflufenacil provide sufficient information on the compliance with GAP, and the M800H11 and M800H35 metabolites are non-detected or present at very low concentration, the Meeting decided, that

The definition of residue in plant commodities for both enforcement and risk assessment purposes is: saflufenacil.

Results of supervised trials on crops

Residue data were submitted by the manufacturer from supervised trials conducted on citrus fruits, pome fruits, stone fruits, berries and small fruits, assorted tropical and sub-tropical fruits-inedible peel, fruiting vegetables, legume vegetables, pulses, root and tuber vegetables, cereals, grasses for sugar or syrup production, tree nuts, oilseeds, seeds for beverages and sweets. The trials were generally conducted at maximum GAP and well documented.

In case of applications on bare soil at early growing season (pre-emergence, pre-planting) The Meeting concluded that the commercial harvesting time of the crop is the relevant primary factor affecting the residues and not the PHI n case of applications on bare soil at early growing season (pre-emergence, pre-planting).

Samples were analysed within the period tested for storage stability of residues. The residues of parent saflufenacil, M800H11 and M800H35 were determined in all samples with method D0603/02 or equivalent. The LOQ for each compound was 0.01 mg/kg, unless otherwise stated. The performance of the methods was verified with concurrent recovery studies.

Where trial plots were at the same location (side-by-side trials), the higher residues were considered from the replicate results. The average of residues measured in replicate samples taken from one field is reported hereunder, and they were used for estimation of the residue levels.

The OECD MRL calculator was used for calculation of maximum residue levels. The reasons for deviation are indicated under corresponding recommendations.

Citrus fruits

Trials were conducted on sweet oranges (12), lemons (5) and grapefruit (6) in five states of the USA. Saflufenacil was applied in WG formulation three times as spray directed to weeds at a rate of 0.05 kg ai/ha with a re-treatment interval of 20–22 days in compliance with US GAP (1–3 broadcast, banded or spot spraying application at 0.05 kg ai/ha (max. annual dose 0.15) and 0 day PHI).

Saflufenacil residues were present below the LOQ of 0.01 mg/kg in all samples.

Three trials were performed in Brazil in oranges applying saflufenacil three times as spray directed to weeds at a rate of 49 g ai/ha in a spray volume of 200 L/ha. Citrus fruit were taken 7 days after the last application. (No GAP.) Saflufenacil residues were present below the calculated limit of detection (< 0.002 mg/kg) in all samples.

Based on the US trial data the Meeting estimated a maximum residue level of 0.01* mg/kg and STMR of 0 mg/kg for citrus fruits.

Pome fruits

Fifteen trials in apples and 10 trials in pears were conducted in the USA according to GAP (1–3 broadcast applications directed to weeds at 0.025–0.05 kg ai/ha (max annual dose 0.15) and 0 day PHI. In addition three trials were performed in Brazil (no GAP).

No residues were detectable in any of the samples taken at day 0 up to 14 days.

Based on the US trial data the Meeting estimated a maximum residue level of 0.01* mg/kg and STMR of 0 mg/kg for pome fruits.

Stone fruits

In the USA six trials in cherries (3 tart, 3 sweet), 13 in peaches and 10 in plums were conducted according to US GAP for stone fruits (1–3 Broadcast banded or spot spraying applications directed to weeds at 0.05 kg ai/ha (max annual dose 0.15) and 0 day PHI). None of the samples taken between day 0 and 21 contained detectable residues (< 0.01 mg/kg).

For stone fruits, the Meeting estimated a maximum residue level of 0.01* mg/kg and STMR values of 0 mg/kg.

Berries and other small fruits

Twelve trials were conducted in the USA in grapes according to US GAP (1–3 Broadcast banded or spot spraying applications directed to weeds at 0.025 kg ai/ha (max annual dose 0.075 kg ai/ha) and 0 day PHI). Two trials were conducted in Brazil in grapes (no GAP).

None of the samples taken 0–17 days after last application contained detectable residues (< 0.01 mg/kg).

Based on the US trial data, the Meeting estimated a maximum residue level of 0.01* mg/kg and STMR of 0 mg/kg for grapes.

Assorted tropical and sub-tropical fruits—inedible peel

Bananas

Four trials were conducted in bananas in Brazil where plantations were sprayed with saflufenacil as a directed application to weeds at a rate of 0.049 kg ai/ha. Fruits were taken directly after last application and a day later (No GAP). None of the samples contained detectable residues < 0.01 mg/kg for parent and < 0.003 mg/kg for metabolites.

Ten supervised trials in bananas were conducted in Costa Rica (two trials), Columbia (one trial), Ecuador (three trials), Guatemala (one trial), Honduras (two trials), and Panama (one trial). Applications of saflufenacil directed to weeds were performed five times at rates between 0.072 and 0.08 kg ai/ha in a spray volume of 191–213 L/ha and re-treatment intervals of 20 ± 5 days. Banana fruit were sampled directly after the application and one day later. Saflufenacil is registered in Columbia with one application directed to weeds at 0.028–0.039 kg ai/ha, the PHI is not specified. Five applications were made at 0.08 kg ai/ha instead of the maximum 3 at 0.05 kg ai/ha, but the residues in all samples were below LOQ/LOD.

The Meeting noted that in the Central American trials five applications were made instead of one, and at 0.08 kg ai/ha instead of 0.05 kg ai/ha, but the residues in all samples were below LOQ/LOD.

As the samples did not contain any detectable residues, the Meeting estimated a maximum residue level of 0.01* mg/kg and STMR of 0 mg/kg for bananas.

Mangoes

Four supervised trials were conducted in Brazil applying saflufenacil three times as a directed spray to weeds. None of the samples contained detectable residues: < 0.01 mg/kg for parent, < 0.01–0.003 mg/kg for metabolites. As the product is not registered in Brazil, the residue data could not be evaluated.

Sweet corn

Five residue trials in sweet corn were conducted in the USA with a single application of saflufenacil either incorporated into the soil before planting or applied post-planting pre-emergence at 0.15 kg ai/ha. (GAP: ≥ 1 ground or aerial spraying applications at 0.065–0.1 kg ai/ha, max annual dose 0.15 kg ai/ha, and 80 day PHI)

The residues were below the LOQ of 0.01 mg/kg in all samples taken 91–106 days after treatment.

The Meeting estimated a maximum residue level of 0.01* mg/kg and STMR of 0 mg/kg for sweet corn.

Legume Vegetables, Pulses

Beans, dry

Five trials were conducted in Brazil in beans. The first application was done at a rate of 0.098 kg ai/ha on the day of sowing; the second (0.098 kg ai/ha) took place before harvest as a desiccant. Bean seed samples were taken at PHI of 7 days after the last application, and in three trials also after 0, 3, 10 and 14 days. None of the 17 dried bean samples contained any detectable residues (< 0.01 mg/kg) regardless of the PHI of 0–14 days. (No GAP).

Ten trials in beans were conducted in the USA and Canada applying saflufenacil at 0.05 kg ai/ha as a single late season treatment. Samples of mature dried bean seed were harvested at a 2-day pre-harvest interval (PHI). (GAP: 1× 50 g, as pre-harvest desiccant, PHI 2 days.)

The average residues of parent saflufenacil in dried bean seed sampled in US trials at the 2 day PHI were: < 0.01 (5), 0.01, 0.046, 0.096, 0.136, and 0.157 mg/kg. The maximum residue detected in one of the replicate samples from a single pot was 0.23 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg and STMR value of 0.01 mg/kg for dried bean seeds.

Peas and soya bean immature seed with or without pods

Thirteen trials on peas and 11 trials on chick peas were conducted in the USA and Canada as pre-plant or pre-emergence application of saflufenacil directed to soil at 0.1 kg ai/ha rate according to the maximum annual label rate for peas in the USA (USA GAP: ≥ 1 ground or aerial spraying applications at 0.025–0.05 kg ai/ha, maximum annual dose 0.05–0.1, and a 65 day PHI). Succulent seed samples with and without pod were taken 63–81 days after the application.

None of the 28 succulent pea (with or without pods) samples contained detectable residues (< 0.01 mg/kg), regardless of the PHI.

Fifteen trials were conducted in the USA on soya beans with a single broadcast, pre-plant incorporated or pre-emergence application of saflufenacil (70% WG) at 0.10 kg ai/ha. (US GAP: > 1

Pre-plant or pre-emergence application at 14 days intervals at 0.025 kg ai/ha and seasonal maximum rate of 0.1 kg/ha with PHI of 65 days).

The immature soya bean (succulent seed with pod and succulent seed without pod) samples were harvested at 62–119 days after treatment

Succulent soya beans seed samples (42) with or without pods at 62–126 days did not contain detectable residues.

The Meeting estimated a maximum residue level and STMR of 0.01 mg/kg for immature seeds of peas (with or without pods) and immature soya beans seeds.

Peas, dry

Thirteen trials on peas and 11 trials on chick peas were conducted in the USA and Canada as pre-plant or pre-emergence application of saflufenacil at 0.1 kg ai/ha rate according to maximum annual label rate for peas in the USA (USA GAP: ≥ 1 ground or aerial spraying applications at 0.025–0.05 kg ai/ha, max annual dose 0.05–0.1, and 65 day PHI). Dried seed samples were taken at harvest 82–117 DAT.

None of the 22 dried pea samples, and 11 dried chick pea samples contained detectable residues (< 0.01 mg/kg), regardless of the PHI.

Further, nine pea trials were conducted in the USA and Canada with a single late season application of saflufenacil as a desiccant at 0.05 kg ai/ha. (US GAP ≥ 1 ground or aerial spraying applications at 0.025–0.05 kg ai/ha, max annual dose 0.05 kg ai/ha, and 3 day PHI). Samples of mature pea dried seed and vines were harvested at a 2–4 day pre-harvest interval (PHI).

Three days after one late season application of saflufenacil at 0.05 kg ai/ha, the average residues of parent saflufenacil in two replicate dried pea seed samples were: < 0.01 (3), 0.01, 0.0.02, and 0.03 mg/kg.

The maximum of saflufenacil residue measured in one of the replicate samples from a single trial was 0.05 mg/kg at day 2 and 0.03 mg/kg at day 3.

For dried pea and chickpea seeds, the Meeting estimated a maximum residue level of 0.05 mg/kg and STMR of 0.01 mg/kg.

Soya beans

Twenty trials were conducted in the USA and Canada with a single late-season broadcast application of the 70% water-dispersible granule (WG) formulation of saflufenacil as a harvest aid/ desiccant at 0.05 kg ai/ha. (US GAP: ≥ 1 application at 0.025–0.05 kg ai/ha, max annual rate 0.05 kg ai/ha, 3-day PHI).

The average parent saflufenacil residues in dry soya bean seed samples at a 3-day PHI were: < 0.01 (14), 0.01 (2), 0.015 (2), 0.02 and 0.05 mg/kg.

Five trials were performed with saflufenacil in Brazil. The first application took place on the day of the planting at a rate of 0.049 kg ai/ha. The second application at a rate of 0.098 g ai/ha was applied to the crop as a pre-harvest desiccant. Soya bean seed was sampled 7 days after the last application. In three trials samples were also collected at 0, 3, 10 and 14 DAT. Soya bean seed samples contained 0.01, 0.02 and 0.03 mg/kg parent saflufenacil residues at day 0. Soya bean samples taken at days 3–14 did not contain any detectable saflufenacil residues, i.e., < 0.01 mg/kg (No GAP).

Based on the US trials, the Meeting estimated a maximum residue level of 0.07 mg/kg and STMR of 0.01 mg/kg for dried soya bean seeds

(OECD calculator gave 0.05 mg/kg which is equal to the highest residues in two samples.)

Potatoes

In Brazil four trials were conducted on potatoes applying saflufenacil as a WG formulation once at a rate of 98 g ai/ha as a pre-harvest desiccant. Potato tubers were sampled 7 days after treatment, and in two trials at 0, 3, 10 and 14 DAT. In potato tubers, saflufenacil residues were not detected above their calculated limit of detection, i.e., 0.009 mg/kg, throughout the study.

As the compound is not registered in Brazil, a maximum residue level could not be estimated.

Cereals

In the USA and Canada a total of 61 trials were conducted in wheat (25), barley (6), sorghum (9), rice (6) and field corn (15) with saflufenacil applied as a single broadcast pre-plant incorporated or pre-emergence application to the soil surface at 0.142–0.158 kg ai/ha. The cereal RAC samples were collected at commercial maturity. The US GAP permits ≥ 1 applications at 0.05–0.13 kg ai/ha (maximum annual rate 0.15 kg ai/ha) with PHI of 80 days for maize; ≥ 1 applications at 0.05–0.1 kg ai/ha (maximum annual rate 0.15 kg ai/ha) with a PHI of 30 days for barley, sorghum, rice and wheat.

In all trials no samples of wheat (64) taken 76–280 DAT, barley (12) taken 81–100 DAT, sorghum (18) taken 68–150 DAT, maize (32) taken 118–158 DAT and rice grains (12) taken 121–146 DAT contained detectable residues, i.e., < 0.01 mg/kg.

In Brazil two trials in wheat and four trials in rice were conducted applying saflufenacil once at a rate of 0.049 kg ai/ha at planting. No samples contained detectable residues in wheat or rice grain taken at normal harvest maturity (No GAP).

Based on the US data, the Meeting estimated a maximum residue level 0.01* mg/kg and STMR of 0 mg/kg for cereal grains.

Sugarcane

In Brazil five trials were conducted in sugar cane applying saflufenacil once at a rate of 98 g ai/ha as pre-harvest desiccant. Sugar cane stalk samples were taken after 7 and 10 days, and in two trials also after 0, 14 and 21 days.

In sugar cane stalk between 0 and 14 DAT residues of parent saflufenacil were below its calculated limit of detection (0.006 mg/kg) or below LOQ (0.01 mg/kg). After 21 days, no residues of saflufenacil were detected above LOD.

As the compound is not registered in Brazil, the maximum residue levels could not be estimated.

Tree nuts

In the USA five trials were conducted in almonds and five in pecans applying saflufenacil three times as broadcast applications to the orchard floor at a rate of 0.05 kg ai/ha. The last application made on the day of harvest. The US GAP permits up to 3 treatments at 0.05 kg ai/ha rate (annual maximum of 0.15 kg ai/ha) with a 7-day PHI.

No residues were detected in any of the samples taken between 0 and 28 days after last application.

For tree nuts, the Meeting estimated a maximum residue level, of 0.01* mg/kg and an STMR of 0 mg/kg.

Oilseeds

Cotton

In the USA 12 trials were conducted in cotton applying saflufenacil once as at-planting pre-emergence broadcast spray to the soil. The application rate was between 0.024–0.036 kg ai/ha and

0.049–0.072 kg ai/ha. The US GAP permits ≥ 1 application at 0.013–0.05 kg ai/ha with maximum annual rate of 0.05 kg/ha and a PHI of 5 days.

Undelinted cotton seed samples (24 for low rate and 22 for high rate) harvested at normal maturity did not contain any residues above the limit of quantitation (0.01 mg/kg).

In 2009, a study was conducted in the US with 12 trials in cotton in which saflufenacil was applied as a single late-season, broadcast application as a harvest aid/ desiccant at a rate of 0.05 kg ai/ha. Cotton seed samples were taken 5 days after the application, in one trial samples were also collected 1, 4, 5, 10 and 15 days after treatment.

In the US trials matching GAP, the residues in undelinted cotton seed were: < 0.01, 0.02, 0.025 (3), 0.075, 0.095, and 0.125 mg/kg.

In Brazil four trials were conducted in cotton applying saflufenacil three times: the first application took place on the day of planting, the second as a post-emergent directed spray, both applications were made at a rate of 0.049 kg ai/ha. The third application was done pre-harvest as desiccant at a rate of 0.098 kg ai/ha. Cotton seed samples were taken at the PHI of 7 days, in two trials and 0, 3, 10 and 14 DAT (there is no GAP).

The residues in delineated cotton seed samples at 7-day PHI were: < 0.01, 0.02, 0.02 and 0.09 mg/kg

Based on the US late season trial data the Meeting estimated a maximum residue level of 0.2 mg/kg and a STMR of 0.025 mg/kg for cotton seed.

Rape seed

In Canada and the USA 16 trials were conducted with a single late-season, broadcast application of the 70% water-dispersible granule (WG) formulation of saflufenacil as a harvest aid/ desiccant at 0.049–0.051 kg ai/ha. The US GAP permits one application at 0.053–0.178 kg ai/ha maximum seasonal rate 0.05 kg ai/ha, PHI 3 days (allowing up to 7 days for optimum desiccation effect depending on environmental conditions).

In addition, at three trial sites, a bridging comparison plot was treated in the same manner with a single late-season, broadcast application of a 342 g/L suspension concentrate (SC) formulation of saflufenacil applied as a harvest aid /desiccant at 0.046–0.052 kg ai/ha. The bridging trials comparing the two formulations (WG vs. SC) demonstrated that there was no observable difference in residues in canola treated with the two formulations.

The residues of parent saflufenacil in dried seeds at 3 days PHI were in rank order: 0.017, 0.0215, 0.044, 0.044, 0.0445, 0.0555, 0.0595, 0.066, 0.068, 0.0695, 0.096, 0.098, 0.0995, and 0.429 mg/kg. The highest residue observed in one of the replicate samples was 0.48 mg/kg.

For rape seed the Meeting estimated a maximum residue level of 0.6 mg/kg and a STMR of 0.054 mg/kg (the OECD calculator's estimate of 0.5 mg/kg does not cover adequately the maximum residue observed).

Sunflowers

In the USA eight trials were conducted in sunflowers applying saflufenacil in two late-season, over-the-top broadcast applications at a rate of 0.05 kg ai/ha and a re-treatment interval of 7 days. The US GAP permits ≥ 1 treatments with 0.025–0.05 kg ai/ha (maximum annual rate 0.1 kg ai/ha and a 7 day PHI).

The average residues of parent saflufenacil in replicate samples taken between 6 and 8 DAT were: 0.056, 0.0586, 0.0644, 0.089, 0.152, 0.163, 0.19, and 0.437 mg/kg

In Brazil four trials were conducted applying saflufenacil once at a rate of 0.098 kg ai/ha as pre-harvest desiccant. Sunflower seeds were taken 7 (the PHI) and 10 days after the last application, in two trials also after 0, 3 and 14 DAT. The residues of saflufenacil in sunflower seed samples taken 7 days after treatment were: < 0.01, < 0.01, 0.04 and 0.07 mg/kg (There is no GAP).

Based on the residue data obtained in the US trials, the Meeting estimated a maximum residue level of 0.7 mg/kg, and a STMR of 0.12 mg/kg for sunflower seed.

Coffee

In Brazil three trials were conducted in coffee applying saflufenacil three times directed to weeds at a rate of 0.049 kg ai/ha. Coffee grains were taken 7 days after the last application. (No GAP.)

Further trials were conducted in Costa Rica (2), Columbia (2) and Mexico (1) with four direct to base applications at rates between 0.098 and 0.104 kg ai/ha. Samples of commercially mature coffee beans (red coffee cherries) were harvested at a 0-day or 1-day pre-harvest interval (PHI) and processed according to typical commercial practices to produce the coffee raw agricultural commodity (RAC), green bean. (Columbian GAP permits one treatment at 0.028–0.03 kg ai/ha PHI is not specified.)

In all trials the residues of saflufenacil in coffee bean samples were below the limit of detection (0.003 mg/kg) or below quantitation (0.01 mg/kg).

Taking into account that no residue was detectable in any samples, the Meeting estimated a maximum residue level, of 0.01 mg/kg and a STMR of 0 mg/kg for green coffee beans.

Animal feeds

The details of the trials are provided under the respective commodities.

Soya bean forage and hay

In soya beans 15 trials were conducted in the USA with a pre-plant incorporated or pre-emergence application at 0.10 kg ai/ha. In soya bean forage and hay residues were all below the LOQ of < 0.025 mg/kg.

Based on the residue data in soya bean forage, the Meeting estimated a highest residue of 0.025 mg/kg and median of 0.025 mg/kg.

Straw, fodder and forage of cereals

The residues in forage, hay and straw samples derived from of all trials (25 in wheat, 9 in sorghum) were below the LOQ of 0.025 mg/kg at all PHI-s.

The Meeting considered that the results are applicable to barley as well.

For wheat, barley and sorghum forage, fodder and straw, the Meeting estimated a highest reside and median of 0.025 mg/kg.

For wheat, barley and sorghum straw and fodder, the Meeting estimated a maximum residue level of 0.05 mg/kg.

The results of 15 field trials on field corn indicated that the residues were below the LOQ of 0.025 mg/kg in maize forage sampled 86–114 days and maize stover sampled 120–158 days after the single pre-plant treatment at max GAP.

For maize forage and stover, the Meeting estimated a highest reside and median of 0.025 mg/kg.

For maize fodder, the Meeting estimated a maximum residue level of 0.05 mg/kg.

Almond hulls

The results of five field trials on almonds indicated that the residues were below the LOQ of 0.025 mg/kg in almond hulls sampled 7–28 days after the last of three treatments at maximum GAP.

For almond hulls, the Meeting estimated highest residue and median residue of 0.025 mg/kg.

Cotton gin by-product

The average residues of saflufenacil in cotton gin by-product samples, taken 5 days after last treatment, were in rank order: 0.09, 0.18, 0.19, 0.215, 1.84 and 2.08 mg/kg.

The highest residue observed in one of the replicate samples was 2.25 mg/kg

For cotton gin by-product, the Meeting estimated a median residue of 0.2025 mg/kg.

Fate of residues during processing

Studies were conducted for determination of the residues of saflufenacil in processed products of soya beans.

The processing factors, Pf, estimated by the meeting and the corresponding STMR-P values are summarized hereunder.

RAC	Processed product	Pf	STMR for RAC mg/kg	STMR-P, mg/kg
Soya beans	refined soya bean oil	0.25	0.01	0.0025
	soya bean meal	0.65	0.01	0.0065
	soya bean hulls	7.9	0.01	0.079
Sunflower	refined sunflower oil	0.03	0.12	0.0036
	sunflower meal	0.8	0.12	0.096

Field trials were conducted on oranges, apples, plums, wheat, maize, rice and cotton at exaggerated and maximum GAP rates. The saflufenacil residues were not detectable in the RAC samples, indicating that no processing studies were necessary.

Nevertheless, residues in citrus oil were determined because of the 1000× theoretical concentration factor for this commodity. Residues were < 0.01 mg/kg in the two oil samples derived from the orange fruit samples.

Residues in animal commodities

Farm animal dietary burden

Maximum residue level recommendations are not made for some processed and forage commodities as no maximum residue level is needed) but they are used in estimating livestock dietary burdens. Those commodities are listed here.

Commodity	High residue (mg/kg)	Median (mg/kg)
Almond hull		0.025
Cotton gin by-products	2.25	0.215
Maize forage and stover	0.025	0.025
Soya bean forage	0.025	0.025
Soya bean hulls		0.079
Soya bean meal		0.0065
Straw and fodder, forage of cereals	0.025	0.025
Sunflower meal		0.096

Applying the OECD feed table for maximum proportion of agricultural commodities in animal feed (FAO Manual 2nd ed 2009, appendix IX) the maximum and mean saflufenacil intake was calculated from the estimated high and STMR residues. Residue data from field pea vines were not taken into consideration because following the desiccation treatment it is practically dry and not used for feed. **(**The vines used for feed contains about 25% dry matter.)

	Livestock dietary burden, saflufenacil, ppm of dry matter diet							
	US-Canada		EU		Australia		Japan	
	max	mean	max	mean	max	mean	max	mean
Beef cattle	0.157[a]	0.043	0.078	0.080	0.101	0.101[b]	0.019	0.011

Dairy cattle	0.080	0.080	0.059	0.061	0.096	0.096[c]	0.041	0.011
Poultry, broilers	0.035	0.035	0.021	0.021	0.026	0.025	0.013	0.010
Poultry, layers	0.035	0.035	0.037[d]	0.037[e]	0.026	0.025	0.009	0.009

[a] Highest maximum beef or dairy cattle dietary burden suitable for Maximum residue level estimates for mammalian meat.

[b] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat.

[c] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

[d] Highest maximum broiler or layer poultry dietary burden suitable for Maximum residue level estimates for poultry meat and edible offal and eggs

[e] Highest mean broiler or layer poultry dietary burden suitable for STMR estimates for poultry meat and edible offal and eggs

Lactating dairy cows

The saflufenacil was administered orally to 14 lactating cows over a period of 28 days. Based on the proposed usage of the test substance as pre-emergence treatment and a maximal anticipated dietary intake from feed, the target dose level of 0.1 ppm in feed (1×) was determined. The actual dose levels of 0.15 ppm (1×), 0.48 ppm (3×) and 1.7 ppm (10×) were calculated based on actual feed intake.

No residues were detected in any milk specimens at any of the dosing levels.

No residues were detected in muscle or fat specimens at any of the dosing levels.

In the liver samples from the 1× dose group, the residue levels ranged from 0.17 mg/kg to 0.26 mg/kg (mean 0.21 mg/kg). In the 3× dose group, the residue levels ranged from 0.67 mg/kg to 0.88 mg/kg (mean 0.77 mg/kg). In the 10× dose group, the residue levels ranged from 2.09 mg/kg to 3.49 mg/kg (mean 2.61 mg/kg). A good correlation between feeding level and residue level was obtained for liver. Residues in the 10× dose group were 1.66 mg/kg and 0.34 mg/kg after 2 and 7 days of withdrawal, respectively.

No residues were detected in the kidney samples at the 1× dose level. Residues at the 3× dose level were 0.02 mg/kg; those at the 10× dose level ranged from 0.03 to 0.04 mg/kg (mean 0.04 mg/kg). The residues in the 10× group declined to 0.03 mg/kg after 2 days of withdrawal and were below the LOQ after 7 days of withdrawal.

The residues expected in animal commodities based on the calculated animal burden are shown in the table below.

	Feed level (ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Residues (mg/kg) in			
				Muscle	Liver	Kidney	Fat
Maximum residue level beef or dairy cattle							
Feeding study [a]	0.15	< 0.01	0.15	< 0.01	0.26	< 0.01	< 0.01
Dietary burden and residue estimate	0.096	< 0.01	0.157	< 0.01	0.26	< 0.01	< 0.01
STMR beef or dairy cattle							
Feeding study [b]	0.15	< 0.01	0.15	< 0.01	0.21	< 0.01	< 0.01
Dietary burden and residue estimate	0.096	< 0.01	0.101	< 0.01	0.14	< 0.01	< 0.01

[a] Highest residues for tissues and mean residue for milk

[b] Mean residues for tissues and milk

The Meeting estimated maximum residue levels of 0.01 mg/kg for milk and milk cream, muscle and fat, 0.01 mg/kg kidney, and 0.3 mg/kg for edible offal of mammals based on residues in liver. The estimated STMR and HR values are 0.01 mg/kg for milk and milk cream and muscle, and HR of 0.26 mg/kg and STMR of 0.14 mg/kg for edible offal of mammals.

Laying hens

The calculated feed burden for poultry based on feed items with highest residues resulted in 0.035 ppm total dry matter feed. Thus, the trigger value of 0.1 mg/kg dry matter feed for conducting a farm animal feeding study was not reached.

In addition, it can be concluded from the data of the hen metabolism study that there are no residues to expect in any of the edible hen matrices assuming a hen feeding level of 0.035 ppm dry matter feed. This feeding level would be lower by a factor of more than 300 compared to the feeding level of 12.6–12.7 mg/kg in the hen metabolism study.

Therefore, by extrapolation from the residue levels in the metabolism study the residues in a hen feeding study would be far below the LOQ of 0.01 mg/kg of the residue analytical method for any of the edible hen matrices even at a 10× feeding level. Thus a hen feeding study has not been conducted.

Establishment of maximum residue limit for poultry product is not necessary.

RECOMMENDATIONS

On the basis of the data from supervised trials, the Meeting concluded that the residue concentrations listed below are suitable for establishing MRLs and for assessing IEDIs and IESTIs.

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for plant and animal commodities: saflufenacil.

The residue is not fat soluble.

CCN	Commodity	MRL, mg/kg	STMR or STMR-P, mg/kg	HR or HR-P, mg/kg
FI 0327	Banana	0.01	0	0
AS 0640	Barley straw and fodder, dry	0.05	0.025	0.025
VD 0071	Beans (dry)	0.3	0.01	
GC 0080	Cereal grains	0.01	0	
FC 0001	Citrus fruits	0.01	0	0
SB 0716	Coffee beans	0.01	0	
SO 0691	Cotton seed	0.2	0.025	
MO0105	Edible offal (Mammalian)	0.3	0.14	0.26
FB 0269	Grapes	0.01	0	0
AS 0645	Maize fodder	0.05	0.025	0.025
MF 0100	Mammalian fats (except milk fats)	0.01	0.01	0.01
MM 0095	Meat (from mammals other than marine mammals)	0.01	0.01	0.01
ML 0106	Milks	0.01	0.01	0.01
VP 0063	Peas (pods and succulent = immature seeds)	0.01	0.01	
VD 0072	Peas, dry	0.05	0.01	
VP 0064	Peas, shelled (succulent seeds)	0.01	0.01	
FP 0009	Pome fruits	0.01	0	0
SO 0495	Rape seed	0.6	0.054	
AS 0651	Sorghum straw and fodder, dry	0.025	0.025	0.025
VP 0541	Soya beans (immature seed)	0.01	0.01	
VD 0541	Soya beans seed (dry)	0.07	0.01	
FS 0012	Stone fruits	0.01	0	0
SO 0702	Sunflower seed	0.7	0.12	
GC 0447	Sweet corn	0.01	0	0
TN 0085	Tree nuts	0.01	0	
AS 0654	Wheat straw and fodder, dry	0.05	0.025	0.025
OR 0702	Sunflower seed oil, edible		0.0036	
AL 1265	Soya beans forage		0.025	0.025
AB 1265	Soya beans meal		0.0065	
OR 0541	Soya beans oil, refined		0.0025	
AB1203	Cotton seed meal		0.0065	

DIETARY RISK ASSESSMENT

Long-term intake

The evaluation of saflufenacil resulted in recommendations for maximum residue levels and STMR values for raw and processed commodities. Where data on consumption were available for the listed food commodities, dietary intakes were calculated for the 13 GEMS/Food Consumption Cluster Diets. The results are shown in Annex 3 of the 2011 JMPR Report.

The IEDIs in the thirteen Cluster Diets, based on estimated STMRs were 0% of the maximum ADI of 0.05 mg/kg bw. The Meeting concluded that the long-term intake of residues of saflufenacil from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The Meeting concluded that establishment of acute reference dose is not necessary. The estimation of short-term intake of residues of saflufenacil was not necessary.

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